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Original Research Article

Ramifications of coronary angiography with effect to time comparing two groups: undergoing off pump coronary artery bypass grafting within or more than seven days of coronary angiography

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ABSTRACT

Background: Acute kidney injury (AKI) following off pump coronary artery bypass grafting (OPCABG) within short interval from coronary angiography (CAG) has been well documented. This prospective study is aimed to delineate perioperative effects and effects of elective 7 days interval between CAG and off pump CABG, to observe its outcome on renal functions.
Methods: The present study was conducted in a total of 1102 consecutive patients who underwent coronary angiography following coronary artery bypass surgery in Fortis hospital, Mohali. Patients were divided into 2 groups - group A (patients undergoing CABG within 7 days of CAG) and group B (patients undergoing CABG beyond 7 days of CAG). Comparison was made between the two groups, in relation to the timing between CAG and CABG, with its impact on perioperative renal functions.
Results: Statistically it was found highly significant higher values of 1st and 3rd day serum creatinine and high incidence of postoperative AKI in patients of group A in comparison to patients of group B.
Conclusions: Thus, our study confirms that patients with a shorter interval between CAG and subsequent OPCAB are more likely to present higher peak creatinine level as well as lower minimum eGFR. A gap of 7 days for elective cases is more likely to present less postoperative AKI.

Keywords: Off pump coronary artery bypass grafting, Acute kidney injury, Peri-operative renal functions, Time interval between CAG and CABG

INTRODUCTION

Coronary artery bypass grafting (CABG) often follows coronary angiography (CAG) using a radio contrast dye, which can result in contrast-induced nephropathy (CIN), following angiographic procedures to exacerbate the risk of AKI.[1-3]

Previous studies of post-operative kidney dysfunction defined AKI as a rise in the serum creatinine level >0.5 mg/dl or >25% from baseline.[4] In a given previous study post-operative AKI was defined as an absolute increase >0.3 mg/dl or a relative increase >50% in the serum creatinine level within 48 h following off pump CABG compared to baseline or a requirement for post-operative haemodialysis. Use of these widely accepted post-operative AKI criteria helps us to delineate post-operative outcomes in patients undergoing off pump CABG.[5]

Patients who have to undergo CABG within short duration following CAG is at greater risk of developing postoperative AKI. The use of CPB and other factors are associated with increased morbidity and mortality, as the use of cardiopulmonary bypass (CPB) is the greatest risk

factor of AKI after CABG. Over the time, with switch of patients undergoing off-pump CABG (OPCAB) rather than on-pump CABG have a positive outcome regarding postoperative renal function.[4,5]

Though off-pump coronary artery bypass surgery (OPCAB) technique avoids cardiopulmonary bypass (CPB) circuit induced adverse effects on renal function, multiple other factors cause postoperative renal dysfunction in these group of patients.[6]

Objective of this study was to retrospectively delineate the effects of coronary angiography on the postoperative renal functions in patients undergoing off pump CABG, with respect to time interval between coronary angiography and surgery.

METHODS

This study was conducted in the department of cardiothoracic and vascular surgery, Fortis hospital Mohali, Punjab, India. This study was analysed retrospectively in consecutive patients, for 2 years from January 2013 to December 2014 undergoing CABG within 7 days of CAG and patients undergoing CABG beyond 7 days of CAG. Institutional medical ethics committee approved the study protocol and was in coherent to the declaration of Helsinki.

Patients undergoing elective isolated OPCAB with normal blood urea nitrogen and serum creatinine levels 0.8-1.3mg/dl, without a past history of kidney disease or chronic renal failure, and no inflammatory diseases that required therapy with steroids or non-steroidal anti-inflammatory drugs were included in study. Patients with preoperative unstable hemodynamic requirement of inotropic drugs and/or intra-aortic balloon pump (IABP) before OPCAB, on pump CABG and conversion of off pump CABG to on pump during surgery CPB were excluded from study.

Study protocol

Post-operative AKI is defined as absolute increase >0.3 mg/dl or relative increase >50% in the serum creatinine level within 48 hours after surgery compared to the preoperative baseline value or requiring postoperative haemodialysis. After ethical committee approval all selected patients underwent consent, preoperative ECG, chest X-ray, echocardiography and diagnostic CAG.

All selected patients were divided into either group A or B according to the time elapsed from CAG until subsequent surgery. Group A patients undergoing off pump CABG within 7 days of coronary angiography. Group B patients undergoing off pump CABG beyond 7 days of coronary angiography.

Pre-operative parameters of selected patients included, age, sex, body mass index, diabetes mellitus, hypertension, atrial fibrillation (AF), recent myocardial infarction (MI) (evidence of MI in the last 30 days before surgery), congestive heart failure (NYHA class III or IV), left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVEDD), use of medications angiotensin-converting enzyme inhibitor (ACEI), angiotensin-receptor blocker (ARB), diuretics, and antiplatelet drugs, and serum creatinine levels before and after CAG.

Surgical variables included number of grafts; redo surgery, low mean perfusion pressure (mean pressure <50 mm hg for >30 minutes), no-touch aorta technique, and duration of anaesthesia (minutes).

Post-operative parameters included postoperative AKI, haemodialysis, re-exploration for bleeding, drainage during first 24 h (ml) postoperatively, blood transfusion, ventilator support over 72 h, re-intubation, new onset AF, stroke (new permanent neurological event; early stroke: within 24h; delayed stroke >24 h post-operatively), the length of stay in the intensive care unit (ICU), as well as hospital stays.

The post-operative peak inotrope score was calculated using; dopamine (×1), dobutamine (×1), amrinone (×1), milrinone (×15), epinephrine (×100), norepinephrine (×100), and isoproterenol (×100). The eGFR were calculated using the modification of diet in renal disease (MDRD) formula; eGFR = 186×creatinine -1.154×age -0.203×1.212 (if black) ×0.742 (if female).[7]

Comparison were made for above aforementioned peri-operative parameters between two groups and were analysed for ramifications on renal functions in content to serum creatinine level and estimated glomerular filtration rate (eGFR) obtained on 1 day before surgery (baseline creatinine and baseline eGFR) and on postoperative 1st, 3rd and 7th days.

Surgical technique

All patients received general anaesthesia. Inotropic infusion was used to maintain the mean systemic arterial pressure over 60mmHg during the period of heart displacement and grafting. Allogenic packed red blood cells were transfused when the haematocrit level is <25%. All surgical procedures were performed by the same surgeon through a median sternotomy, and the heart being displaced using a posterior pericardial stitch, large (12×70 cm) gauze swabs and a tissue stabilizer (Octopus, Medtronic, Minneapolis, MN, USA) and urchin positioner (Medtronic/Maquet). Dual pacing was done with pacing wires, by fixing one to right atria and another to left ventricle for pacing heart. The sequence of grafting begins with the left internal mammary artery anastomosis to the left anterior descending coronary artery , followed by grafting of the circumflex coronary artery and right coronary artery using a radial artery or saphenous vein. After aortic side cross-clamping, proximal anastomoses

of grafts were performed. A 'no-touch' aorta technique was used when there was moderate to severe sclerosis or calcification. The blood flow of the grafts is to be checked followed by distal grafting. An intracoronary shunt (Medtronic, chase) was used during grafting. Haemostasis was achieved following closure. All patients were transferred to the ICU following surgery for a minimum of 3 days stay.

Statistical analysis

Evaluation of the data was carried out by microsoft excel and Medcalc calculator. The statistical analyses for parametric and non-parametric values were undertaken. The student 't' test was used for testing the significance of parametric values between the two groups. Odds ratio (OR) and 95% confidence interval (CI) were calculated for non-parametric variables. value less than 0.05 and 0.01 were considered significant and highly significant respectively.

RESULTS

Total of 1336 consecutive patients with CAD underwent isolated CABG in span of 2 years. Out of these, 1102 patients undergoing isolated OPCAB met the inclusion criteria and were enrolled in the study. This retrospective case study was conducted on 1102 patients who underwent CABG after CAG, attending the department of cardiothoracic vascular surgery, Fortis hospital, Mohali. The patients were divided into two groups; group A, consisting of 564 patients, who underwent CABG within 7 days of CAG; and group B, consisting of 538 patients, who underwent CABG after 7 days of CAG. A comparison was made between the two groups, regarding perioperative renal functions.

The mean values with standard deviations of various parameters (age; BMI; ejection fraction; LVEDD; time elapsed between CAG and CABG; number of grafts; low mean perfusion pressure; duration of anaesthesia; drainage during first 24 hours; length of ICU stay; length of hospital stay; post-operative peak inotrope score; pre-operative serum creatinine; 1st, 3rd and 7th day values of serum creatinine; preoperative eGFR; 1st, 3rd and 7th day values of eGFR) have been tabulated in (Table 1). From the p values attained, it has been concluded that there is a statistically significant higher ejection fraction (%) of patients of group B as compared to group A. The time elapsed between CAG and CABG is statistically significantly higher in patients of group B as compared to group A.

There are statistically highly significant higher values of 1st and 3rd day serum creatinine of patients of group A in comparison to patients of group B. Also, there is a statistically significant higher 7th day serum creatinine value of patients of group A in comparison to patients of group B. There are statistically highly significant higher values of 1st and 3rd day eGFR of patients of group A in comparison to patients of group B. Also, there is a statistically significant higher incidence of postoperative AKI in patients of group A in comparison to patients of group B.

Table 1: Comparison of parametric data for patients in group A and group B.

Parametric values	Group A (n=564) mean±SD	Group B (n=538) mean±SD	P value	Inference
Age (years)	62.36±9.37	61.78±9.11	0.15	NS
BMI (kg/m^2)	24.99±3.79	25.29±4.24	0.12	NS
Ejection fraction (%)	48.06±9.32	49.03±8.59	0.04	Significant*
LVEDD (mm)	51.23±3.79	51.31±3.55	0.35	NS
Time elapsed between CAG and CABG (days)	2.69±2.06	28.34±31.14	2.32E-73	HS*
Number of grafts	2.82±0.80	2.89±0.93	0.10	NS
Duration of anaesthesia (minutes)	306.66±14.71	307.32±19.56	0.26	NS
Drainage during first 24 hours (ml)	250.35±136.45	245.37±126.72	0.26	NS
Length of ICU stay (days)	3.06±0.37	3.05±0.37	0.41	NS
Length of hospital stay (days)	7.07±0.45	7.05±0.44	0.31	NS
Postoperative peak inotrope score	10.45±2.04	10.64±1.97	0.0556	NS
Preoperative serum creatinine (mg/dl)	1.04±0.15	1.05±0.15	0.12	NS
1st day serum creatinine (mg/dl)	1.22±0.23	1.15±0.18	3.49 E-08	HS*
3rd day serum creatinine (mg/dl)	1.19±0.19	1.12±0.16	7.63 E-13	HS*
7th day serum creatinine (mg/dl)	1.10±0.44	1.07±0.14	0.047	Significant*
Preoperative eGFR (ml/min)	90.88±17.67	89.70±17.21	0.13	NS
1st day eGFR (ml/min)	76.67±16.76	81.13±16.43	4.52E-06	HS*
3rd day eGFR (ml/min)	77.86±15.62	83.75±16.55	8.17E-10	HS*
7th day eGFR (ml/min)	86.91±16.29	87.94±15.88.	0.14	NS

Table 2: Comparison of non-parametric data for patients in group A and B.

Non-parametric values	Odds ratio (OR)	95% confidence interval (CI)	Value of p	Inference
Diabetes mellitus	1.14	0.90-1.45	0.27	NS
Hypertension	1.20	0.94-1.52	0.13	NS
AF	1.13	0.68-1.87	0.65	NS
Recent MI	1.00	0.64-1.57	0.99	NS
CHF	1.05	0.73-1.53	0.77	NS
Previous heart operation	0.24	0.03-2.13	0.20	NS
Previous PCI	1.05	0.67-1.64	0.82	NS
2 vessels disease	0.96	0.71-1.31	0.83	NS
3 vessels disease	1.03	0.77-1.37	0.84	NS
Left main trunk disease	1.09	0.74-1.63	0.65	NS
ACEI	1.40	1.05-1.87	0.02	Significant*
ARB	0.77	0.56-1.06	0.11	NS
Diuretics	1.25	0.95-1.65	0.11	NS
Preoperative use of antiplatelets	0.93	0.73-1.18	0.54	NS
Low mean perfusion pressure	1.43	0.40-5.11	0.58	NS
No-touch aorta technique	2.09	0.79-5.54	0.14	NS
Postoperative AKI	2.59	1.80-3.72	<0.0001	HS*
Hemodialysis	2.87	0.12-70.53	0.52	NS
Requiring blood transfusion	0.82	0.64-1.07	0.14	NS
Re-exploration for bleeding	1.34	0.42-4.25	0.62	NS
Ventilator support over 72h	0.79	0.24-2.61	0.70	NS
Re-intubation	0.38	0.07-1.96	0.25	NS
New onset AF	0.86	0.59-1.26	0.45	NS
Mortality	0.95	0.06-15.29	0.97	NS

Table 2 denotes there is a statistically significant difference in the preoperative use of ACEI drugs among both groups A and B. Patients of group A were more likely for preoperative use of ACEI drugs. There was no significant difference found between the two groups for sex, previous history of diabetes, hypertension or AF, recent MI, previous heart operation, preoperative congestive heart failure, extent of coronary artery disease, preoperative use of diuretics, ARB or antiplatelet drugs, use of no-touch aorta technique, requiring blood transfusion, re-exploration for bleeding, and hospital mortality.

DISCUSSION

The reported incidence of contrast-induced nephropathy after coronary angiography is 1-15%. Renal insufficiency tends to develop 24 to 96 hours after contrast administration. Post catheterization nephropathy is a well-known complication of cardiac catheterization among patients with chronic renal insufficiency. Contrast agents leads to vasoconstriction mediated medullary ischemia, and direct cytotoxicity on glomerular cells. The studies suggested that patients having undergone cardiac catheterization within the 5 days period preceding surgery may be more vulnerable to further renal deterioration peri-operatively. The non-physiologic, non-pulsatile flow during bypass, activation of inflammatory cascades, and coagulation abnormalities may all be responsible for part of the observed alterations in renal function. In addition, during bypass, the renal parenchyma is exposed to lower perfusion pressures and reduced oxygen tension. These results are consistent in suggesting a deleterious effect caused by longer pump times, and underline the significance of optimizing perioperative renal protection for cases in which longer CPB periods are anticipated, such as complex operations, reoperation cases, and combined coronary artery bypass grafting and valvular surgery.[8,9]

Multiple mechanisms contribute to the renal damage, including non-pulsatile flow, embolization, trauma to the blood constituents, hypothermia, and activation of known inflammatory pathways. CIN develops in up to 10% of patients with normal renal function and may develop in up to 25% of patients with pre-existing renal impairment. Baseline renal impairment, diabetes mellitus, congestive heart failure, and higher doses of contrast media increase the risk of CIN. In the presence of a reduced nephron mass, the remaining nephrons are vulnerable to injury. Iodinated contrast, after causing a brief (minutes) period of vasodilation, causes sustained (hours to days) intrarenal vasoconstriction and ischemic injury. The ischemic injury sets off a cascade of events largely driven by oxidative injury, causing death of renal tubular cells. If a sufficient mass of nephron units is affected, then a recognizable rise in serum creatinine will occur. In as much as CIN is usually a time-limited phenomenon, with

an effect that peaks after 3 to 5 days from contrast administration, and in as much as contrast dose is an important factor in development of CIN, surgery soon after angiography may impose a second insult to the kidneys and induce ARF. The association of high contrast dose and operation up to 5 days after angiography has an additive effect on the prevalence of ARF.[10]

The studies demonstrated that having cardiac catheterization within 5 days before surgery is a significant risk factor for postoperative ARF. Efforts to maximize the delay between cardiac catheterization and operation beyond at least 5 days, when clinically feasible, may allow more recovery from the effects of contrast nephropathy, especially in patients with impaired baseline renal function.[9,11]

Patients with a shorter interval between CAG and subsequent OPCAB are more likely to present higher serum creatinine levels and lower eGFR in the early postoperative period, compared to patients with a longer interval. Although the serum creatinine level is used as a guide to the diagnosis of AKI, the eGFR is also evaluated as a renal function index. A rise in the serum creatinine level and a reduction in the eGFR in the early postoperative period explain impaired kidney function. The studies showed that the degree of damage to kidney function increased gradually following OPCAB, reached a peak within 3 days, and then decreased slowly in both groups. Patients with a shorter interval between CAG and subsequent OPCAB are more likely to present higher peak creatinine level as well as lower minimum eGFR following OPCAB compared to patients with longer interval, which shows that patients with a shorter interval suffer from more serious kidney injury in the early postoperative period and are more likely to present postoperative AKI. Thus, performing post-CAG OPCAB after the 5 days limit (if feasible), especially in elective cases, has the potential to minimize the additive adverse effect of CAG. However, it is only a hypothesis and remains to be proven in future studies. A clinical decision should be made for those needing early surgery based on the perceived risk of immediate surgery on renal function versus that for an ischemic event and its consequences while waiting longer. If early surgery is indeed warranted, all efforts should be directed at minimizing the deleterious effects of contrast on renal tubules. Strategies to prevent contrast-induced nephropathy, such as preoperative discontinuation of drugs inducing kidney damage for days, use of isosmotic and non-ionic contrast agent, volume expansion therapy using isosmotic crystalloids, and administration of statins and vitamin C, should be routinely adopted during angiography and continued in the post-angiography period, with the hope that this may help reduce postoperative AKI in those needing early cardiac surgery following CAG.[11]

Our results were similar to those observed by Duca et al, Medalion et al and Ji et al who also concluded that beginning OPCABG early after diagnostic CAG did affect postoperative renal function and increased the incidence of AKI in patients with normal preoperative renal function.[9-11] These findings suggest that delaying the procedure beyond 7 days after exposure to contrast agents (if feasible) has the potential to decrease the incidence of postoperative AKI in patients undergoing elective OPCABG.

Limitations

The primary limitation of our study is that it was applicable to patients undergoing elective isolated OPCAB. The study excluded patients undergoing emergency procedures or CABG with CPB or CABG plus other cardiac surgery. We did not take into account factors such as; amount and type of contrast agents used during coronary angiography, which have an influence on renal functions of the patients. The peri-operative use of intravenous fluids, diuretics and various anaesthetic agents, which may have an influence on renal functions of the patients.

CONCLUSION

We thus conclude from our study that beginning off-pump coronary artery bypass graft surgery early after diagnostic CAG affects post-operative renal function and increases the incidence of AKI in patients with normal preoperative renal function. These findings suggest that delaying the procedure beyond 7 days after exposure to contrast agents (if feasible) has the potential to decrease the incidence of postoperative AKI in patients undergoing elective OPCABG.

Keeping this normative data as baseline, further studies can be done in this line of research of effect of timing between CAG and CABG on perioperative renal functions of the patients.

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