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Original Article

Influence of the timing of cardiac catheterization and amount of contrast media on acute renal failure after cardiac surgery

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Abstract

BACKGROUND: There is limited data about the influence of timing of cardiac surgery in relation to diagnostic angiography and/or the impact of the amount of contrast media used during angiography on the occurance of acute renal failure (ARF). Therefore, in the present study the effect of the time interval between diagnostic angiography and cardiac surgery and also the amount of contrast media used during the diagnostic procedure on the incidence of ARF after cardiac surgery was investigated.

METHODS: Data of 1177 patients who underwent different types of cardiac surgeries after cardiac catheterization were prospectively examined. The influence of time interval between cardiac catheterization and surgery as well as the amount of contrast agent on postoperative ARF were assessed using multivariable logistic regression.

RESULTS: The patients who progressed to ARF were more likely to have received a higher dose of contrast agent compared to the mean dose. However, the time interval between cardiac surgery and last catheterization was not significantly different between the patients with and without ARF ($p = 0.05$). Overall, postoperative peak creatinine was highest on day 0, then decreased and remained significantly unchanged after this period. Overall prevalence of acute renal failure during follow-up period had a changeable trend and had the highest rates in days 1 (53.57%) and 6 (52.17%) after surgery. Combined coronary bypass and valve surgery were the strongest predictor of postoperative ARF (OR: 4.976, CI = 1.613-15.355 and $p = 0.002$), followed by intra-aortic balloon pump insertion (OR: 6.890, CI = 1.482-32.032 and $p = 0.009$) and usage of higher doses of contrast media agent (OR: 1.446, CI = 1.033-2.025 and $p = 0.031$).

CONCLUSIONS: Minimizing the amount of contrast agent has a potential role in reducing the incidence of postoperative ARF in patients undergoing cardiac surgery, but delaying cardiac surgery after exposure to these agents might not have this protective effect.

KEYWORDS: Contrast Media, Iodine Compounds, Adverse Effects, Acute Renal Failure, Cardiac Surgery, Angiography, Coronary Artery Bypass Grafting.

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Acute renal failure (ARF) is a serious and even life-threatening event occurring after isolated or combined cardiac procedures in up to 30% of patients and might be associated with 20% mortality after cardiac catheterization.[1] A series of risk factors have been

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identified for the occurrence and progression of acute ARF after these procedures such as history of chronic renal failure, diabetes mellitus, advanced age, heart failure, and periprocedural hemodynamic alterations.[2,3] Contrast-induced nephrotoxicity is another important risk factor accounting for the hospitalization of a large number of cases. Some studies have shown that the use of high volumes of contrast medium is related to the development of ARF in patients undergoing coronary bypass surgery and combination cardiac procedures.[4] Furthermore, a temporal relationship between the timing of cardiac catheterization and the development of ARF has been suggested.[5,6] Therefore, the timing between angiography and surgery might be an important factor in the development of this complication.[7] Some studies have shown that steroids and low osmolality contrast media have high impact to decrease the adverse reaction rates.[8] On the other hand, others have demonstrated that atherosclerosis has an impact on the type of the contrast-induced coronary vasomotor reaction. According to the presence/absence of, and the distance from a coronary atherosclerotic lesion located in their proximity, angiographically normal coronary segments show divergent vasomotor reactions to iodixanol or iopromide.[8] However, the existing data about the influence of timing of cardiac surgery in relation to diagnostic angiography and/or the impact of the amount of contrast used during preceding angiography on the appearance of acute renal failure (ARF) is limited. The aim of this study was to investigate the effect of the time interval between diagnostic angiography and cardiac surgery and the amount of contrast used during this diagnostic procedure on the incidence of ARF after cardiac surgery.

Methods

The study population included 1177 patients who underwent different types of cardiac surgeries with cardiopulmonary bypass method at Sina private Hospital (Isfahan, Iran), between April 2008 and September 2009. All patients underwent a cardiovascular diagnostic procedure requiring the use of a contrast agent for left ventriculography, coronary or carotid angiography, and thoracic and/or abdominal aorta angiography before their surgeries. Thus, the patients requiring emergency dialysis therapy or those that underwent the off-pump method surgery were excluded. Data for the studied patients including demographics, clinical characteristics, laboratory data, medical treatments, angiographic data ,(including amount and type of the contrast agent used), comorbid conditions and cardiac procedural data (including its timing in relation to the preceding angiography), were collected by reviewing hospital record files in a computerized database. The study was approved by the research ethics committee of Isfahan University of Medical Sciences, Isfahan Sina Heart Center.

The contrast agent used were Meglumine compound 76% (Urografin, Bayer, USA) as hyperosmolar, iopromide 370 (Ultravisit, Berlex Montville, USA, Mfd. In: Germany) and Iohexol 300 (Iopaque, Iran or Omnipaque 300, USA) as low-osmolar contrast agents. Use of nonsteroidal anti-inflammatory agents and other nephrotoxic drugs were avoided or withheld for 48 hours before angiography. Creatinine clearance was determined using the Cockcroft- Gault equation. Postoperative renal risk was assessed using 2 different risk scores of a simplified predictive index for renal replacement therapy after cardiac surgery and a risk score for prediction of contrast-induced nephropathy.[9]

The main outcome of interest was the incidence of postoperative ARF, defined as postoperative serum creatinine > 2 times baseline and/or the need for renal replacement therapy. The mean value of baseline creatinine was 0.99 mg/dl.[6]

Statistical analyses

The obtained results are presented as mean ± SD, frequency, and percentage. Comparisons were made using chi-square test or Fisher's exact test for categorical variables and nonparametric test for continuous variables. Patients were grouped according to the time (days) be-

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tween angiography and surgery. The amount of contrast media was entered into the model as both a linear (continuous variable) and a dichotomous term (median or less and greater than median value). Multivariable logistic regression analysis was used to identify independent predictors of ARF using variables found to have marginal association (p > 0.10) on univariate analysis. Odds ratio (OR) and 95% confidence interval (CI) were constructed to provide an estimate of adjusted risk posed by post-procedural ARF.

Results

Of 1177 patients who underwent different types of cardiac surgeries after angiography, ARF occurred in 465 subjects, 2 of these patients needed dialysis. Mean dose of hyperosmolar and low-osmolar contrast agents used overall were 1.23 and 1.21 ml/kg, respectively. Mean overall postoperative peak serum creatinine was 1.23 mg/dl. Baseline clinical features between the two cohorts with and without postoperative ARF are listed in Table 1. Postoperative ARF was more prevalent in older and male patients (p = 0.003 and 0.002, respectively), and those with a higher history of hypertension(p = 0.012), but prevalence of other risk factors as well as left ventricular ejection fraction were similar in both group of patients. There was a significant difference between last pre and post- operative creatinine in both groups (p < 0.001). Patients with ARF were also more likely to have undergone combined coronary artery bypass grafting and valve surgery the same day as angiography and also underwent more postoperative intra-aortic balloon pump insertion (IABP) (Table 2). The patients with ARF were more likely to have received higher doses of both hyper-osmolar and

Table 1. Clinical and demographic characteristics of the studied population

Variable	Overall (n = 1177)	Postoperative ARF (n = 465)	No Postoperative ARF (n = 712)	P–value*
Age (year)	59.35 ± 9.49	61.02 ± 9.12	60.01 ± 9.38	< 0.001
Body mass index (kg/m^2)	26.80 ± 3.95	26.40 ± 3.80	26.65 ± 3.91	0.09
Last pre operative creatinine	0.96±0.21	0.92±0.23	0.989±0.195	0.000
Hypertension	478 (40.6%)	212 (45.6%)	266 (37.4%)	0.01
Current smoking	173 (14.7%)	76 (16.4%)	97 (13.7%)	0.43
Previous MI	448 (38.1%)	196 (42.1%)	252 (35.5%)	0.12
Congestive heart failure	38 (3.2%)	16 (3.4%)	22 (3.1%)	0.74
Male gender	889 (75.5%)	368 (79.1%)	521 (73.2%)	0.02
IABP** used intraoperatively	10 (0.8%)	5 (1.1%)	5 (0.7%)	0.53
IABP** used postoperatively	11 (0.9%)	9 (1.9%)	2 (0.3%)	<0.001
Pre-procedure creatinine (mg/dl)	0.99 ± 0.20	0.92 ± 0.23	0.96 ± 0.21	< 0.001
Post-procedure creatinine (mg/dl)	1.23 ± 0.22	1.81 ± 0.84	1.46 ± 0.62	< 0.001
Ejection fraction	50.72 ± 11.45	49.99 ± 11.43	50.43 ± 11.44	0.28

Data are expressed as mean ± SD and number (%)
* P value are calculated by chi-square test or 2-sided Fisher's exact test
** Intra aortic balloon pump

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Table 2. Contrast agent and cardiac surgery data

Variable	Overall (n = 1177)	Postoperative ARF (n = 465)	No Postoperative ARF (n = 712)	P -value
Type of contrast agent used				
Hyperosmolar	926 (78.7%)	367 (78.9%)	559 (78.5%)	0.86
Low-osmolar	251 (21.3%)	98 (21.1%)	153 (21.5%)	
Dose of contrasted agent used				
Hyperosmolar	122.88 ± 16.84	124.52 ± 18.11	123.53 ± 17.37	0.03
Low-osmolar	121.31 ± 15.33	127.65 ± 26.86	123.78 ± 20.79	0.04
Contrast agent dose > median value	58 (8.1%)	56 (12.0%)	114 (9.7%)	0.03
Days between surgery and catheterization				
≤ 7 days	3.27 ± 2.01	3.27 ± 2.27	3.27 ± 2.11	0.99
7-30 days	18.79 ± 6.44	18.47 ± 6.01	18.67 ± 6.01	0.64
30-476 days	102.96 ± 95.95	110.82 ± 101.61	106.00 ± 98.17	0.34
Cardiac procedure				
Isolated CABG**	1097 (93.3%)	428 (92.0%)	669 (94.1%)	0.16
CABG** and other surgeries	25 (2.1%)	8 (1.7%)	17 (2.4%)	0.41
Isolated valve surgery	31 (2.6%)	16 (3.4%)	15 (2.1%)	0.17
Valve surgery and other surgeries	3 (0.3%)	0 (0.0%)	3 (0.4%)	0.17
CABG** and valve surgery	20 (1.7%)	13 (2.8%)	4 (1.0%)	0.02

Data are expressed as mean ± SD and number (%)
* P-values are calculated by chi-square test
** Coronary artery bypass grafting

Table 3. Independent correlates of acute renal failure after surgery

Variable	B	Odds Ratio	95% CI	p-value
Male gender	-0.0780	0.925	0.774-1.104	0.386
Age	-0.5924	0.553	0.075-2.095	0.068
Hypertension	-0.1997	0.819	0.661-1.016	0.069
IABP* insertion	1.9301	6.890	1.482-32.032	0.009
Contrast agent dose	0.3688	1.446	1.033-2.025	0.031
Combined surgery	1.6046	4.976	1.613-15.355	0.002

* Intra aortic balloon pump

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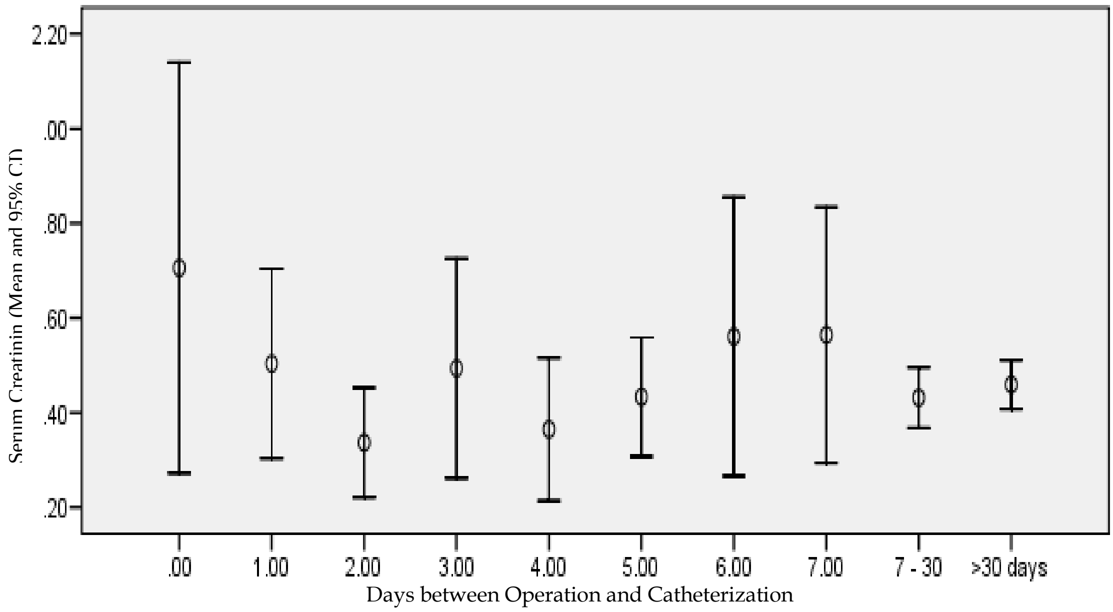

Figure 1. Relationship between the time interval flanked by angiography and surgery and post-operative serum creatinine

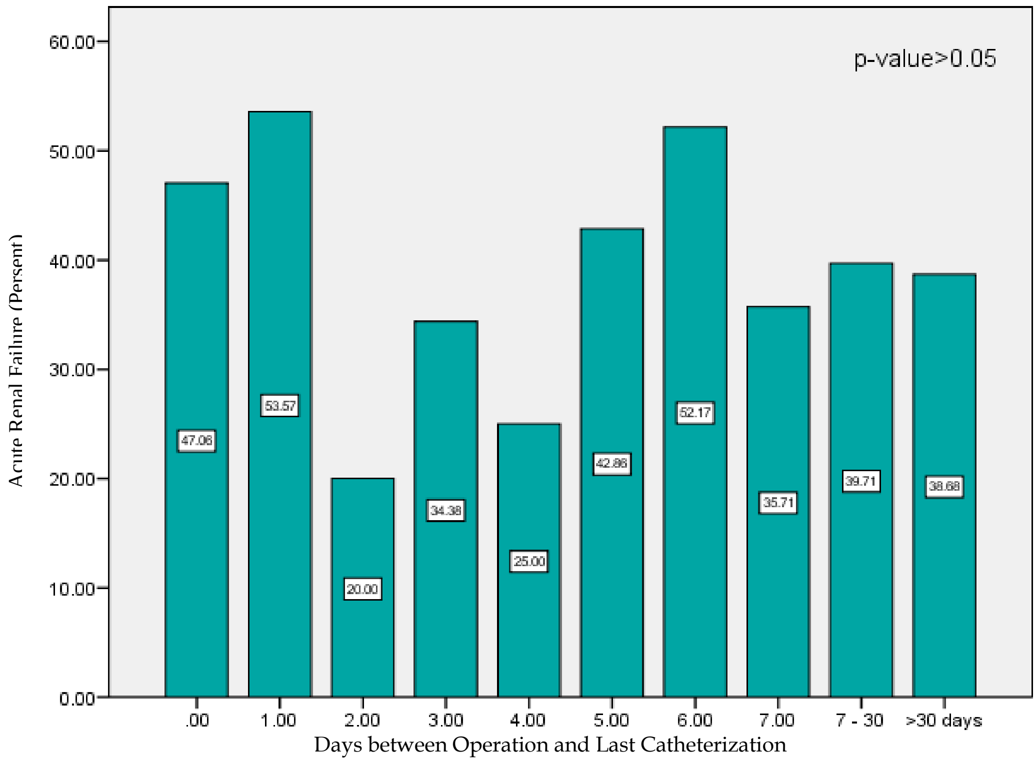

Figure 2. Relationship between the time interval flanked by angiography and surgery and post-operative acute renal failure

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low-osmolar contrast agents compared to mean doses ($p = 0.17$ and 0.035, respectively). However, the time interval between cardiac surgery and last catheterization was not different between the patients with and without ARF ($p > 0.05$) (Table 2).

Overall postoperative peak creatinine was highest on day 0 (Figure 2), then decreased and remained significantly unchanged after this period ($p < 0.05$). However, overall prevalence of acute renal failure during follow-up period (figure 2) had a changeable trend and had the highest rates in days 1 (53.57%) and 6 (52.17%) ($p < 0.05$).

Independent correlates of postoperative ARF in a multivariate model are listed in Table 3. Combined coronary artery bypass grafting (CABG) and valve surgery was the strongest predictor of postoperative ARF (OR: 4.976, $p = 0.002$), followed by intra-aortic balloon pump insertion (OR: 6.890, $p = 0.009$) and higher dose of contrast agent (OR: 1.446, $p = 0.031$).

Discussion

The major findings of the present study were that the higher dose of the used contrast agents besides some other determinants such as combined coronary bypass and valvular surgery as well as IABP insertion could effectively predict post-procedure acute ARF. On the other hand, the use of high dose of contrast agent was strongly related to the incidence of ARF after combined cardiac surgery. In fact, our data confirmed findings of other investigations that ARF after cardiac surgery was associated with the amount of prescribed contrast agents. In a similar study by Ranucci and his colleagues,[6] cardiac surgery performed on the day of cardiac catheterization and higher dose of contrast agent were both independently associated with increased risk of postoperative ARF. Although these investigators demonstrated a correlation between the time interval of cardiac catheterization and surgical procedure with the incidence of acute ARF, we could not demonstrate this relationship in our multivariable regression model. In another study by Del Duca et al[4] cardiac catheterization performed within 5 days before operation, baseline glomerular filtration rate of less than 60 ml/min and prolonged cardiopulmonary bypass duration, were significant risk factors for acute renal failure after cardiac surgery. Moreover, other studies established similar clinical and surgical characteristics associated with increased risk of ARF after cardiac surgery, including age,[1,6–8] baseline serum creatinine,[10] diabetes mellitus,[11-13] congestive heart failure,[10,12] emergency surgery,[11,14] concomitant valve surgery with coronary artery bypass grafting,[11] preoperative use of IABP,[14] and low cardiac output syndrome in the postoperative course.[14,15] However, these studies consistently failed to account for the influence of the timing between previous angiography and cardiac surgery and the amount of the contrast agent used in this event.

Multiple mechanisms have been suggested to contribute to the renal damage following cardiac diagnostic procedures, including nonpulsatile flow, embolization, and trauma to the blood constituents, hypothermia, and activation of known inflammatory pathways.[16]

Iodinated contrast as a common contrast agent, after causing a brief period of vasodilation, can cause sustained 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 are affected, then a recognizable rise in serum creatinine will occur.[17-18] Therefore, minimizing the amount of contrast agent during preceding angiography is recommended. Similar studies need to be conducted regarding alternate imaging modalities that do not use iodine-based contrast agents to obtain information about ventricular function, valvular dysfunction and aortic pathologic characteristics.[6] Finally, strategies to prevent contrast-induced nephropathy during angiography that is continued in the postoperative period may also have the potential to decrease ARF after early cardiac surgery.

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Conflict of Interests

Authors have no conflict of interests.

Authors' Contributions

MMS designed the study and drafted this manuscript; MG carried out the study and drafted the tables; PN carried out the study and drafted the tables; HSH helped in designing the study; HMS helped in final drafting; AK helped in designing and carried out the study; PMS data analysis; and NF Data collection. All authors have read and approved the final manuscript.

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