Evaluating the relative frequency and predicting factors of acute renal failure following coronary artery bypass grafting

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Original Article

Abstract

BACKGROUND: Renal dysfunction or acute renal failure in patients undergoing coronary artery bypass grafting (CABG) is an important cause of morbidity and mortality. The great impact of acute renal failure (ARF) in the outcomes of cardiac surgery demands its study in our population, encouraging to the elaboration of this study, which aimed to identify the incidence and risk factors of ARF after CABG.

METHODS: Since March 2010 to 2011, 589 patients were studied who underwent CABG in Sina Hospital (Isfahan, Iran). In this cross-sectional study, patients were divided into two groups based on the occurrence of ARF after CABG and measured variables were compared between the two groups was also statistically significant. P value less than 0.05 was set as a significant level.

RESULTS: A total of 434 men and 155 women were enrolled in the study. The mean age of the study subjects was 57.6 years. ARF was seen in about 22% of patients after CABG. The mean age of ARF group was more than 3 years higher than that in the other group and the difference was significant between the two groups. Serum creatinine level after the surgery was different between the two groups. Moreover, the history of diabetes mellitus was significantly different between the two groups. Pump time comparison also showed was also statistically significant.

CONCLUSION: Our data showed older patients were more prone to affected by ARF. In addition, diabetic patients should be considered as high risk patients and are more likely to deteriorate by ARF. Despite increased prevalence of renal insufficiency in CABG patients, studies show that in most cases, this is not a serious problem and it is easily treatable. A lower proportion of patients (1.0 to 1.7% in different large series) develop ARF severe enough to require dialysis.

Keywords: Coronary Artery Bypass, Acute Kidney Injury, Creatinine

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Introduction

Coronary artery bypass graft (CABG) surgery has been shown to be an effective method for treating angina pectoris and prolonging life in patients with severe coronary artery disease.[1] Each year, 600,000 patients undergo myocardial revascularization with cardiopulmonary bypass and sustain profound physiologic perturbations that precipitate ischemia and infarction in several organ systems.[2] Although the conduct of CABG with cardiopulmonary bypass (CPB) has evolved with continual improvement in morbidity and mortality, cardiopulmonary bypass is known to induce a proinflammatory state with several adverse consequences.[3,4] Clinically, the manifestations of cardiopulmonary bypass associated with morbidity include neurological dysfunction,[5,6] pulmonary dysfunction,[7] renal dysfunction,[8] and possibly infectious-related complications.[9]

Renal dysfunction or acute renal failure in patients undergoing CABG is an important cause of morbidity and mortality.[10] A decrease in cardiac output in the early stage after cardiac surgery is a frequent cause of acute renal failure and a very important risk factor as well.[11] Nonpulsatile blood flow, increased levels of circulating catecholamines and inflammatory mediators, macro embolic and micro embolic insults to kidney, and release of free hemoglobin from traumatized erythrocytes result in numerous pathophysiologic renal responses.[12,13] Many studies have shown that patients who have

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undergone cardiac surgery developed maldistributed renal blood flow, increased renal vascular resistance, and substantive decrease (25% to 75%) in renal blood flow and glomerular filtration rate.[14,15] In a study, the incidence of post-operative renal impairment varied from 3.5% to 31%[16] and the risk of developing a need for dialysis in the post-operative period has varied from 0.5 to 15%.[17-25] The prognosis of ARF in this setting is poor, with mortality rates ranging from 28 to 64%.[18-24] These patients often stayed longer in intensive care units and had higher costs.[2] Survival rate associated with ARF has remained dismal over the past few decades; multiple attempts at therapeutic interventions have failed to demonstrate clear benefits in either amelioration of renal injury or improved survival,[26] possibly because improvements in therapy have been balanced by increasing pre-operative comorbidity.[27] The great impact of ARF in the outcomes of cardiac surgery demand its study in our population, encouraging to the elaboration of this study, which aimed to identify the relative frequency and predicting factors of ARF after myocardial coronary artery bypass surgery.

Materials and Methods

Since March 2010 to 2011, 589 patients were studied who underwent CABG in Sina Hospital in Isfahan, Iran. In this cross-sectional study, patients were divided into two groups based on the occurrence of ARF after CABG and measured variables were compared between the two groups.

The following patients were excluded: Those who had positive history of chronic renal failure (CRF), acute renal failure (ARF), renal stone or serum creatinine > 2.1 mg/dl pre-operatively, patients who had been subjected to off pump CABG or other surgical procedures, those who were receiving renal replacement therapy or who had active endocarditis at the time of operation, patients who required preoperative dialysis, preoperative extracorporeal membrane oxygenation, preoperative tracheostomy or mechanical ventilation, those who underwent procedures for automated implantable cardioverter-defibrillator, left ventricular assist devices or sternal work and finally, patients who passed away within the first 24 hours after the operation (minimum time required for laboratory assessment of renal function).

Acute renal dysfunction was defined based on peak serum creatinine level > 2 mg/dl or more than 2 folds increase in postoperative creatinine level. ARF was defined as deterioration in renal function sufficient to require dialysis within 30 days following surgery. The indications for dialysis included uremia, volume overload or biochemical abnormalities and were measured based on clinical judgment. Creatinine clearance was estimated from serum creatinine, age, weight and gender by the formula of Cockcroft and Gault.

We examined the following variables as possible predictors of ARF: age, gender, body mass index (weight divided by height squared), pre and post operative serum creatinine (mg/dl), pre and post operative hemoglobin, pre and post operative ejection fraction (assessed by preoperative contrast ventriculography, radionucleotide ventriculography or two-dimensional echocardiography), cross-clamp time, CPB time, history of diabetes mellitus (requiring therapy with oral agents or insulin), history of cerebral vascular disease (manifested by previous stroke or transient ischemic attack), history of myocardial infarction (MI which was defined as either a Q-wave or a non-Q-wave infarction. A Q-wave MI was diagnosed centrally by the presence of a new Q wave on each of two postoperative 12-lead electrocardiograms, as defined by Minnesota Code criteria that were scored by a consensus panel of cardiologists. A non-Q-wave myocardial infarction was determined by an elevated creatine kinase-MB level, a new wall-motion abnormality detected by echocardiography or a new perfusion defect on a scintigraphy scan, and history of chronic obstructive pulmonary disease (resulting in functional disability or hospitalization or requiring chronic bronchodilator therapy or $FEV_1 < 75\%$ predicted).

Statistical analyses were carried out with SPSS for Windows 20.0 (SPSS Inc., Chicago, IL, USA), t-test for quantitative variables and chi-square test for qualitative variables were used to find out any association. P value less than 0.05 was set as a significant level.

Results

A total of 434 men and 155 women were enrolled in our study. The mean age of the study subjects was 57.62 years. ARF was observed in about 22% of the patients after CABG. The characteristics of patients with and without postoperative renal dysfunction are listed in table 1.

The mean age of ARF group was more than 3 years higher than that in the other group and the difference was significant between the two groups. About 37.5% patients in non-ARF group and 29% in ARF group were female. The mean changes of serum creatinine level after surgery was statistically

different between the two groups. Moreover, the history of hypertension and the history of diabetes mellitus were significantly different between the two groups. There was a statistically significant difference between the two groups in pump time.

As depicted in table 1, there is no statistically significant association between the gender as well as BMI and occurrence of ARF. Nevertheless, older patients are more prone to affected by ARF. We also compared other cardiac and non-cardiac risk factors between two groups in table 2.

Discussion

Acute renal failure (ARF) is a potential complication of CABG that can arise from a variety of causes including intraoperative hypotension, postoperative cardiac complications that impair renal perfusion, atheroemboli, and exposure to contrast media.[28] One problem with the available data on the incidence of ARF after CABG is the variable definitions used for ARF.[29] The incidence was higher with smaller compared to larger reductions in estimated glomerular filtration rate (e.g. 25% increase in serum creatinine compared to a 100% increase or the requirement for dialysis). In two studies with 843 and 649 patients undergoing cardiac surgery (mostly CABG), the incidence of ARF (defined as a rise in the serum creatinine of only 25%) was 17 and 24%.[30,31]

Other contemporary studies that used a more restrictive definition noted a much lower rate of ARF. The following two studies used the Society of Thoracic Surgeons (STS) definition: either an increase of serum creatinine to > 2 mg/dl (177 μmol/l) with a minimum doubling of the preoperative value, or a new requirement for dialysis. In a review of over 51,000 CABG procedures performed from 1999 to 2002, the incidence of ARF was constant over the four years, ranging from 4 to 5%.[32] In a 2006 data analysis report from the STS, the incidence of ARF was 3.6% after isolated CABG, and 7.5 and 12.9% after CABG combined with aortic or mitral valve replacement, respectively.[16]

Table 1. Baseline characteristics of the patients

Risk Factors		Non-ARF group (n = 458)	ARF group (n = 129)	P
Gender	Female (n)	125	29	ns
	Male (n)	333	100	
Age (mean)		56.90	60.10	0.01
Body mass index (mean)		26.86	27.05	ns

ARF: Acute renal failure; NS: Non significant

Table 2. Compare risk factors between the two groups

Risk Factors		Non-ARF group (n = 458)	ARF group (n = 129)	P
Mean creatinine level (mg/dl)	Preoperative	1.21	1.07	ns
	Postoperative	1.44	2.27	0.001
Postoperative-Preoperative		0.23	1.17	0.020
Mean ejection fraction (%)	Preoperative	49.49	49.29	ns
	Postoperative	47.18	46.18	
Mean cardiac clamp time (minute)		53.77	56.14	ns
Mean pump time (minute)		85.91	91.62	
History of diabetes mellitus	Yes (n)	228	77	0.050
	No (n)	230	52	
History of cerebrovascular accident	Yes (n)	431	126	ns
	No (n)	10	2	
History of MI within recent 30 days	Yes (n)	403	117	ns
	No (n)	42	8	
History of COPD	Yes (n)	19	3	ns
	No (n)	423	123	
Hemoglobin level (g/dl)	Preoperative	14.30	14.32	ns
	Postoperative	10.40	10.48	

ARF: Acute renal failure; MI: Myocardial infarction; COPD: Chronic obstructive pulmonary disease; NS: Non significant

ARF was observed in about 22% of the patients after CABG in this cross-sectional study. In different studies, the incidence of post-operative renal impairment in cardiac surgery patients varied from 3.5% to 31%.[19] Although, based on the results of the present study, only three important risk factors were associated with the ARF in patients undergoing CABG and no other appreciable differences were found between the two groups (ARF vs. non-ARF), several studies have demonstrated some associations among preoperative, intraoperative and postoperative risk factors with ARF. One important risk factor according to our study was history of hypertension. Cooper et al. also showed that among coronary artery bypass patients, the risk of ARF rose monotonically from 0.6% to 1.6% as preoperative systolic blood pressure rose from < 120 to ≥ 160 mmHg. In addition, they found that body mass index, a measure of obesity, was unrelated to the risk of ARF, similar to our study. In contrast, body surface area, an anthropometric measure estimating overall body size, was inversely correlated with ARF risk.[33] The results of our study also revealed another risk factor that obviously increased the possibility of ARF among patients undergoing CABG and that was history of diabetes mellitus. In the study of Mangano et al. patients, who had previously had a history of type I diabetes mellitus, had a 50% higher risk of postoperative renal dysfunction.[2]

A similar association between ARF requiring dialysis and impaired baseline renal function has been noted in other studies.[17,34] Other important independent risk factors in these reports included New York Heart Association functional class IV valve surgery, peripheral arterial disease, emergency surgery, and the need for preoperative intraaortic balloon pump. These risk factors have permitted the creation of risk scores that can stratify patients into categories of risk ranging from 0.4% to 21.4%.[26]

ARF requiring dialysis has also been associated with increased mortality. In the Veterans Administration study cited above, the 30-day mortality rate in such patients was 63.7% compared to 4.3% in those without ARF requiring dialysis.[34]

It is still controversial whether or not age is important in predisposing to ARF. Although reduced functional capacities of the kidney in the older patients is documented, a number of previous studies failed to demonstrate any statistical association between advanced age and the incidence of renal complications, whereas some others reported it ARF is more likely to develop in older patient.[2] To explain the positive correlation, it has been suggested that older patients may have a reduced ability to cope with a critical circulation or that they more frequently undergo high-risk procedures.[17] In our study, the mean age of ARF patients was higher than that in the other group.

In contrast to our study, other studies demonstrated that factors such as female gender,[26] peripheral artery disease,[19] congestive heart failure (defined by New York Heart Association class III or IV criteria), chronic obstructive pulmonary disease,[26] previous CABG surgery, aortic cross-clamp and total cardiopulmonary bypass lasting at least 2 hours were associated with an increased risk of post-operative renal dysfunction. However, they were not able to reveal low ejection fraction (≤ 0.3) and previous unstable angina as statistically significant risk factors of ARF.[2] In Mangano et al. the use of at least three inotropic drugs was associated with an increased risk of postoperative renal dysfunction. Moreover, the administration of "renal-dose" dopamine did not decrease the likelihood of postoperative renal dysfunction.[2]

This wide variability of the results could be due to different criteria used for diagnosis, the number and characteristics of centers involved in each study, the patients' features, and the size of the sample which hinders data comparison among the several performed studies.[19] Furthermore, the definition chosen for renal dysfunction was arbitrary in each study so the reported incidence of renal dysfunction after cardiac surgery was significantly influenced by the definition used in a given study.[2] We defined postoperative renal dysfunction on the basis of an absolute creatinine value (≥ 2 mg/dl) coupled with a relative change in creatinine level (≥ 2 folds) between the preoperative and the postoperative period. This study showed that the mean changes of creatinine level after surgery could be associated with ARF.

Our study had the limitation of choosing patients from a single center. Therefore, the generalizability of the findings is limited. The model needs to be tested broadly at multiple centers and to be well represented by differences in gender, race, and other risk factors to substantiate its applicability to our society.[26]

Despite the increased prevalence of ARF in the CABG patients, studies showed that in most cases, this is not a serious problem and it is easily treatable. A lower proportion of patients (1.0 to 1.7% in different large series) develops ARF severe enough to require dialysis.[2,35]

Conclusion

Our data showed older patients were more prone to affected by acute renal failure. Diabetic patients should be considered as high risk patients and are more likely to deteriorate by ARF.

Suggestions

1. Performing studies similar this study with larger sample size
2. Sharing our results to other cardiac surgeon for better management
3. And design studies with longer follow-up

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Conflict of Interests

Authors have no conflict of interests.

References

1. Eagle KA, Guyton RA, Davidoff R, Ewy GA, Fonger J, Gardner TJ, et al. ACC/AHA Guidelines for Coronary Artery Bypass Graft Surgery: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1991 Guidelines for Coronary Artery Bypass Graft Surgery). American College of Cardiology/American Heart Association. J Am Coll Cardiol 1999; 34(4): 1262-347.
2. Mangano CM, Diamondstone LS, Ramsay JG, Aggarwal A, Herskowitz A, Mangano DT. Renal dysfunction after myocardial revascularization: risk factors, adverse outcomes, and hospital resource utilization. The Multicenter Study of Perioperative Ischemia Research Group. Ann Intern Med 1998; 128(3): 194-203.
3. Levy JH, Tanaka KA. Inflammatory response to cardiopulmonary bypass. Ann Thorac Surg 2003; 75(2): S715-S720.
4. Boyle EM, Pohlman TH, Johnson MC, Verrier ED. Endothelial cell injury in cardiovascular surgery: the systemic inflammatory response. Ann Thorac Surg 1997; 63(1): 277-84.
5. Taylor KM. Central nervous system effects of cardiopulmonary bypass. Ann Thorac Surg 1998; 66(5 Suppl): S20-S24.
6. Almassi GH, Sommers T, Moritz TE, Shroyer AL, London MJ, Henderson WG, et al. Stroke in cardiac surgical patients: determinants and outcome. Ann Thorac Surg 1999; 68(2): 391-7.
7. Asimakopoulos G, Smith PL, Ratnatunga CP, Taylor KM. Lung injury and acute respiratory distress syndrome after cardiopulmonary bypass. Ann Thorac Surg 1999; 68(3): 1107-15.
8. Ascione R, Lloyd CT, Underwood MJ, Gomes WJ, Angelini GD. On-pump versus off-pump coronary revascularization: evaluation of renal function. Ann Thorac Surg 1999; 68(2): 493-8.
9. Jensen RH, Storgaard M, Vedelsdal R, Obel N. Impaired neutrophil chemotaxis after cardiac surgery. Scand J Thorac Cardiovasc Surg 1995; 29(3): 115-8.
10. Hickey PR, Buckley MJ, Philbin DM. Pulsatile and nonpulsatile cardiopulmonary bypass: review of a counterproductive controversy. Ann Thorac Surg 1983; 36(6): 720-37.
11. Yavuz S, Ayabakan N, Goncu MT, Ozdemir IA. Effect of combined dopamine and diltiazem on renal function after cardiac surgery. Med Sci Monit 2002; 8(5): I45-I50.
12. Donohoe JF, Venkatachalam MA, Bernard DB, Levinsky NG. Tubular leakage and obstruction after renal ischemia: structural-functional correlations. Kidney Int 1978; 13(3): 208-22.
13. Lowe MB. Effects of nephrotoxins and ischaemia in experimental haemoglobinuria. J Pathol Bacteriol 1966; 92(2): 319-23.
14. Mazzarella V, Gallucci MT, Tozzo C, Elli M, Chiavarelli R, Marino B, et al. Renal function in patients undergoing cardiopulmonary bypass operations. J Thorac Cardiovasc Surg 1992; 104(6): 1625-7.
15. Mori A, Watanabe K, Onoe M, Watarida S, Nakamura Y, Magara T, et al. Regional blood flow in the liver, pancreas and kidney during pulsatile and nonpulsatile perfusion under profound hypothermia. Jpn Circ J 1988; 52(3): 219-27.
16. Santos FO, Silveira MA, Maia RB, Monteiro MD, Martinelli R. Acute renal failure after coronary artery bypass surgery with extracorporeal circulation-incidence, risk factors, and mortality. Arq Bras Cardiol 2004; 83(2): 150-4.
17. Zanardo G, Michielon P, Paccagnella A, Rosi P, Calo M, Salandin V, et al. Acute renal failure in the patient undergoing cardiac operation. Prevalence, mortality rate, and main risk factors. J Thorac Cardiovasc Surg 1994; 107(6): 1489-95.
18. Ostermann ME, Taube D, Morgan CJ, Evans TW. Acute renal failure following cardiopulmonary bypass: a changing picture. Intensive Care Med 2000; 26(5): 565-71.
19. Chertow GM, Lazarus JM, Christiansen CL, Cook EF, Hammermeister KE, Grover F, et al. Preoperative renal risk stratification. Circulation 1997; 95(4): 878-84.
20. Fortescue EB, Bates DW, Chertow GM. Predicting acute renal failure after coronary bypass surgery: cross-validation of two risk-stratification algorithms. Kidney Int 2000; 57(6): 2594-602.
21. Conlon PJ, Stafford-Smith M, White WD, Newman MF, King S, Winn MP, et al. Acute renal failure

following cardiac surgery. Nephrol Dial Transplant 1999; 14(5): 1158-62.
22. Suen WS, Mok CK, Chiu SW, Cheung KL, Lee WT, Cheung D, et al. Risk factors for development of acute renal failure (ARF) requiring dialysis in patients undergoing cardiac surgery. Angiology 1998; 49(10): 789-800.
23. Andersson LG, Ekroth R, Bratteby LE, Hallhagen S, Wesslen O. Acute renal failure after coronary surgery--a study of incidence and risk factors in 2009 consecutive patients. Thorac Cardiovasc Surg 1993; 41(4): 237-41.
24. Frost L, Pedersen RS, Lund O, Hansen OK, Hansen HE. Prognosis and risk factors in acute, dialysis-requiring renal failure after open-heart surgery. Scand J Thorac Cardiovasc Surg 1991; 25(3): 161-6.
25. Schmitt H, Riehl J, Boseila A, Kreis A, Putz-Stork A, Lo HB, et al. Acute renal failure following cardiac surgery: pre- and perioperative clinical features. Contrib Nephrol 1991; 93: 98-104.
26. Aronson S, Blumenthal R. Perioperative renal dysfunction and cardiovascular anesthesia: concerns and controversies. J Cardiothorac Vasc Anesth 1998; 12(5): 567-86.
27. Rosner MH, Okusa MD. Acute kidney injury associated with cardiac surgery. Clin J Am Soc Nephrol 2006; 1(1): 19-32.
28. Palevsky PM. Epidemiology of acute renal failure: the tip of the iceberg. Clin J Am Soc Nephrol 2006; 1(1): 6-7.
29. Loef BG, Epema AH, Smilde TD, Henning RH, Ebels T, Navis G, et al. Immediate postoperative renal function deterioration in cardiac surgical patients predicts in-hospital mortality and long-term survival. J Am Soc Nephrol 2005; 16(1): 195-200.
30. Del Duca D, Iqbal S, Rahme E, Goldberg P, de Varennes B. Renal failure after cardiac surgery: timing of cardiac catheterization and other perioperative risk factors. Ann Thorac Surg 2007; 84(4): 1264-71.
31. Mack MJ, Brown PP, Kugelmass AD, Battaglia SL, Tarkington LG, Simon AW, et al. Current status and outcomes of coronary revascularization 1999 to 2002: 148,396 surgical and percutaneous procedures. Ann Thorac Surg 2004; 77(3): 761-6.
32. Bridgewater B, Keogh B, Kinsman R, Walton P. The Society for Cardiothoracic Surgeryin Great Britain and Ireland, Sixth National Adult Cardiac Surgical Database Report 2008 [Online]. 2008; Available from: URL: http://www.e-dendrite.com/files/13/file/Pages%20from%20NACSD%202008.pdf/
33. Cooper WA, O'Brien SM, Thourani VH, Guyton RA, Bridges CR, Szczech LA, et al. Impact of renal dysfunction on outcomes of coronary artery bypass surgery: results from the Society of Thoracic Surgeons National Adult Cardiac Database. Circulation 2006; 113(8): 1063-70.
34. Thakar CV, Arrigain S, Worley S, Yared JP, Paganini EP. A clinical score to predict acute renal failure after cardiac surgery. J Am Soc Nephrol 2005; 16(1): 162-8.
35. Eriksen BO, Hoff KR, Solberg S. Prediction of acute renal failure after cardiac surgery: retrospective cross-validation of a clinical algorithm. Nephrol Dial Transplant 2003; 18(1): 77-81.

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