Incidence and Complications of Acute Kidney Injury Following Coronary Artery Bypass Graft

A Retrospective Cohort Study

Fardin Yousefshahi,[1] Ali Mohammad Fakhre Yasseri,[2] Khosro Barkhordari,[1] Manouchehr Amini,[3] Abbas Salehi Omran,[4] Mohsen Rezaei Hemami,[5] Mahboobeh Asadi[2]

[1]Department of Anesthesia and Critical Care, Tehran University of Medical Sciences, Tehran, Iran
[2]School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[3]Department of Nephrology, Tehran University of Medical Sciences, Tehran, Iran
[4]Department of Cardiac Surgery, Tehran University of Medical Sciences, Tehran, Iran
[5]Department of Epidemiology, Rasul-Akram Hospital, Iran University of Medical Sciences, Tehran, Iran

Keywords. acute kidney injury, coronary artery bypass, length of stay, hemodialysis, mortality

Introduction. Acute kidney injury (AKI) is a common complication of coronary artery bypass graft with several serious complications. This study aimed to find the incidence of AKI after coronary artery bypass graft and its complications based on the Acute Kidney Injury Network (AKIN) criteria.
Materials and Methods. This study was done on 3470 patients who had undergone isolated coronary artery bypass graft. Acute kidney injury's incidence was based on the AKIN criteria (only based on serum creatinine irrespective of urine output). Patients' demographic data, in-hospital complications, and out-hospital mortality were collected from hospital databases and compared between the patients with and without AKI.
Results. Based on serum creatinine, the incidence of AKI was 27.7% (958 patients) on the 1st postoperative day. Nine patients (0.3%) needed hemodialysis during their hospital stay, and 31 patients (0.7%) developed persistent kidney failure until the discharge day. The number of patients undergoing hemodialysis was not significantly difference but persistent kidney failure was significantly more frequent in patients with AKI ($P < .001$). Those with AKI also experienced longer length of stay ($P = .04$) and longer length of stay in intensive care unit ($P < .001$), and their mortality rate was higher in hospital ($P < .001$) and during the 3-year follow-up period ($P < .001$).
Conclusions. Although AKI is associated with great patients' morbidity and in-hospital and long-term mortality, most of AKI episodes after coronary artery bypass graft are mild with no need for hemodialysis, and they mostly improve spontaneously.

IJKD 2015;9:113-8
www.ijkd.org

INTRODUCTION

Acute kidney injury (AKI) is a common complication after coronary artery bypass graft surgery that causes many complications, such as increasing length of stay in hospital and intensive care unit (ICU), risk of hemodialysis, persistent kidney failure, and mortality rate.[1] Acute kidney injury can affect coronary artery bypass graft (CABG) results and worsen the operation outcomes. On the other hand, CABG operation is usually done in high-risk patients and that are at risk of AKI after the operation.[2]

There are two classifications used for AKI staging, including the Acute Kidney Injury Network

(AKIN) and the Risk, Injury, Failure, Loss, and End-stage Renal Disease (RIFLE) classifications. In the AKIN classification, there are 3 stages for AKI. Stage 1 is defined as increasing by at least 0.3 mg/dL of serum creatinine or 1.5- to 2-folds or oliguria (urine output lower than 0.5 mL/kg/h) in 6 hours; stage 2, increasing serum creatinine at least 1.5- to 2-folds or oliguria (urine output lower than 0.5 mL/kg/h) in 12 hours; and stage 3, increasing serum creatinine at least 2- to 3-folds or 4-folds with an acute rise of 0.5 mg/dL or the need for renal replacement therapy regardless of prior stage or oliguria (urine output lower than 0.3 mL/kg/h) in 24 hours or anuria in 24 hours.[3,4] The incidence of AKI after CABG is reported from 7.6% to 48.5% in previous studies based on the AKIN classification.[3-5]

Risk factor for AKI include female sex, preoperative heart failure, left ventricular dysfunction, peripheral vascular disease, diabetes mellitus, the need for intra-aortic balloon pump, urgent operation, preoperative rise in creatinine level, use of diuretic medications, long cross-clamp time, use of aprotinin, blood transfusion, cardiopulmonary bypass time, preoperative anemia, erythrocyte transfusion, blood albumin, β2-microglobulin, blood uric acid, postoperative re-exploration, dosage of mannitol, hypertension, number of grafts, mechanical ventilation time, and preoperative percutaneous angiography. [6-13] Consequences of AKI is the need for dialysis, mortality, increased length of stay, and increased costs.[3] Unfortunately, about 64% of those undergoing hemodialysis will remain dependent on hemodialysis. Mortality rate is increased in these patients and their 1-year survival is only 10%.[14] Hemodialysis incidence is reported from 1% to 5%.[15]

There is a strong relationship between AKI and mortality after CABG even in lower AKI stages. Post-AKI mortality was reported from 15% to 30%, and it was as high as 60% in some studies.[15,16] Nonetheless, AKI definition was different in these studies. The mortality was 60% to 70% in patients requiring hemodialysis. Mortality rate after 1-year follow-up was 4.5-fold higher in patients developing AKI.[14] Hemodialysis causes hemodynamic instability, ventricular ectopy, catheter-related infection, and visceral ischemia. There are also immunologic incoordination and platelet dysfunction after AKI that play a role in mortality. Infection is a major cause of death in AKI following CABG accounting for 40% of deaths. Risk of sepsis is significantly increased in hemodialysis after CABG in comparison with other post-CABG patients (58.5% versus 3.3%).[14] Kidney injury is one of the factors used in the EuroSCORE as a useful scoring system to estimate mortality after CABG.[17]

Increase in length of stay in hospital is one of the AKI consequences after CABG operation. Length of stay was reported to be longer in AKI patients in comparison with CABG patients without AKI (11 days versus 5 days), and also, length of stay in the ICU was longer (3.2 days versus 1.4 days).[18] The postoperative costs were increased by 1.6-fold in AKI after CABG compared to the control group even for lower stages of AKI.[18] A cost study proved that the cost was 42% higher (average, US $ 5807 per person) in post-CABG kidney dysfunction.[19] Overall, kidney dysfunction after CABG adds up to US $ 643 million in hospital costs in the United States.[19]

The first studies based on the AKIN classification were published in 2009. Li and colleagues[6] reported AKI in 27.9% in 68 patients undergoing CABG. Later Machado and coworkers[3] reported the incidence of 48.5% in 817 patients, with a hemodialysis rate of 3.8% and mortality rate 11-folds higher with AKI (11.2% versus 1%). In 2011, Englberger and colleagues[20] studied on 4800 patients and reported that AKI incidence after CABG was 18.9% based on the AKIN and mortality was higher in the AKI group (odds ratio, 4.5). Kim and colleagues[4] reported an incidence of 7.6% in the same year. Gong and coworkers[21] assessed 1400 post-CABG patients in 2012. The receiver operator characteristic curve determined AKI classification with RIFLE a powerful predictor of delayed extubation, failure to extube, and mortality. In the same year Vellinga and colleagues[22] assessed 565 patients, and the incident was 14.7% based on the AKIN classification. In 2013, Chew and colleagues[23] published a study about the role of ethnicity in AKI. In their study, the incidence of AKI after CABG was 35.3%. Indians and Malays had a higher risk of developing AKI than the Chinese in a South East Asian population.

Most studies on AKI based on AKIN and RIFLE classifications were retrospective and used only the creatinine component of criterion. In only

12% of the analyzed population, the creatinine and urine output criteria were used together.[24] A brief review of the literature shows that not many studies determined the incident of AKI after CABG based on the AKIN classification and most of them were done on inadequate sample sizes. Also, studies on complications based on the AKIN criteria are scarce. There is not any qualified study that includes all complications.[6,20-23]

Nowadays, many physicians use the AKIN classification to describe their patients and an increasing number of studies use this new classification.[6,20-23] This study was aimed to determine AKI incidence after CABG based on the AKIN classification and the rates of mortality, need for hemodialysis, persistent kidney failure, and longer stay in hospital and ICU in these patients as compared with other patients with CABG. Results of this study could help physicians to manage these patients better.

MATERIALS AND METHODS

This retrospective cohort study was done between March 2010 and March 2012 in Tehran University of Medical Sciences and Tehran Heart Center. This study was done on patients who had undergone isolated on pump coronary artery bypass graft. The inclusion criteria were age older than 18 years, serum creatinine level lower than 2 mg/dL, and an ejection fraction greater than 30%. Patients on nephrotoxic medications a week before the surgery, those with a history of preoperative hemodialysis and sepsis, those undergoing urgent CABG surgery were excluded. Also, patients with incomplete information in their charts were not included.

The sample size was estimated to be 3400 patients (d = 1.5). In 3 years, 72 500 patients had been operated and their data was recorded on an electronic database. We identified patients with CABG who would meet the inclusion criteria; 2800 patients were excluded because of low ejection fraction (lower than 30%), 1080 because of high serum creatinine level, and others because of urgent operations or age under 18 years old. Overall 3548 patient came into this study. From these patients, 75 were excluded from this study due to other exclusion criteria and finally analysis was done on 3473 patients.

The incidence of acute kidney injury incidence was determined based on the AKIN classification (only based on serum creatinine irrespective of urine output): a 0.3-mg/dL increase or greater in creatinine level or 50% increase in the base creatinine (despite urine output). These were based on the two serum creatinine levels recorded in the database: morning of the operation day and the day after the operation. Therefore, serum creatinine was not measured exactly 24 hours after the surgery, because some patients were operated in the afternoon. The difference between these values was considered as AKI "within 24 hours."

The overall length of stay and ICU days were calculated based on the admission and discharge day and the ICU hours recorded in the database. The need for hemodialysis was determined from consultation note of the nephrologist, but reasons for hemodialysis were not available. Postoperative persistent kidney failure was defined as a creatinine level elevation over 2 mg/dL during hospital stay. In-hospital mortality was recorded from patients' charts. The patients had followed-up visits after discharge in 3-month intervals. Their mortality and the cause of death were recorded in the database. Out-of-hospital mortality was collected for a maximum 3-year follow-up period.

The included patients were divided into 2 groups of AKI-positive and AKI-negative patients. Postoperative in-hospital complications, length of stay, and mortality data were compared between these groups.

Analysis was done using the SPSS software (Statistical Package for the Social Sciences, version 19.0, SPSS Inc, Chicago, Ill, USA). The length of stay variables were compared by the *t* test. Dialysis, kidney failure, and in-hospital mortality were compared with the chi-square test. The Kaplan-Meier estimator and log-rank test were used for survival analysis. The summary values for age, weight, height, body mass index, preoperative serum creatinine, cardiopulmonary bypass time, and cross-clamp time were shown as mean ± standard deviation. Values of $P < .05$ were considered significant.

RESULTS

This study was done on 3473 patients. There were 997 women (28.7%) and 2476 men (71.3%). The mean age was 60.75 ± 9.46 years (range, 22 to 88 years). The mean weight, height, and body mass index were 73.48 ± 12.11 kg (range, 37 kg to 183 kg), 164.80 ± 9.84 cm (range, 71 cm to 191 cm), and 27.01 ± 4.10 kg/m^2 (range, 14.71 kg/m^2 to 52.50 kg/m^2), respectively. The mean preoperative creatinine level was 0.94 ± 0.36 mg/dL. The mean cardiopulmonary bypass time was 72.88 ± 28.95 minutes and the mean cross-clamp time 43.41 ± 129.45 minutes.

Overall, 3467 patients had 2 365 099 days of follow-up records that varied between 1 to 1259 days (median, 690 days; mean, 685.17 ± 322.62 days). The incidence of AKI was 27.7% (958 patients) based on serum creatinine of the 1st postoperative day. The staging based on the AKI classification was 1 or higher in 958 patients (27.7%), 2 or higher in 62 (1.8%), and 3 or higher in 31. In this study, 9 patients (0.3%) needed hemodialysis during the hospitalization. Thirty-one patients (0.7%) developed persistent kidney failure before the discharge day.

The number of patients undergoing hemodialysis was not significantly difference (P = .22), but persistent kidney failure was significantly more frequent in patients with AKI (P < .001). The patients with AKI also experienced longer length of stay (15.78 ± 7.78 days versus 15.15 ± 9.43 days, P = .04) and longer length of stay in ICU (3.10 ± 4.29 days versus 2.65 ± 3.65 days, P < .001), and their mortality rate was higher in hospital (P < .001) and during the 3-year follow-up period (P < .001). Tables 1 and 2 show the comparisons of these variables between the two groups. In-hospital mortality was 2.3% among patients with AKI and 0.7% in those without AKI (P < .001), and mortality during the 3-year follow-up period was 4.8% versus 1.9%, respectively (P < .001). Table 2 shows the comparisons of these variables between the two groups. Patient survival was significantly lower in the AKI-positive patients (Figure; P < .001).

Table 1. The Effect of Acute Kidney Injury on Length of Stay*

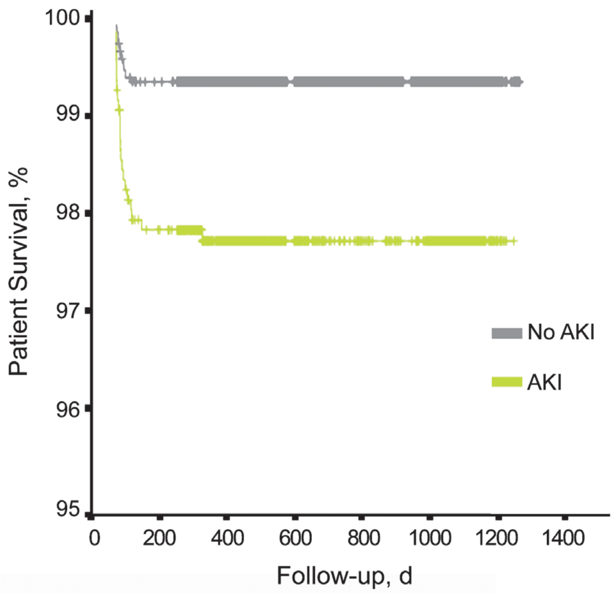
	Patients With CABG		
Parameter	AKI	No AKI	P
Length of stay, d	15.15 ± 9.43	15.78 ± 7.78	.04
Intensive care unit stay, d	2.65 ± 3.65	3.10 ± 4.29	.002

*AKI indicates acute kidney injury and CABG, coronary artery bypass graft.

Table 2. Complications in Patients With and Without Acute Kidney Injury*

	Patients With CABG		
Parameter	AKI	No AKI	P
Postoperative hemodialysis	4 (0.2)	5 (0.2)	.22
Persistent kidney failure	9 (0.4)	16 (1.7)	< .001
In-hospital mortality	18 (0.7)	22 (2.3)	< .001
Mortality in 3 years	47 (1.9)	46 (4.8)	< .001

*AKI indicates acute kidney injury and CABG, coronary artery bypass graft.



Survival function of patients with and without acute kidney injury (AKI)

DISCUSSION

The AKI incidence was 27.7% in this study. Li and colleagues in China reported a rate of 27.9% for AKI incidence after CABG, which is very similar to this study.[6] The incidence rate was different reported in different countries. It was 48.5% in Brazil, 26.3% in the United States, and 14.7% in Belgium.[3,20,22] The role of ethnicity could explain the difference between the incidence rates in different studies. Chew and coworkers documented that Indians and Malays have a higher risk of developing AKI than Chinese in a South-East Asian population.[23] Machado and colleagues[3] excluded preoperative kidney failure, and the AKI incidence was measured in 48 hours. Although transient AKI in 24 hours after surgery was excluded, the incidence was higher (48.5%) than that in other similar studies. Considering exclusion criteria and lack of data regarding urine output, underestimation of mild forms of AKI is possible in our study.

The average length of stay was 0.63 days longer and ICU stay was 0.45 days longer in patients with AKI than those without AKI, and the differences was significant. This result is similar to previous studies, but the differences were smaller in this study. Dastal and colleagues showed that length of stay was 11 days in their AKI group and 5 days in the control group. In that study, the average ICU stay was 3.2 days in the AKI group versus 1.4 in the control group.[18]

In this study, postoperative persistent kidney failure was about 4-fold higher with AKI (1.7% versus 0.4%), but postoperative hemodialysis rate was not significantly different between the two groups, and this was not similar to previous studies. In both groups, persistent kidney failure and the need for hemodialysis were in few cases, which could be the result of intraoperative insults to the kidney or the result of any later unrecorded complication. In this study, overall 0.3% of the patients needed hemodialysis, as compared to 1% in Rosner and colleagues' study[14] and 3.8% in Machado and colleagues' study.[3] This difference may rise from excluding preoperative kidney failure in our study. Although 27% of the patients develop AKI, fortunately most of the patients did not progress to persistent kidney failure and dependence on dialysis. It is probable that most of these injuries were only transient ischemia and it does not cause permanent injury in most of cases.

In the present study, in-hospital mortality rate in was about 3 times higher in patients with AKI than in those without AKI (3.2% versus 7.0%). Mortality after 3 years of follow-up in was 2.5 times higher in these patients (8.4% versus 9.1%), and these differences were significant, nearly similar to previous studies. In Eagleburger and coworkers' study,[20] mortality risk was 4.5-fold higher in the AKI group. In Machado and colleagues' study,[3] mortality was 11-fold higher (11.2% versus 1%). Gong and associates[21] demonstrated that AKI classification was the predictor of death. This is an important point that even mild and transient AKI could increase mortality rate. Therefore, it would be a justified argument to prevent even minimal insults to the kidney.

Many studies are carried out on AKI after CABG, but the studies that based on the AKIN classification are very few. Unfortunately, most of these studies were done with small sample sizes and without reporting AKI complications incidence.[6,20-23] There was no study on AKI after CABG based on the AKIN classification on Iranians. These causes show why this study was necessary. However, there were several limitations in this study. First, only 2 creatinine levels were recorded from the patients in the database (operation day and day after operation). Variation in creatinine level that could even lead to hemodialysis in the first postoperative day was not considered. Second, the time of the operation was in the afternoon in some of those patients; therefore, the AKI measurement was not exactly within 24 hours. Third, unfortunately urine output was not recorded in the database and caused the underestimation at least for mild forms of AKI incidence rate. Fourth, in the follow-up clinic database, only death and cause of death were recorded. Out-of-hospital creatinine changes and kidney function of patients was not recorded. The real contribution of AKI in this mortality rate is however difficult to assess. Fifth, the follow-up time was different between the patients. Finally, any causes of renal hypoperfusion were not come in this study or were excluded; so, there may be an underestimation of the incidence rate in this study, as compared to others. We suggest databases upgrading could help researchers to study on AKI better. Further studies should be performed on post-CABG AKI and its complications to define patients who are at risk for serious morbidity and mortality.

CONCLUSIONS

Even mild and transient AKI could be associated with an increase in ICU length of stay and long-term mortality rate obviously, without any increase in hemodialysis rate.

ACKNOWLEDGEMENTS

The authors would like to thank Dr Hashem Fakhre Yaseri for his help and Dr Binaa for contributing to extracting data from the electronic database.

REFERENCES

1. Loef BG, Epema AH, Smilde TD, et al. Immediate postoperative renal function deterioration in cardiac surgical patients predicts in-hospital mortality and long-term survival. J Am Soc Nephrol. 2005;16:195-200.
2. Barkhordari K, Karimi A, Shafiee A, et al. Effect of pentoxifylline on preventing acute kidney injury after cardiac surgery by measuring urinary neutrophil gelatinase - associated lipocalin. J Cardiothorac Surg. 2011;6:8.
3. Machado MN, Miranda RC, Takakura IT, et al. Acute

kidney injury after on-pump coronary artery bypass graft surgery. Arq Bras Cardiol. 2009;93:247-52.

4. Kim MY, Jang HR, Huh W, et al. Incidence, risk factors, and prediction of acute kidney injury after off-pump coronary artery bypass grafting. Ren Fail. 2011;33:316-22.
5. Yousefshahi F, Bashirzadeh M, Abdollahi M, et al. Effect of Hypertonic Saline Infusion versus Normal Saline on Serum NGAL and Cystatin C Levels in Patients Undergoing Coronary Artery Bypass Graft. J Tehran Heart Cent. 2013;8:21-7.
6. Li XH, Xiao F, Li Y, et al. [Investigations of influential factors of acute renal injury after coronary artery bypass grafting]. Beijing Da Xue Xue Bao. 2009;41:554-7. Chinese.
7. Karkouti K, Wijeysundera DN, Yau TM, et al. Acute kidney injury after cardiac surgery: focus on modifiable risk factors. Circulation. 2009;119:495-502.
8. Perez-Valdivieso JR, Monedero P, Vives M, Garcia-Fernandez N, Bes-Rastrollo M. Cardiac-surgery associated acute kidney injury requiring renal replacement therapy. A Spanish retrospective case-cohort study. BMC Nephrol. 2009;10:27.
9. Mazandarani M, Yousefshahi F, Abdollahi M, et al. Comparison of hypertonic saline versus normal saline on cytokine profile during CABG. Daru. 2012;20:49.
10. 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;16:162-8.
11. Ling LG, Zeng N, Liu J, et al. [Risk factors for acute kidney injury following 5100 cardiac surgeries with extracorporeal circulation]. Zhong Nan Da Xue Xue Bao Yi Xue Ban. 2009;34:861-6.
12. Pakfetrat M, Nikoo MH, Malekmakan L, et al. Risk Factors for contrast-related acute kidney injury according to risk, injury, failure, loss, and end-stage criteria in patients with coronary interventions. Iran J Kidney Dis. 2010;4:116-22.
13. Mahdavi-Mazdeh M. Re: risk factors for contrast-related acute kidney injury according to risk, injury, failure, loss, and end-stage criteria in patients with coronary interventions. Iran J Kidney Dis. 2010;4:269-70.
14. Rosner MH, Okusa MD. Acute kidney injury associated with cardiac surgery. Clin J Am Soc Nephrol. 2006;1:19-32.
15. Conlon PJ, Stafford-Smith M, White WD, et al. Acute renal failure following cardiac surgery. Nephrol Dial Transplant. 1999;14:1158-62.
16. Levy MM, Macias WL, Vincent JL, et al. Early changes in organ function predict eventual survival in severe sepsis. Crit Care Med. 2005;33:2194-201.
17. Nashef SA, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). Eur J Cardiothorac Surg. 1999;16:9-13.
18. Dasta JF, Kane-Gill SL, Durtschi AJ, Pathak DS, Kellum JA. Costs and outcomes of acute kidney injury (AKI) following cardiac surgery. Nephrol Dial Transplant. 2008;23:1970-4.
19. Callahan M, Battleman DS, Christos P, Efimba M, Whitelaw G. Economic consequences of renal dysfunction among cardiopulmonary bypass surgery patients: a hospital-based perspective. Value Health. 2003;6:137-43.
20. Englberger L, Suri RM, Li Z, et al. Clinical accuracy of RIFLE and Acute Kidney Injury Network (AKIN) criteria for acute kidney injury in patients undergoing cardiac surgery. Crit Care. 2011;15:R16.
21. Gong ZY, Gao CQ, Li BJ, et al. [Acute kidney injury early after cardiac surgery with cardiopulmonary bypass: clinical analysis]. Zhonghua Yi Xue Za Zhi. 2012;92:3283-7.
22. Vellinga S, Verbrugghe W, De PR, Verpooten GA, Janssen van DK. Identification of modifiable risk factors for acute kidney injury after cardiac surgery. Neth J Med. 2012;70:450-4.
23. Chew ST, Mar WM, Ti LK. Association of ethnicity and acute kidney injury after cardiac surgery in a South East Asian population. Br J Anaesth. 2013;110:397-401.
24. Cruz DN, Ricci Z, Ronco C. Clinical review: RIFLE and AKIN--time for reappraisal. Crit Care. 2009;13:211.

Correspondence to:
Fardin Yousefshahi, MD
Women Hospital & Tehran Heart Center, Tehran, Iran
Tel: +98 912 619 0811
E-mail: yousefshahi@tums.ac.ir
Received April 2014
Accepted July 2014