ORIGINAL ARTICLE

Coronary Artery Bypass Surgery and Acute Kidney Injury: Impact of the Off-Pump Technique

E Ghanei[1]*, SA Hogat[1], T Orouji Jokar[1], AA Kolahi[2]

[1]Urology and Nephrology Research Center (UNRC), Department of Internal Medicine, Shohada-e-Tajrish Hospital, [2]School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract

Background: Acute kidney injury (AKI) is a common major complication after coronary artery bypass grafting (CABG) especially when the cardiopulmonary bypass is performed. This study was conducted to evaluate the impact of the off-pump technique on the incidence of AKI, also to determine the major risk factors for AKI.

Methods: In this prospective cohort study, 535 consecutive adult patients who underwent CABG between January 2007 and May 2010 in a tertiary Hospital. Some 64 of 535 patients were operated through the off-pump coronary artery bypass (OPCAB) technique and another 471 patients by the on-pump coronary artery bypass graft (CABG) technique. Stratified sampling was used to assign patients to be operated either by the OPCAB or ONCAB technique. The AKI incidence and severity were compared between the two groups.

Results: In OPCAB group 9.4% (6 patients) and in ONCAB group 4.1% (19 patients) developed AKI with no significant difference. Furthermore, the AKI severity was alike in the two groups and 10.5% (2 patients) in ONCAB and 33.3% (2 patients) in OPCAB group had mild AKI, 78.9% (15 patients) in ONCAB and 50% (3 patients) in OPCAB group had moderate AKI, and 10.5% (2 patients) in ONCAB and 16.7% (1 patients) in OPCAB group had severe AKI.

Conclusion: As the differences of incidence and severity of postoperative AKI between OPCAB and ONCAB groups were not significant, further studies to find other useful protective methods such as free-radical scavengers, anti-inflammatory agents, and other modalities are recommended to prevent AKI.

Keywords: Acute kidney injury; Coronary artery bypass grafting; Off-pump

Introduction

Acute kidney injury (AKI) is a common major complication after on-pump coronary artery bypass graft (ONCABG) surgery[1] occurring in 9 to 19% of patients.[2-4] The ischemic injury is the main cause of nephropathy in these patients,[5-6] but performing coronary angiography using a radiocontrast dye, before coronary artery bypass grafting (CABG), may result in contrast-induced nephropathy.[7] Therefore, patients undergoing coronary angiography before CABG are at higher risk of AKI.[8] The matter should be considered because of the point that any rise in serum creatinine following CABG is associated with increased mortality and morbidity resulting in prolonged hospital stay and higher costs.[9-13] The best way to decrease the burden of AKI is prevention.[3,14]

Performing no cardiopulmonary bypass that may be achieved in off-pump coronary artery bypass (OPCAB) grafting technique, could be associated with a lower incidence of AKI.[15,16] However, previous studies have shown different results. Available randomized clinical trials are insufficient to detect a difference in AKI requiring RRT after OPCAB; evidence from observational studies suggests a reduction in renal replacement therapy (RRT) requirement.[11] Most studies lack consistency in defining AKI.[3,11] Since, the CABG may be considered as a modifiable risk factor for AKI and the use of OPCAB may result in reduction of postoperative AKI after CABG,[3] this study

***Correspondence:** Esmat Ghanei, MD, Urology and Nephrology Research Center (UNRC), Shahid Beheshti University of Medical Sciences, No.103, Boostan 9th St, Pasdaran Ave., Tehran, Iran. Tel: +98-21-22567222, Fax: +98-21-22567282, e-mail: dr_e_ghanei@yahoo.com
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was conducted to evaluate the impact of the OPCAB technique on the incidence of AKI, and also to determine the major risk factors for AKI.

Material and Methods

In this prospective cohort study, some 535 consecutive adult patients who underwent CABG between January 2007 and May 2010 in a tertiary Hospital and had normal serum creatinine and estimated creatinine clearance values before operation were included. Shaheed Beheshti Ethical Committee approved this study, and the study was conducted in accordance with the declaration of Helsinki. Only patients who completed the informed consent form were included.

Some 64 out of 535 patients were operated through the OPCAB technique and the other 471 patients by the ONCAB technique. All 535 patients were candidates for CABG by either OPCAB or ONCAB technique. One cardiovascular surgeon performed all OPCAB cases, and another surgeon performed all the ONCAB cases. Both surgeons were experienced in CABG through the ONCAB technique, but only one was expert in OPCAB surgery. Patients were randomly assigned to operation by either surgeon, namely the OPCAB or the ONCAB technique. The exclusion criteria were as follows: The patients under 14 and above 90 years old, those who had undergone emergency surgery and the patients with end-stage renal disease receiving hemodialysis before operation. Required clinical and laboratory data were extracted from the patients records. The serum creatinine was measured with a kinetic enzymatic colorimetric assay, before operation (baseline) and then twice a day until discharge.

Postoperative AKI was diagnosed by a serum creatinine of higher than 2 mg/dL or 0.3 mg/dl or more compared with baseline, within 72 hours after operation. Severity of AKI was classified as stage 1 (serum creatinine increase by 50–100% or $\geq$0.3 mg/dL), stage 2 (serum creatinine increase by 101–200%), and stage 3 (serum creatinine increase by >200% and the need for dialysis).[17]

After testing for normal distribution by Kolmogorov-Smirnov test, continuous data were compared by Student's *t*-test or the one-way ANOVA, and categorical data were compared by the Chi-Square or Fisher's Exact test. Potential risk factors associated with AKI after CABG were coded as present or absent and assessed by bivariate analysis. Continuous data were shown as mean±SD.

Results

Age, sex, weight, prevalence of diabetes mellitus, congestive heart failure and chronic kidney disease, and preoperative renal function (as measured by serum creatinine and estimated glomerular filtration rate) were alike in the two groups (Table 1). Moreover, the severity of coronary heart disease did not differ between the two groups (Table 1). The mean preoperative ejection fraction was 45.59±11.15 percent in ONCAB group and 47.34±10.03 in OPCAB group with no significant difference (p>0.05).

In OPCAB group, 9.4% (6 patients) and in ONCAB group, 4.1% (19 patients) developed AKI with no significant difference (p=0.06). Furthermore, the AKI severity was alike in both groups and 10.5% (2 patients) in ONCAB and 33.3% (2 patients) in OPCAB group with mild AKI, 78.9% (15 patients) in ONCAB and 50% (3 patients) in OPCAB group with moderate AKI, and 10.5% (2 patients) in ONCAB

Table 1: Baseline and demographic characteristics of the patients.

Variable	ONCAB (No.=471) No. (%)	OPCAB (No.=64) No. (%)	*P value*
CVP>9 mmHg	155 (32.9)	16 (25)	0.215
Age (Mean±SD)	59.35±10.41	57.56±9.25	0.192
Diabetes mellitus	153 (32.5)	17 (26.6)	0.340
Hypertension	256 (54.4)	31 (48.4)	0.373
Obesity	100 (21.2)	11 (17.2)	0.454
Hyperlipidemia	231 (49)	27 (42.2)	0.303
CVA history	11 (2.3)	---	0.217
MI	121 (25.7)	10 (15.6)	0.709
Smoking	174 (36.9)	26 (40.6)	0.568

*Values were presented as mean±SD. OPCAB=off-pump coronary artery bypass; ONCAB=on-pump coronary artery bypass.

and 16.7% (1 patients) in OPCAB group with severe AKI (p=0.340). The creatinine and glomerular filtration rate (GFR) values were similar in the two groups during the study period (Table 2).

The mean ICU stay was 3.56±2.23 days in ONCAB and 3.08±1.22 days in OPCAB group with no statistically significant difference (p=0.095). The mean hospital stay was 14.9±5.96 days in the ONCAB, and 11.77±4.32 days in the OPCAB group with a statistically significant difference (p<0.001). None of the patients died in OPCAB group, but 10 subjects (2.1%) died in the ONCAB group (p=0.246) None of the patients in OPCAB group and only one subject in ONCAB group required postoperative dialysis (p=1.000). In the OPCAB group, 62.5% (40 patients), and in the ONCAB group, 77.3% (364 patients) had urination within an hour after their operation with a statistically significant difference (p=0.010). Sixteen patients in OPCAB group (25%) and 154 subjects (32.8%) in ONCAB group had a central venous pressure of higher than 9 mmHg (p=0.215). However, the preoperative platelet counts were similar in the two groups (210.19 and 208.73 per microliter in the ONCAB and the OPCAB groups, respectively); the postoperative platelet count differed in the aforesaid groups (165.96 and 198.03 per microliter in ONCAB and OPCAB groups, respectively) (p<0.001).

In bivariate analysis, age, sex, positive history of diabetes, hyperlipidemia, myocardial infarction (MI), family history of MI, smoking, ejection fraction, center venous pressure (CVP), platelet count, and cerebro vascular accident (CVA) history had no impact on AKI developing in none of the groups (p>0.05). The hypertensive patients in OPCAB group developed more AKI (19.4% versus zero) with a significant difference (RR=1.24, [CI 95%]=1.04-1.47, p=0.010), but the AKI severity was not different in the groups (p>0.05). The obese patients had no higher rate of AKI (p>0.05), but the severe AKI cases were more common in the obese patients in the ONCAB group (40% versus zero) with a significant difference (p=0.024). The patients with 3-vessel and 2-vessel involvements, especially those with left main artery disease, had more occurrence of AKI (p<0.05) and also the AKI severity was significantly higher in the ONCAB group with 3-vessel involvement (p<0.05). However, none of these factors showed statistically significant impact on AKI occurrence in multivariate analysis (p>0.05).

Discussion

This study was performed to compare the incidence rate of AKI in patients undergoing coronary artery bypass with ONCAB or OPCAB techniques. This study was conducted in a prospective manner despite vast majority of previous similar studies. We had ONCAB/OPCAB ratio of 467/64 and the number of the patients in the ONCAB group was almost seven times higher than that of the OPCAB group. Nevertheless, the strength of the study was satisfactory.

Our results showed that the OPCAB technique was not protective against AKI in patients undergoing CABG. Besides, it did not affect AKI severity. The only risk factors for AKI in our study were hypertension and the number of the involved coronary vessels in angiography. However, even these two factors were not effective in multivariate analysis. In addition, the mortality rate, and creatinine and GFR values were not significantly different in the two groups in the current study. The only significant difference found between the ONCAB and the OPCAB techniques in our study was for the mean hospital stay that was longer in the ONCAP group. Yet, the mean ICU stay was not different between the two groups.

In the current study, none of the patients in the OPCAB group, and only one subject in the ONCAB group required postoperative dialysis. Ten patients died in this study that all were in the ONCAB group,

Table 2: Baseline and follow up serum creatinine and GFR measurements*

Variable	ONCAB	OPCAB	*P value*
Baseline serum creatinine (mg/dL)	1.1±0.33	1.3±1.15	0.213
Serum creatinine after 72 hours (mg/dL)	1.24±0.47	1.5±1.29	0.125
Serum creatinine at hospital discharge (mg/dL)	1.19±0.38	1.42±1.24	0.152
Baseline GFR (mL/min/1.73 m2)	71.51±24.31	72.3±30.93	0.845
GFR after 72 hours (mL/min/1.73 m2)	67.3±25.46	67.46±31.27	0.963
GFR at hospital discharge (mL/min/1.73 m2)	68.28±23.41	71.53±31.83	0.433

*Values were presented as mean±SD. OPCAB=off-pump coronary artery bypass; ONCAB=on-pump coronary artery bypass.

but no significant difference was observed between the two groups. In a non-congruent manner, the AKI rate and severity were higher in the OPCAB group (two-fold higher) and this matter may be due to inequality and the lack of matching for some confounding factors such as frequency of involved coronary arteries.

In our study the patients with AKI had non-significant higher mortality, but hospital stay was significantly longer among them. This matter shows the importance of AKI prevention in patients under coronary artery bypass procedures. However, this may not be achieved by the use of the OPCAB technique, according to our study. The post-CABG AKI is a multi-factorial entity, therefore, preventive programs should not be focused only on the type of procedure, and perhaps the application of other factors such as prolonging the interval between angiography and CABG is beneficial. Since cell injuries and cellular damages are present in patients with AKI after CABG,[18] it may also be suggested to use cytoprotective agents especially in animal models. Moreover, the use of angiotensin-converting enzyme (ACE) inhibitors has been recommended in some studies with good protective effects.[2] The role of inflammatory processes should be considered too, and the evaluation of anti-inflammatory agents could be helpful.[19]

There are only a few studies with results similar to our findings.[20-22] Maganti *et al*. showed that the OPCAB method is effective in preventing AKI only in men and not in women. Moore *et al*. showed that OPCAB is equally safe in carefully selected high and low-risk patients. Berdat *et al*. also showed similar rate of AKI in patients who had undergone the OPCAB technique, also in those in whom the ONCAB method was used. In addition, vast majority of studies were reported beneficial effects of the OPCAB technique in comparison with the ONCAB method.[15,16,23]

On the whole, this study demonstrated that the OPCAB technique has no additional renoprotective advantages in patients under coronary artery bypass surgery. Thus, further researches for finding other useful protective methods such as free-radical scavengers, anti-inflammatory agents, and the other modalities are recommended to prevent AKI and to reduce its incidence and the subsequent complications.

Conflict of interest: None declared.

References

1 Benedetto U, Luciani R, Goracci M,Capuano F , Refice S, Angeloni E, Roscitano A, Sinatra R. Miniaturized cardiopulmonary bypass and acute kidney injury in coronary artery bypass graft surgery. *Ann Thorac Surg* 2009;**88**:529-35. [19632407]

2 Benedetto U, Sciarretta S, Roscitano A, Fiorani B, Refice S, Angeloni E, Sinatro R. Preoperative Angiotensin-converting enzyme inhibitors and acute kidney injury after coronary artery bypass grafting. *Ann Thorac Surg* 2008;**86**:1160-5. [18805152]

3 Massoudy P, Wagner S, Thielmann M, Herold U, Kottenberg-Assenmacher E, Marggraf G, Kribben A, Philipp T, Jakob H, Herget-Rosenthal S. Coronary artery bypass surgery and acute kidney injury--impact of the off-pump technique. *Nephrol Dial Transplant* 2008;**23**:2853-60. [18388121] [http://dx.doi.org/10.1093/ndt/gfn153]

4 Gu TX, Zhang WF, Xiu ZY, Fang Q, Zhang YH, Wang C. Incidence and risk factors of acute kidney injury post off-pump and on-pump coronary artery bypass grafting. *Zhonghua Xin Xue Guan Bing Za Zhi* 2008;**36**:1092-6. [19134277]

5 Emmiler M, Yaveri A, Koçoğullari CU, Ela Y, Sahin DA, Sivaci RG, Cekirdekci A. Gastrointestinal ischemia related mortality in patients undergoing off- or on-pump coronary artery bypass grafting. *Heart Surg Forum* 2009;**12**:E79-84. [19383592] [http://dx.doi.org/10.1532/HSF98.20081114]

6 Boyle JM, Moualla S, Arrigain S, Worley S, Bakri MH, Starling RC, Heyka R, Thakar CV. Risks and outcomes of acute kidney injury requiring dialysis after cardiac transplantation. *Am J Kidney Dis* 2006;**48**:787-96. [17059998] [http://dx.doi.org/10.1053/j.ajkd.2006.08.002]

7 Kim NY, Kim SY, Lee NH, Kwak YL. Impact of the interval between coronary angiography and off-pump coronary bypass surgery on postoperative renal function. *Korean J Anesthesiol* 2010;**58**:142-7. [20498792] [http://dx.doi.org/10.4097/kjae.2010.58.2.142]

8 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**:1264-71. [17888981] [http://dx.doi.org/10.1016/j.athoracsur.2007.05.016]

9 Puskas JD, Edwards FH, Pappas PA, O'Brien S, Peterson ED, Kilgo P, Ferguson TB Jr. Off-pump techniques benefit men and women and narrow the disparity in mortality after coronary bypass grafting. *Ann Thorac Surg* 2007;**84**:1447-54. [17954045] [http://dx.doi.org/10.1016/j.athoracsur.2007.06.104]

10 Abelha FJ, Botelho M, Fernandes V, Barros H. Determinants of postoperative acute kidney injury. *Crit Care* 2009;**13**:R79. [19463152] [http://dx.doi.org/10.1186/cc7894]

11 Nigwekar SU, Kandula P, Hix JK, Thakar CV. Off-pump coronary artery bypass surgery and acute kidney injury: a meta-analysis of randomized and observational studies. *Am J Kidney Dis* 2009;**54**:413-23. [19406542] [http://dx.doi.org/10.1053/j.ajkd.2009.01.267]

12 Novick RJ, Fox SA, Stitt LW, Kiaii BB, Abu-Khudair W, Lee A, Benmusa A, Swinamer SA, Rayman R, Menkis AH, McKenzie FN, Quantz MA, Boyd WD. Effect of off-pump coronary artery bypass grafting on risk-adjusted and cumulative sum failure outcomes after coronary artery

surgery. *J Card Surg* 2002;**17**:520-8. [12643463] [http://dx.doi.org/10.1046/j.1540-8191.2002.01008.x]

13 Al-Ruzzeh S, George S, Yacoub M, Amrani M. The clinical outcome of off-pump coronary artery bypass surgery in the elderly patients. *Eur J Cardiothorac Surg* 2001;**20**:1152-6. [11717020] [http://dx.doi.org/10.1016/S1010-7940(01)00978-2]

14 Zhang WF, Gu TX, Diao C, Zhang YH, Wang C, Fang Q, Wang HL. Comparison of transient changes in renal function between off-pump and on-pump coronary artery bypass grafting. *Chin Med J (Engl)* 2008;**121**:1537-42. [18982864]

15 Bucerius J, Gummert JF, Walther T, Borger MA, Doll N, Falk V, Mohr FW. Impact of off-pump coronary bypass grafting on the prevalence of adverse perioperative outcome in women undergoing coronary artery bypass grafting surgery. *Ann Thorac Surg* 2005;**79**:807-12. [15734382] [http://dx.doi.org/10.1016/j.athoracsur.2004.06.013]

16 Massoudy P, Wagner S, Thielmann M, Herold U, Kottenberg-Assenmacher E, Marggraf G, Kribben A, Philipp T, Jakob H, Herget-Rosenthal S. Coronary artery bypass surgery and acute kidney injury--impact of the off-pump technique. *Nephrol Dial Transplant* 2008;**23**:2853-6. [18388121] [http://dx.doi.org/10.1093/ndt/gfn153]

17 Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, Levin A; Acute Kidney Injury Network. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. *Crit Care* 2007;**11**:R31. [17331245] [http://dx.doi.org/10.1186/cc5713]

18 Rosner MH, Okusa MD. Acute kidney injury associated with cardiac surgery. *Clin J Am Soc Nephrol* 2006;**1**:19-32. [17699187] [http://dx.doi.org/10.2215/CJN.00240605]

19 Kim DH, Shim JK, Hong SW, Cho KR, Kang SY, Kwak YL. Predictive value of C-reactive protein for major postoperative complications following off-pump coronary artery bypass surgery: prospective and observational trial. *Circ J* 2009;**73**:872-7. [19282606] [http://dx.doi.org/10.1253/circj.CJ-08-1010]

20 Maganti M, Rao V, Cusimano RJ. Sex differences in resource use after on-pump and off-pump coronary artery bypass surgery: a propensity score-matched cohort. *Can J Cardiol* 2009;**25**:e151-6. [19417865] [http://dx.doi.org/10.1016/S0828-282X(09)70498-2]

21 Moore GJ, Pfister A, Trachiotis GD. Outcomes for off-pump coronary artery bypass grafting in high-risk groups: a historical perspective. *Heart Surg Forum* 2005;**8**:E19-22. [15769707] [http://dx.doi.org/10.1532/HSF98.20041148]

22 Berdat PA, Muller K, Schmidli J, Kipfer B, Eckstein F, Carrel T. Total arterial off-pump versus on-pump coronary revascularization: comparison of early outcome. *J Card Surg* 2004;**19**:489-94. [15548179] [http://dx.doi.org/10.1111/j.0886-0440.2004.04104.x]

23 Yu HY, Wu IH, Chen YS, Chi NH, Hsu RB, Tsai CH, Wang SS, Lin FY. Comparison of outcome of off-pump coronary artery bypass surgery and conventional coronary artery bypass surgery. *J Formos Med Assoc* 2003;**102**:556-62. [14569321]