

Impacts of non-dialysis-dependent renal insufficiency on the early surgical outcomes after isolated coronary artery bypass graft surgery

İzole koroner arter baypas greft cerrahisinden sonra diyalize bağımlı olmayan renal yetersizliğin erken cerrahi sonuçlar üzerindeki etkileri

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Background: This study aims to investigate the effects of non-dialysis-dependent renal dysfunction on postoperative mortality and complications assessed by creatinine clearance and serum creatinine.

Methods: Between August 2007 and March 2011, a total of 1,359 consecutive patients (975 females, 384 males; mean age 58.6±10.1 years; range 23 to 87 years) who underwent isolated coronary artery bypass grafting (CABG) surgery in Shariati Hospital, Tehran, Iran were retrospectively analyzed. Patients were classified based on the preoperative creatinine clearance values to group renal (group R; n=21) (<30 mL/min) and group control (group C; n=1338) (≥30 mL/min). Two groups were compared for preoperative characteristics. Effects of preoperative renal insufficiency on post-CABG mortality and morbidity rates were measured using stepwise multivariate logistic regression analyses.

Results: Post-coronary artery bypass grafting surgery renal failure (9.5% vs. 0.4%) and mortality rates (19.0% vs. 3.3%) were higher in group R compared to group C (p<0.001). Renal impairment was an independent predictor for post-CABG surgery renal insufficiency and dialysis (OR=1.05, 95% CI: 1.02-1.07; p=0.001) and early mortality (OR=1.16, 95% CI: 1.07-1.25; p=0.001).

Conclusion: Preoperative non-dialysis-dependent renal insufficiency is the most important risk factor for post-CABG surgery renal failure and mortality. A specific attention is warranted to patients with pre-existing risk factors especially renal impairments.

Key words: Coronary artery bypass graft; mortality; non-dialysis-dependent renal insufficiency.

Amaç: Bu çalışmada kreatinin klirensi ve serum kreatinin ile değerlendirilen diyalize bağımlı olmayan renal yetersizliğin ameliyat sonrası mortalite ve komplikasyonlar üzerindeki etkileri araştırıldı.

Çalışma planı: Ağustos 2007 - Mart 2011 tarihleri arasında İran, Tahran Shariati Hastanesi'nde izole koroner arter baypas greft (KABG) cerrahisi yapılan toplam 1359 ardışık hasta (975 kadın, 384 erkek; ort. yaş 58.6±10.1 yıl; dağılım 23-87 yıl) retrospektif olarak incelendi. Hastalar ameliyat öncesi kreatinin klirensi değerlerine göre renal (R grubu; n=21) (<30 mL/dk.) ve kontrol grubu (K grubu; n=1338) (≥30 mL/dk.) olarak sınıflandırıldı. İki grup ameliyat öncesi özellikler açısından karşılaştırıldı. Ameliyat öncesi renal yetersizliğin KABG sonrası mortalite ve morbidite oranları üzerindeki etkisi, kademeli çok değişkenli lojistik regresyon analizleri kullanılarak incelendi.

Bulgular: Koroner arter baypas greft cerrahisi sonrası renal yetmezlik (%0.4'e kıyasla %9.5) ve mortalite oranı (%3.3'e kıyasla %19.0) grup C'ye kıyasla, grup R'de daha fazlaydı (p<0.001). Renal bozukluk, koroner arter baypas greft cerrahisi sonrası renal yetersizlik ve diyaliz (OR=1.05, %95 CI: 1.02-1.07; p=0.001) ile erken mortalitenin (OR=1.16, %95 CI: 1.07-1.25; p=0.001) bağımsız bir öngördürücüsüdür.

Sonuç: Ameliyat öncesi diyalize bağımlı olmayan renal yetersizlik, KABG cerrahisi sonrası renal yetmezlik ve mortalite için en önemli risk faktörüdür. Özellikle böbrek bozuklukları gibi risk faktörleri taşıyan hastalara özel ihtimam gösterilmelidir.

Anahtar sözcükler: Koroner arter baypas grefti; mortalite; diyalize bağımlı olmayan renal yetersizlik.



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Although the association between preoperative dialysis-dependent renal failure and postoperative mortality after coronary artery bypass grafting (CABG) has been documented,^[1] the impact of non-dialysis-dependent renal insufficiency on the clinical outcomes of CABG patients is still unknown.^[2] However, there are some recent studies that have suggested there is an increased risk of post-CABG mortality and morbidity, events in patients with mild renal insufficiency.^[3-5]

The relationship between mild-to-moderate renal insufficiency and postoperative clinical outcomes after CABG has been assessed in several studies,^[3-10] but until recently,^[9] most only assessed renal function based on the serum creatinine levels and not the glomerular filtration rate (GFR) or calculated creatinine clearance rate (CCr). Renal function tests are indications of the state of the kidneys, and the GFR describes the flow rate of filtered fluid through the kidneys. The CCr signifies the volume of blood plasma that is cleared of creatinine per unit time and is a useful measurement for approximating the GFR. It is important to note that both the calculated CCr or the GFR provide a more accurate estimation of renal function than serum creatinine alone.^[11] In addition, serum creatinine levels are affected by several factors in the body and may not be reliable enough on their own because kidney lesions and decreased glomerular filtration may also be present in individuals with normal serum creatinine values. In the early stages of renal impairment, relatively small changes in serum creatinine concentration may be associated with major changes in glomerular filtration and creatinine clearance. Moreover, most of the existing literatures provide unadjusted outcomes with regard to the effects of mild renal impairment on postoperative outcomes after isolated CABG. In the current study, we conducted multivariate logistic regression analyses using an extensive database containing more than 200 different variables to investigate the effects of non-dialysis-dependent renal dysfunction assessed by both CCr and serum creatinine on postoperative mortality and any associated complications.

PATIENTS AND METHODS

In this retrospective review of an existing data bank of patients with heart diseases, all consecutive cases who underwent isolated CABG in Shariati Hospital, Tehran, Iran between August 2007 and March 2011 were recruited. Patients with additional concomitant procedures such as valve surgery or carotid endarterectomies, those with incomplete data, and those who were also receiving dialysis were excluded. The Cockcroft-Gault formula was used to

estimate the CCr,^[12] and the patients were divided into two groups based on their preoperative CCr, with the renal group (group R) representing those with reduced levels (<30 mL/min) and the control group (group C) signifying those with normal levels (≥30 mL/min).^[13] The two groups were compared with respect to their pre-, peri- and postoperative characteristics such as age, diabetes, hypertension, hypertriglyceridemia, hypercholesterolemia, cerebrovascular disease (CVD), renal function, intraoperative situations, postoperative mortality, and morbidities along with whether or not they had a family history of coronary artery disease (CAD). The study protocol was approved by the ethics committee of the Tehran University of Medical Sciences (TUMS).

Primary and secondary outcomes

Primary outcomes were defined as mortality rate in the first 30 days after surgery; whereas secondary outcomes were defined as morbidities that occurred during hospitalization along with the changes in the serum creatinine levels in the first five postoperative days. Furthermore, infection complications were defined as sternal, deep, or superficial infections, leg infections, or urinary tract infections, and neurological complications consisted of the patients who had suffered a stroke in the first postoperative 72 hours, those who had experienced a transient ischemic attack (TIA), or those who were in a coma. In addition, pulmonary complications included pulmonary embolisms, pneumonia, pleural effusion, and pneumothorax while ventricular arrhythmia included ventricular tachycardia, fibrillation, premature ventricular contraction (PVC), and atrioventricular junctional rhythm (AVJR). Atrial fibrillation, flutter, and paroxysmal atrial tachycardia (PAT) made up the category of supraventricular arrhythmias, and postoperative myocardial infarction (MI) was defined as changes involving increased cardiac enzyme levels or patients with wall motion abnormalities as revealed on postoperative echocardiography.

Intraoperative findings included the average units of packed red blood cells used in transfusion, perfusion time, aortic cross-clamp time (ACCT), mechanical ventilation time, inotropic support, and the proportion of those who underwent on-pump cardiopulmonary bypass (CPB) along with whether or not the patient required an intra-aortic balloon pump (IABP).

Statistical analysis

The results were reported as mean ± standard deviation (SD) for quantitative variables and

percentages for categorical variables, and the groups were compared using Student’s t-test for continuous variables and the chi-square test (or Fisher’s exact test, if required) for categorical variables. Statistical significance was based on two-sided design-based tests evaluated at the 0.05 level of significance.

The potential confounding effects of the risk factors associated with surgical outcomes was first tested using univariate analyses for each dependent variable. When it was statistically significant ($p < 0.2$), the variables were evaluated via stepwise multivariable logistic regression analyses to construct the final model. All of the statistical analyses were performed using the SPSS version 16.0 for Windows (SPSS Inc, Chicago, IL, USA) software program.

RESULTS

Baseline characteristics

A total number of 2,333 patients were initially recruited, but 613 of these were excluded due to valve surgery or surgery for congenital heart disease (CHD), 354 because of incomplete data, and seven because they were under dialysis. In the end, a total number of 1,359 patients (384 males, 975 females; mean age 58.6 ± 10.1 years; range 23 to 87 years) who underwent isolated CABG and were followed up with regard to their postoperative outcomes and complications were included in the study. The patients’ baseline characteristics are summarized

in Table 1. Comparatively, the patients in group R were older and had a higher proportion of smokers. In addition, more patients in group R had hypertension and were class 3 and 4 according to the Canadian Cardiovascular Society (CCS) Angina Grading Scale as compared to group C.

Operative and postoperative outcomes

The comparison of the two groups regarding their operative clinical characteristics are provided in Table 2. A higher proportion of patients in group C underwent on-pump CPB, but the two groups did not differ significantly in the need for inotropic support, IABP, transfused packed red blood cell (PRBC) units, ACCT, perfusion time, or mechanical ventilation time.

The changes in serum creatinine levels are shown in Figure 1. The mortality rate was considerably higher in the patients with lower creatinine clearance compared to the control subjects (19.0% vs. 3.3%; $p < 0.001$). As shown in Table 3, postoperative outcomes were also compared between two studied groups. We found that a higher proportion of the patients in group R developed postoperative renal failure requiring dialysis compared with group C (9.5% vs. 0.4%; $p < 0.001$). Additionally, a univariate analysis determined that a creatinine clearance of < 30 mL/min represented a significant association with renal failure [odds ratio (OR)= 13.3 and 95% confidence intervals (CI)= 1.5-96.5; $p = 0.005$] as well as with the “need for a reoperation due to

Table 1. Patients’ baseline characteristics

Variables	Renal group (n=21)			Control group (n=1,338)			p
	n	%	Mean±SD	n	%	Mean±SD	
Female gender	12	57.1		372	27.8		0.030
Mean age (years)			64.4±11.0			58.6±10.0	0.009
Those over the age of 65	11	52.4		376	28.1		0.014
Smokers	1	2.7		249	18.6		0.101
Addiction to opium	1	2.7		198	14.8		0.192
A family history of CAD	0	0.0		103	7.7		0.186
Previous MI	6	28.6		458	34.2		0.581
CCS angina class 3-4	7	33.3		210	15.7		0.029
NYHA 3-4	7	33.3		309	23.1		0.271
Diabetes mellitus	7	33.3		447	33.4		0.965
Hypertension	17	81.0		643	48.1		0.003
Hypercholesterolemia	11	52.4		616	46.0		0.762
Hypertriglyceridemia	11	52.4		616	46.0		0.722
Creatinine clearance rate (ml/min)			24.5±5.3			73.7±23.6	<0.001
Serum creatinine levels (mg/dl)			2.5±1.3			1.1±0.23	<0.001
Chronic obstructive pulmonary disease	0	0.0		7	0.5		0.739
Cerebrovascular accident	0	0.0		32	2.4		0.473

SD: Standard deviation; CAD: Coronary artery disease; MI: Myocardial infarction; CCS: Canadian Cardiovascular Society; NYHA: New York Heart Association.

Table 2. Patients' operative clinical data

Variables	Renal group (n=21)			Control group (n=1,338)			p
	n	%	Mean±SD	n	%	Mean±SD	
Packed red blood cells transfused			3.2±1.8			2.4±2.1	0.138
Perfusion time (min)			81.9±22.1			81.02±26.1	0.920
Aortic cross-clamp time (min)			33.6±17.4			44.7±32.3	0.330
Mechanical ventilation (min)			170±56			175±61	0.709
Inotropic support	4	19.0		230	17.2		0.823
Intra-aortic balloon pump	3	14.3		91	6.8		0.093
On-pump cardiopulmonary bypass	8	38.1		911	68.1		0.003

SD: Standard deviation.

bleeding” (OR= 4.4 and 95% CI= 1.3-15.4; p=0.012). In the final model based on the stepwise multivariate logistic regression analyses renal impairment was an independent predictor of post-CABG renal failure and dialysis (OR= 1.05 and 95% CI= 1.02-1.07; p=0.001) and the “need for a reoperation due to bleeding” (OR= 1.12 and 95% CI= 1.02-1.20; p=0.008). Furthermore, no significant relationships were detected between the low CCr and the following postoperative complications in either the univariate or multivariate analyses: ventricular (ventricular tachycardia and fibrillation) and supraventricular (atrial fibrillation) arrhythmia, gastrointestinal, pulmonary, neurological, or infection (septicemia, deep sternal infection and leg site infection) complications, postoperative MI, or prolonged ventilation (p>0.05).

Patients of the female gender as well as those who over the age of 65, those with a CCr of <30 mL/min, those categorized as CCS class 3 and 4, and those who underwent on-pump CPB represented independent predictors for early postoperative mortality after CABG in the final model. Furthermore, baseline

renal impairment was the most important predictor of postoperative mortality in the patients who underwent CABG (OR= 1.16). Table 4 shows the final multivariate logistic regression model as it relates to post-CABG mortality as a dependent variable.

DISCUSSION

Preexisting renal insufficiency has been previously proposed as a risk factor for post-CABG renal failure.^[5] Additionally, preoperative renal dysfunction has also been shown to be an independent risk factor for post-CABG mortality,^[3-5] and it is well known that post-CABG renal failure is associated with high surgery-related morbidity and mortality rates.^[5,14-16] The 30-day mortality rate for patients requiring dialysis has been reported to be as high as 63% compared with the corresponding rate of 4.3% among those without renal insufficiency.^[17,18] This remarkable increase played a significant role in the identification of the major predictive factors associated with the development of post-CABG renal failure and subsequent early mortality. Patients with mild renal dysfunction do not require dialysis. Dialysis-dependent renal failure has been linked with poorer clinical outcomes after CABG.^[1] However, it is still not known whether mild renal insufficiency (non-dialysis renal insufficiency) has the same adverse effects on CABG outcomes.

Except recently,^[9] most of the previous investigations have measured serum creatinine levels in order to evaluate renal function.^[3-8] Despite being widely used, these levels alone are not as accurate as the GFR or CCr for determining the presence of chronic kidney disease.^[19] In fact, it has been reported that up to 30% of patients with normal serum creatinine levels (≤1.29 mg/dl) may be in stage 3 of chronic kidney disease and have a reduced GFR.^[9] Therefore, we used the Cockcroft-Gault formula to estimate the CCr in this study,^[12] and the patients were classified into two groups based on their preoperative CCr.

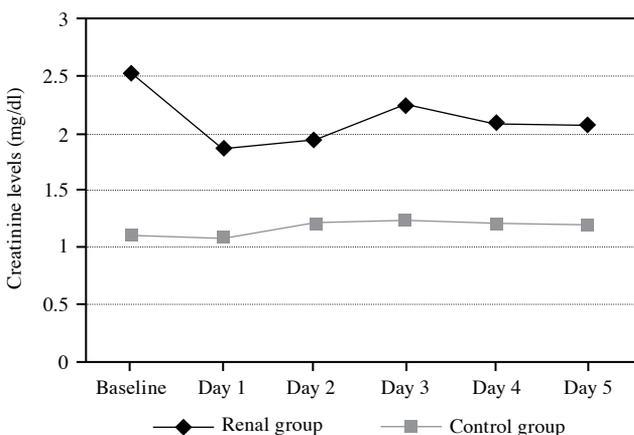


Figure 1. Changes in the creatinine levels in the two groups. In all of the studied times, the differences between the two groups were significant (p<0.05).

Table 3. Comparison of post-coronary artery bypass grafting outcomes

Variables	Renal group (n=21)		Control group (n=1,338)		p
	n	%	n	%	
Mortality	4	19.0	44	3.3	<0.001
Ventricular arrhythmia	6	28.6	247	18.4	0.238
Ventricular tachycardia	0	0.0	24	1.8	0.536
Ventricular fibrillation	0	0.0	16	1.2	0.614
Supraventricular arrhythmia	3	14.3	155	11.6	0.702
Atrial fibrillation	3	14.3	146	10.9	0.673
Postoperative myocardial infarction	0	0.0	4	0.3	0.802
Renal complications	3	14.3	11	0.8	<0.001
Renal failure and dialysis	2	9.5	5	0.4	<0.001
Renal deterioration	1	4.7	6	0.4	0.005
Pulmonary complications	0	0.0	26	1.9	0.519
Neurological complication	0	0.0	31	2.3	0.408
Vascular complications	0	0.0	2	0.1	0.859
Gastrointestinal complications	0	0.0	18	1.3	0.593
Infection complications	0	0.0	13	1.0	0.650
Leg infection	0	0.0	4	0.3	0.809
Deep sternal infection	0	0.0	9	0.7	0.706
Septicemia	0	0.0	3	0.2	0.828
Prolonged mechanical ventilation	1	4.7	38	2.8	0.577
Need for reoperation due to bleeding	3	14.3	49	3.7	0.012

SD: Standard deviation.

Since the patients with preoperative mild renal dysfunction were considerably more likely to develop renal failure after CABG, it was expected that they would have higher post-CABG mortality rates, and we found that the early mortality rate was remarkably higher in those with mild renal dysfunction compared with those with normal renal function (19.0% vs. 3.3%, $p < 0.001$). Moreover, the observed mortality rates in both groups were comparatively higher than those in previous studies.^[5,9] This may be due to the differences in the setting, surgeons and staff, and equipment used in the studies.

In order to treat the effects of the different baseline characteristics and some of the known risk factors, the impact of preoperative mild renal dysfunction on

postoperative mortality was assessed using a stepwise multivariate logistic regression analysis. As revealed in the final model, preoperative renal impairment was the most important predictor of postoperative mortality in the patients who underwent CABG. Consistent with our findings, most recent investigations also have reported that baseline renal dysfunction is a major risk factor for postoperative mortality after CABG.^[3-10] Samuels et al.^[20] found that patients over the age of 70 with chronic renal failure are at a substantial risk for early morbidity and mortality after CABG. Furthermore, the impact of on-pump CPB with regard to the increased risk for mortality and renal failure after CABG has recently been discussed in a various studies involving patients with non-dialysis-dependent

Table 4. Multivariate analysis for predicting early mortality after coronary artery bypass grafting

Variables	OR	(95% CI)	p
Creating clearance <30 ml/min	1.16	(1.07-1.25)	<0.001
Canadian Cardiovascular Society class 3 and 4	1.05	(1.02-1.08)	0.001
Over the age of 65	1.04	(1.01-1.06)	0.002
On-pump cardiopulmonary bypass	1.04	(1.02-1.06)	0.001
Female gender	1.03	(1.01-1.06)	0.003

OR: Odds ratio; CI: Confidence interval.

renal insufficiency.^[8-10,21-24] However, other studies have failed to reach this same conclusion regarding this topic.^[25,26] In addition, other studies agree with our results which concluded that female gender is independent risk factor that is associated with postoperative mortality and complications.^[27-29] Moreover, patients who are referred in the late stages of the disease may require urgent surgery, which could increase the risk of mortality and postoperative renal dysfunction.

In this study a significant association was found between preoperative renal dysfunction and post-CABG renal failure as well as the “need for a reoperation due to bleeding” in both the univariate and multivariate analyses. Hayashida et al.^[5] also found that patients with mild renal insufficiency were more likely to develop postoperative renal failure and bleeding requiring reexploration.

The retrospective nature of our study is one of its limitations as we had to exclude many potential participants. Furthermore, the low number of patients versus the controls in this study may have affected the study power. Another limitation was that referral bias is common in studies like ours that are conducted in tertiary care referral centers. However, we applied the stepwise multivariate logistic regression model to account for the variance in the patients’ baseline characteristics, but there may have been other unknown factors that we did not account for in our study. In addition, we measured the effects of preoperative renal function on all postoperative morbidities in a separate multivariate logistic regression model to also account for the possible referral bias.

Conclusion

Preoperative non-dialysis-dependent renal insufficiency is the most important risk factor affecting postoperative renal failure and mortality. Furthermore, specific attention should be given to patients with major baseline risk factors such as those who are female, those over the age of 65, those categorized as CCS class 3 and 4, and those who will undergo on-pump CPB.

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