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ORIGINAL ARTICLE

EVALUATING THE IMPACT OF RENAL DYSFUNCTION ON POST-OPERATIVE COMPLICATIONS OF CORONARY ARTERY BYPASS GRAFT SURGERY

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ABSTRACT: Increasing prevalence of renal impairment in coronary artery bypass graft surgery (CABG) candidates is an important issue when categorizing patients into different mortality and morbidity risk groups. Renal impairment combined with many other risk factors may predispose patients to poor outcomes after major surgeries such as CABG surgery.In this retrospective study 2700 patients from July 2006 to October 2013 which their basic and follow up information were correctly registered, were recruited. Patients were categorized in three subgroups based on their pre-operative Glomerular Filtration Rate (GFR) level as the predictor of renal function. The association between renal function and post-op adverse outcomes was analyzed. Post-operative adverse outcomes were as follows: sternal wound infection, nosocomial pneumonia, prolonged ventilation, Atrial fibrillation (AF), re-operation for bleeding, stroke, length of hospital stay, post-op mortality and acute kidney injury.Mild renal dysfunction (GFR 60 to 89) was the most prevalent group among CABG surgery candidates (43% of the patients). One unit increase in GFR level was shown to be protective in almost all of the complications. GFR<60 was significantly related to most of the post-operative complications except postoperative stroke and re-operation for bleeding (p value=0.75 and 0.51). GFR<60 was associated with higher mortality rates but the relation was confounded by age in this study (p value=0.089 after adjustment). In our study mild renal dysfunction despite moderate and sever renal dysfunction, was not a strong risk factor for poor outcomes.Mild renal dysfunction in an otherwise healthy patient does not significantly increase post-operative complications, but concomitant HTN, DM and diffuse atherosclerotic disease enhance the risk of morbidity and mortality.

***Keywords*:** Coronary artery bypass graft, renal dysfunction

INTRODUCTION

There is a proved positive correlation between coronary artery disease and renal dysfunction (1). In addition CABG candidates have several features and comorbidities, which are directly or indirectly related to kidney disease such as: old age, Diabetes Mellitus (DM), Hypertension (HTN) and congestive heart failure (2, 3). In past decade the prevalence of patients with renal disease undergoing CABG has increased (4,5). Renal dysfunction, due to definite pathologic pathways, which was interestingly described by McCullough et al (6), predisposes CABG candidates to post-operative complications. Chronic kidney disease is believed to play a remarkable role in long-term post-operative mortality (2). Based on health status data registration, in United States almost 10 to 20% of patients who undergo CABG surgery have creatinine level more than 1.5 mg/dl (3). In this study we wanted to evaluate the outcomes of CABG surgery in patients with renal dysfunction.

MATERIAL AND METHODS

We retrospectively reviewed 2700 patients whom underwent CABG surgery in Imam Khomeini hospital from 2006 to 2013. Patients were categorized in three groups based on GFR, which was considered a reliable marker for renal dysfunction in literature. GFR was calculated with Cockcroft-Gault equation. According to published guidelines we can define renal function as 5 GFR subgroups: normal (GFR≥90 ml/min per 1.73 m2), mild dysfunction (GFR 60 to 90 ml/min per 1.73 m2), moderate (GFR 30 to 59 ml/min per 1.73 m2), sever dysfunction (GFR<30 ml/min per 1.73 m2) (7). For practical usage of this study and better triage and preoperative case selection we

categorized our patients in 3 subgroups: Group 1:GFR≥90 ml/min per 1.73 m2, Group 2: GFR 60 to 89 ml/min per 1.73 m2 and Group 3: GFR<60. We excluded patients with ESRD and also patients on dialysis.

In this study we treated GFR as both continuous and categorical variable. Other comorbidities (known as preoperative) were also included in multivariate regression to adjust the effect of GFR on each post-operative complication. Post-operative complications were: sternal wound infection, nosocomial pneumonia, prolonged ventilation, Atrial fibrillation (AF), operation for re-bleeding, stroke, length of hospital stay, post-op mortality and acute kidney injury. Prolonged ventilation was defined as more than 24 hours, and acute kidney injury as 50% increase in serum creatinine (compared to pre- and post-operative lab results). We also considered the length of stay in hospital a kind of post-operative outcomes and categorized it in two groups (<14 vs. ≥14).

STATISTICAL ANALYSIS

Values are given as mean± SD. Independent sample T-test was used to compare means of quantitative variable. Uni-variate and multivariate analysis in binary logistic regression was also used to define the relation between predictors and outcome in terms of Odds ratio and confidence interval. Analysis was performed in SPSS 11.5 for windows (SPSS Inc., Chicago, IL).

RESULTS

This study population consisted of 30% female patients which 15% had normal renal function (GFR≥90). Prevalence of normal kidney function among male patients was 26%. Overall prevalence of normal kidney function among CABG candidates was 22.6%. Age difference in GFR subgroups was significant (p value<0.001) which, was 51 (in normal function), 58(in 60≤GFR<90) and 66 years old (in GFR<60). Basic and demographic features of patients were shown in Table (1). In all analysis in this article GFR>90 was the reference group and the results (odds ratio and p value) are based on this assumption. Uni-variate analysis with binary logistic regression was done, Table (2). GFR<60 was significantly related to most of the post-operative complications except postoperative stroke and re-operation for bleeding (p value=0.75 and 0.51). When assessing GFR as a quantitative predictor (which better describes the value of 1 unit increase in GFR) it was associated with outcomes except for post-operative stroke and re-operation for bleeding. Mild renal dysfunction was associated with post-operative acute kidney injury, p-value<0.05, OR=2.17(1.63-2.89). Length of stay in hospital after CABG surgery was analyzed and reported, 2.5% of Group1 patients were hospitalized more than 14 days, this was 2.7% and 8.4% for group 2 and 3 respectively. In multivariate logistic regression (GFR and other major preoperative factors) Table 3, in order to find the pure effect of GFR on post-operative outcomes we adjusted for major pre-operative factors (gender, HTN, age, gender and left ventricular ejection fraction). GFR<60 was related to prolonged ventilation after adjustment for gender, HTN, DM, EF<40% but relation was not significant when adjusting for age. The result of adjustment for major risk factors on GFR<60 and pneumonia was similar to non-adjusted analysis.

As shown in Table 3, the relation between GFR<60 and also 60≤GFR<90 before surgery and probability of acute kidney injury was not confounded by major risk factors as it was significant in both analysis.

Mortality was associated to lower GFR in uni-variate analysis, however after adjusting for age this relation was not significant which means the association was confounded by age. Mortality rate is higher in older age not just due to lower renal function in this subgroup. Age was a confounding factor in many associations between GFR and post-operative complications such as, prolonged ventilation, pneumonia, AF, sternal infection and mortality.

Table 1. Basic demographic and health status of patients (n=2574)

	GFR groups		
Preoperative variables	**GFR≥90 (n=624, 22.7%)**	**60≤GFR<90 (n=1176, 42.7%)**	**GFR<60 (n=954, 34.6%)**
Age (years±SD)	51.3±8.2	58.5±9.1	66.4±9
Female gender (%)	19.9	29.9	36.7
Diabetes mellitus (%)	33.3	32.5	32.5
Smokers (%)	39.7	35.9	31
Hyperlipidemia (%)	30.2	31.6	33.5
Hypertension (%)	38.1	41.8	52.8
Previous stroke (%)	1.7	1.5	5.8
Previous MI (%)	18.9	21.1	18.7
LVEF<40 (%)*	31.7	35.4	39.2
BMI (±SD)**	29.8±4.5	26.7±3.6	25.4±4
GFR (±SD)	112.3±21.6	73.5±8.6	45.3±11.7
Mean CPB* time (±SD)**	96±18	98±21	113±28

*Left Ventricular Ejection Fraction **Body mass index ***cardiopulmonary bypass time

Table 2. Univariate analysis. Association of renal dysfunction and post-op complications (n=2754)

Post-operative complications	**P-value in univariate analysis**	**Odds ratio(95% confidence interval)**
Prolonged ventilation		
90≤GFR		1
60≤GFR<90	0.68	1.17(0.55-2.48)
GFR<60	0.001	3.25(1.68-6.47)
GFR	<0.001	0.97(0.96-0.98)
Pneumonia		
90≤GFR		1
60≤GFR<90	0.27	1.86(0.61-5.69)
GFR<60	0.01	4(1.38-11.58)
GFR	0.001	0.97(0.96-0.99)
Atrial fibrillation		
90≤GFR		1
60≤GFR<90	0.76	0.92(0.55-1.54)
GFR<60	0.025	1.73(1.07-2.81)
GFR	0.046	0.99(0.98-1)
Sternal infection		
90≤GFR		1
60≤GFR<90	0.34	2.13(0.45-10.06)
GFR<60	0.04	4.63(1.04-20.45)

GFR	0.008	0.97(0.96-0.99)
Stroke		
90≤GFR		1
60≤GFR<90	0.38	0.66(0.25-1.68)
GFR<60	0.75	1.14(0.47-2.78)
GFR	0.57	0.99(0.98-1.009)
Reoperation for bleeding		
90≤GFR		1
60≤GFR<90	0.37	1.23(0.77-1.98)
GFR<60	0.051	1.59(0.99-2.5)
GFR	0.072	0.99(0.98-1.001)
mortality		
90≤GFR		1
60≤GFR<90	0.67	1.19(0.51-2.76)
GFR<60	0.002	3.37(1.56-7.24)
GFR	<0.001	0.97(0.96-0.98)
PLOS*		
90≤GFR		1
60≤GFR<90	0.63	0.85(0.45-1.61)
GFR<60	<0.001	3.38(1.95-5.85)
GFR	<0.001	0.98(0.97-0.99)
AKI**		
90≤GFR		1
60≤GFR<90	<0.001	2.17(1.63-2.89)
GFR<60	<0.001	4.76(3.28-6.9)
GFR	<0.001	0.977(0.973-0.981)

* Prolonged Length of Stay(>14 days) **Acute Kidney Injury

Table 3. Multivariate analysis. Adjustment of renal dysfunction major factors (n=2754)

Comorbidities / Preoperative complications	**Age**	**Gender**	**Hypertension**	**Diabetes mellitus**	**LVEF***
Prolonged ventilation					
90≤GFR					
60≤GFR<90	OR:1	OR:1	OR:1	OR:1	OR:1
GFR<60	0.88	0.88	0.75	0.67	0.74
	0.067	0.004(OR:2.76, CI:1.38-5.54)	0.003(OR:2.84, CI:1.42-5.69)	0.001(OR:3.27, CI:1.64-6.51)	0.001(OR:3.08, CI:1.54-6.14)
Pneumonia					
90≤GFR	OR:1	OR:1	OR:1	OR:1	OR:1
60≤GFR<90	0.32	0.35	0.30	0.26	0.32
GFR<60	0.033(OR:3.62, CI:1.11-11.83)	0.025(OR:3.41, CI:1.17-9.96)	0.022(OR:3.46, CI:1.19-10.08)	0.01(OR:4.07, CI:1.4-11.83)	0.019(OR:3.5, CI:1.23-10.4)
Atrial fibrillation					
90≤GFR	OR:1	OR:1	OR:1	OR:1	OR:1
60≤GFR<90	0.12	0.90	0.76	0.75	0.70
GFR<60	0.64	0.011(OR:1.88, CI:1.15-3.06)	0.026(OR:1.73, CI:1.06-2.81)	0.026(OR:1.73, CI:1.06-2.8)	0.037(OR:1.67, CI:1.03-2.71)
Sternal infection					

90≤GFR	OR:1	OR:1	OR:1	OR:1	OR:1
60≤GFR<90	0.38	0.31	0.34	0.34	0.35
GFR<60	0.091	0.036(OR:4.92, CI:1.10-21.87)	0.045(OR:4.57, CI:1.03-20.29)	0.044(OR:4.61, CI:1.04-20.36)	0.051
mortality					
90≤GFR	OR:1	OR:1	OR:1	OR:1	OR:1
60≤GFR<90	0.92	0.94	0.72	0.65	0.78
GFR<60	0.089	0.013(OR:2.68, CI:1.23-5.82)	0.005(OR:3.01, CI:1.39-6.50)	0.002(OR:3.44, CI:1.59-7.43)	0.005(OR:3.04, CI:1.41-6.56)
PLOS*					
90≤GFR	OR:1	OR:1	OR:1	OR:1	OR:1
60≤GFR<90	0.21	0.50	0.57	0.65	0.51
GFR<60	0.035(OR:1.98, CI:1.04-3.75)	0.000(OR:3.06, CI:1.76-5.33)	0.000(OR:3.03, CI:1.74-5.26)	0.000(OR:3.43, CI:1.98-5.96)	0.000(OR:3.09, CI:1.78-5.36)
ARF**					
90≤GFR	OR:1	OR:1	OR:1	OR:1	OR:1
60≤GFR<90	0.000(OR:3.49, CI:2.54-4.18)	0.000(OR:2.18, CI:1.64-2.91)	0.000(OR:2.21, CI:1.66-2.94)	0.000(OR:2.17, CI:1.63-2.89)	0.000(OR:2.19, CI:1.64-2.91)
GFR<60	0.000(OR:12.23, CI:7.76-19.27)	0.000(OR:4.80, CI:3.30-6.98)	0.000(OR:5.06, CI:3.48-7.36)	0.000(OR:4.76, CI:3.28-6.90)	0.000(OR:4.82, CI:3.32-6.99)

DISCUSSION

The frequency of renal dysfunction (measured by GFR) in our CABG- candidates was 77%, which was almost similar to previous study by William et al (7). The prevalence of DM, HTN and atherosclerosis disease which all are related to renal impairment is also increasing (8). The explanation for devastating outcomes of CABG surgery in moderate and sever renal dysfunction, which were truly proved in our study were as follows: concomitant comorbidities along with kidney disease and an unknown pathophysiology in accelerated atherosclerosis in these patients (6).

Outcomes of CABG surgery as in other major surgeries are correlated to the pre-operative health status of the patients. Renal impairment is one of the most important major preoperative risk factors (9). Patients with renal disease are at higher risk for three vessel disease which affects the post-operative outcomes (10). In addition renal disease is not an isolated entity and is combined with other concomitant comorbidities such as HTN, DM and old age.

In this study the impact of mild renal dysfunction on post-operative adverse outcomes was not significantly higher than patients with normal kidney. In previous study by William A. et al (7) the odds ratio of the relation was just a little above one (in mild renal dysfunction and post-op complications). May be in their larger sample size the relation was significant.

In this study and several previous studies moderate and sever renal dysfunction, GFR<60, was strongly related to outcomes even after adjusting for other major risk factors (2, 3, 7, 11)

Renal function should be estimated before major surgeries and perioperative cares have to be done to improve renal function (12). Although plasma creatinine is a specific predictor for renal insufficiency its relation to non-renal factors makes it insensitive (13), GFR is considered to be a better marker for renal impairment since it encompass major important features of the patients (gender and age besides creatinine level) (14).

CONCLUSION

Precise case selection before major surgeries is an important concept in this field. Patients with combined risk factors are more likely to have worse outcomes. Renal dysfunction is a powerful multivariable predictor of post CABG adverse outcome. Mild renal dysfunction in an otherwise healthy patient does not significantly increase post-operative complications, but concomitant HTN, DM and diffuse atherosclerotic disease enhance the risk of morbidity and mortality.

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CONFLICT OF INTEREST

There is no conflict of interest in this study.

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