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Original Article

Impact of Chronic Kidney Disease on Short Term Clinical Outcomes of Patients Undergoing Coronary Revascularization

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Abstract

Background: When compared with medical treatment, coronary revascularization is an effective tool to restore cardiac functions in patients suffering from chronic kidney disease but at times it is associated with poor clinical outcome. This study was done to determine the short term clinical outcome in chronic kidney disease patients undergoing coronary revascularization i.e coronary artery bypass graft or percutaneous coronary intervention.
Study type, settings and duration: Cross sectional study, conducted at coronary revascularization center of Aga Khan University Hospital, Karachi between January 2012 and August 2013.
Patients and Methods: All chronic kidney disease patients were enrolled and grouped into mild, moderate and severe kidney disease cases according to creatinine clearance estimated by the Cockroft-Gault equation. The primary outcome was in-hospital major adverse cardiac cerebral events, including myocardial infarction, stroke, and death.
Results: A total of 159 patients were included in the study (122 males and 37 females) whose mean age was 65±9.6 years. Based on the creatinine clearance, 59 cases had severe, 79 moderate and 21 mild chronic kidney disease. Before revascularization, 20 patients with severe, 3 patients with moderate and 2 patients with mild kidney disease were on long term hemodialysis. In the moderate to severe group, 79 patients underwent percutaneous coronary intervention whereas, in the mild group, 15 patients underwent coronary artery bypass graft. Though the rate of failed PCI (uncrossable total occlusions of coronary artery) was similar among the 3 groups but complete revascularization was more evident 18 (85.7% and 60 (75.9%) in mild to moderate cases respectively. During hospitalization, 9 (15.3%) patients died in severe cases out of whom 2 (3.4%) died due to cardiogenic cause and 7 (11.9%) died due to non-cardiogenic causes. Mortality in moderate group was similar 9 (11.4%) and among them, 2 patients died due to cardiogenic cause and rest due to non-cardiogenic cause but none died in mild group.
Conclusion: Though all 3 groups of chronic kidney disease patients had similar clinical and angiographic findings but poor clinical outcome was noted in patients having moderate to severe chronic kidney disease irrespective of whether they underwent PCI or CABG.
Key words: Chronic kidney disease, creatinine clearance, coronary revascularization, percutaneous coronary intervention, coronary artery bypass graft.

Introduction

The incidence of both early stages of chronic kidney disease (CKD) and end stage renal disease (ESRD) is escalating worldwide, in part due to increasing diabetes mellitus and hypertension. The prevalence of CKD has accounted for about 10% of the global population[1-2]. According to the United States Renal Data System (USRDS), at the current growth rate, the number of patients with ESRD will increase to 534,000 by the year 2020[3]. With the beginning of renal replacement therapy (RRT), more than 12% patients will develop acute myocardial infarction (AMI), more than 60% will have a diagnosis of congestive heart failure (CHF), within 18-24 months and by 3 years 38% will die suddenly presumably due to cardio vascular causes[3]. CKD is considered to be an independent risk factor for coronary artery disease (CAD)[4]. As glomerular filtration rate (GFR) declines, the frequency and severity of obstructive CAD increases[5-6]. The increased risk occurs even when renal insufficiency is mild; with a doubling of mortality at 1 year[7]. Several observational studies have found higher frequency of various CAD risk factors among CKD patients as

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opposed to patients with normal kidney function[8]. CKD patients with CAD have multi-vessel coronary disease, calcified coronary vessels and higher mortality and morbidity than those with normal kidney function[9]. To reduce cardiac mortality and improve prognosis in patients with CAD and concomitant CKD, coronary revascularization is considered to be an effective strategy than medical treatment alone[10-13]. Similarly, the incidence of CKD in developing countries like Pakistan is increasing, in a study done in Karachi which harbors 9% of the total population of Pakistan, 25.3% of adults had some degree of renal impairment and 5% had moderate CKD (GFR <60ml/min)[14]. However, to the best our knowledge, there is paucity of data on CAD and concomitant CKD and impact of CKD on clinical outcomes in patients undergoing coronary revascularization The aim of the present study is to determine the in-hospital major adverse cardiac cerebral events (MACCE) in patients with mild, moderate and severe CKD following percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) and evaluate the clinical and angiographic characteristics among these CKD groups.

Patients and Methods

In this cross sectional study, all patients with chronic kidney disease who underwent coronary revascularization at Aga Khan University Hospital Karachi, between January 2012 and August 2013, were included in the analysis. The mode of revascularization included percutaneous coronary intervention (PCI) using stents (excluding Balloon Angioplasty) or Coronary Bypass Graft (CABG). Patients were excluded, if they had severe anemia or liver disease.

All patients had serum creatinine measured 24-48 hours before the revascularization. Renal functions were assessed by the creatinine clearance estimated using the Cockcroft-Gault formula[15] and based on creatinine clearance, were stratified into three groups i.e. severe (<30ml/min), moderate (30-59ml/min) and mild CKD (60-89ml/min). Baseline demographics, clinical and angiographic features were recorded. All patients were observed after the procedure while in the hospital for any adverse clinical outcomes like hospital major adverse cardiac cerebral events (MACCE) including all-cause death, new onset myocardial infarction, and stroke. Within 7 days of revascularization, myocardial infarction (MI) was defined by appearance of new abnormal Q-wave (according to Minnesota Code[16] plus a ratio of serum creatinine kinase MB (CK-MB) iso- enzyme to total cardiac enzyme >0.1 or a Creatinine kinase MB elevated at least 3-fold the upper limit of the normal. After 7 days of the revascularization, abnormal Q-waves or enzymatic changes were enough to diagnose MI[17-18]. Stable angina was defined according to Canadian Cardiovascular Society (CCS)[19]. Unstable angina was defined according to the Braunwald classification[20]. The number of diseased coronary vessels was defined as number of coronary arteries with luminal diameter narrowing ≥70% and the left main coronary artery stenosis ≥50% was considered to be 3-vessel coronary artery disease (3V-CAD). Left anterior descending (LAD) proximal lesion was defined as stenosis ≥70% in the proximal half of the LAD. Long lesion was defined as stenosis > 20mm. Osteal lesion was defined as stenosis within 3mm of the origin of the vessel. Complete revascularization was defined if there was no remaining stenosis ≥70% in the coronary artery luminal diameter ≥ 2mm. Failed PCI is defined as uncrossable total occlusions of coronary artery.

Data was analysed using the Statistical package for social science SPSS (19.0). Descriptive analysis was performed for demographic and clinical characteristics while participants with CKD treated with CABG and PCI with stenting were assessed by using the Chi-square or Fisher exact test. For continuous variables, Independent t-test was used to assess the difference of means. In univariate analysis, compare the association of PCI with clinical outcomes and other covariates. Logistic regression analysis was performed to assess factors that predict favorable outcome. Comparisons among groups were made by pearson chi-square test for categorical variables and ANOVA test for variance for continuous variables. All p-values were two sided and considered as statistically significant if < 0.05. This study was reviewed and approved by the institutional ethical review committee of Aga Khan University Hospital.

Results

A total of 159 patients with chronic kidney disease underwent coronary revascularization (85 PCI and 74 CABG). There were 122 males and 37 females with a mean age of 65±9.6 years. Based on the creatinine clearance, 59 cases had severe CKD followed by 79 with moderate and 21 with mild CKD. As shown in Table-1, patients having moderate to severe chronic kidney disease were older, had lower hemoglobin level, had history of ischemic stroke, and more had STEMI when compared with those having mild CKD. Almost one third of patients (34%) with severe CKD were on long term hemodialysis before the revascularization compared to only 2 and 3 patients with mild and moderate disease respectively were on long term hemodialysis. Other conditions like hypertension, diabetes mellitus, hemorrhagic stroke, valvular heart disease, prior MI, prior revascularization, Left ventricular ejection fraction (LVEF<40%) and indications for revascularization were not significantly different among the 3 groups except ST-elevation myocardial infarction (STEMI) (Table-1).

Table 1: Demographic characteristics of CKD groups. creatinine clearance (ml/min)

	Severe CKD Cases (<30) (n=59)	*Moderate CKD Cases (30-59) (n=79)*	*Mild CKD Cases (60-89) (n=21)*	*p value*
Age, years	68.46 ± 9.41	65.29 ± 9.32	58.29 ± 8.14	<0.001
Male	43 (72.9%)	61 (77.2%)	18 (85.7%)	0.48
Female	16 (27.1%)	18 (22.8%)	3 (14.3%)	
Hemoglobin	10.70 ± 1.35	12 ± 1.75	12.65 ± 1.80	<0.001
WBC	11.76 ± 6.20	11 ± 4.76	10 ± 2.34	0.32
Current smoking history	5 (8.5%)	9 (11.4%)	4(19%)	0.42
Hypertension	55(93.2%)	69 (87.3%)	20(95.2%)	0.37
Diabetes melitus	43(72.9%)	50 (63.3%)	15 (71.4%)	0.45
History of ischemic stroke	11(18.6)	4(5.1)	1 (4.8)	0.04
History of hemorrhagic stroke	0	1	0	
Valvular heart disease	11 (18.6%)	20 (25.3%)	3 (14.3%)	0.44
Prior MI	27 (45.8%)	26 (32.9%)	6 (28.6%)	0.20
Prior kidney disease	58 (98.3%)	79 (100%)	20 (95.2%)	0.20
On dialysis	20 (33.9%)	3 (3.8%)	2 (9.5%)	<0.001
Without dialysis	38 (64.4%)	76 (96.2%)	20 (95.2%)	<0.001
Peripheral vascular	0	1	0	
Prior revascularization	20 (33.9%)	18 (22.8%)	2 (9.5%)	0.06
LVEF <40%	30 (51.7%)	37 (46.8%)	10 (47.6%)	0.84
Indications for revascularization				
Stable angina	6 (10.2%)	20 (25.3%)	5 (23.8%)	0.07
Unstable angina	9 (15.3%)	15 (19%)	3 (14.3%)	0.79
NSTEMI	27 (45.8%)	30 (38%)	12 (57.1%)	0.26
STEMI	18 (30.5%)	15 (19%)	1 (4.8%)	0.03

CKD, chronic kidney disease; CrCl, creatinine clearance; WBC, white cell count; MI, myocardial infarction; LVEF, left ventricular ejection fraction; NSTMI, non-ST-elevation MI; STEMI, ST-elevation MI.

Table 2: Angiographic and Procedural Characteristics of CKD groups. CrCl (ml/min)

	Severe CKD Cases (<30) (n=59)	*Moderate CKD Cases (30-59) (n=79)*	*Mild CKD Cases (60-89) (n=21)*	*p value*
No.of disease vessels	2.20 ± 0.80	2.51 ± 0.69	2.52 ± 0.68	0.03
Multivessel disease	45 (76.3%)	69 (88.5%)	19 (90.5%)	0.10
LM lesion	12 (20.3%)	18 (23.1%)	4 (19%)	0.88
LAD proximal lesion	26 (44.1%)	36 (46.2%)	10 (47.6%)	0.95
Ostial lesion	19 (32.2%)	25 (32.1%)	6 (28.6%)	0.94
CTO	20 (33.9%)	26 (33.3%)	7 (33.3%)	0.99
ISR	8 (13.6%)	4 (5.1%)	0	0.06
Long lesion	19 (32.2%)	35 (44.9%)	8 (38.1%)	0.32
Complex lesion	15 (25.4%)	15 (19.2%)	3 (14.3%)	0.49
PCI	51 (86.4%)	28 (35.4%)	6 (28.6%)	<0.001
CABG	8 (13.6%)	51 (64.6%)	15 (71.4%)	<0.001
Complete revascularization	30 (50.8%)	60 (75.9%)	18 (85.7%)	0.001
Failed PCI	1(1.7)	3(3.8)	0	0.54

LM, left main; LAD,left anterior descending; CTO, chronic total occlusion; ISR, in-stent restenosis; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft

All 3 groups of CKD had multivessel coronary artery disease with almost similar evidence of left main lesion, LAD proximal lesion, osteal lesion, chronic total occlusion, in-stent restenosis, long lesion or complex lesion. In the moderate to severe groups, 79 patients underwent PCI whereas, in the mild CKD group, 15 patients underwent CABG. Though the rate of failed PCI (uncrossable total occlusions of coronary artery) was similar among the 3 groups of kidney disease patients but complete revascularization was more evident in patients having mild to moderate disease (Table-2).

During hospitalization, mortality was seen in 9 severe CKD cases, out of whom 2 died due to cardiogenic cause and 7 died due to non-cardiogenic death. Mortality was seen in 8 moderate CKD cases, out of whom 2 died due to cardiogenic cause and rest died due to non-cardiogenic cause. However, one patient in mild CKD cases died due to cardiogenic cause. Stroke was only seen in 3 moderate CKD cases. The frequency of new onset MI in moderate to severe CKD groups was almost similar 10 (16.9%) and 6 (7.6%) respectively. Only one patient in mild CKD group suffered from new

Table 3: Characteristics of patients with CKD after PCI and CABG.

	Total (n=159)	*PCI (n=85)*	*CABG (n=74)*	*p value*
Age (years)		67±9	63±9	0.003
Male	122 (76.7%)	63 (74.1%)	59 (79.7%)	0.45
Female	37 (23.3%)	22(25.9%)	15 (20.3%)	
Hemoglobin	11.5 ± 1.76	11.4 ± 1.8	11.6 ± 1.6	0.66
WBC	11.1 ± 5.1	12.4 ± 6.2	9.5 ± 2.8	<0.001
Baseline creainine(mg/dl)	2.3 ± 1.5	2.7 ± 1.7	1.7 ± 0.9	<0.001
Creatinine on admission(mg/dl)	2.6 ± 2.0	3.4 ± 2.3	1.8 ± 1.04	<0.001
Creatinine Clearance (ml/min)				
<30	59 (37.1%)	51 (60%)	8 (10.8%)	<0.001
30-59	79 (49.7%)	28 (32.9%)	51 (68.9%)	
60-89	21 (13.2%)	6 (7.1%)	15 (20.3%)	
Current smoking history	159 (100%)	5 (5.9%)	13(17.6%	0.02
Hypertension	144 (90.6%)	77 (90.6%)	67(90.5%)	0.99
Diabetes mellitus	108 (67.9%)	60 (70.6%)	48(64.9%)	0.99
History of ischemic stroke	16 (10.1%)	11 (12.9%)	5(6.8%)	0.27
History of hemorrhagic stroke	1 (0.6%)	0 (0.0%)	1(1.4%)	0.36
Valvular heart disease	34 (21.4%)	19 (22.4%)	15(20.3%)	0.84
Prior MI	59 (37.1%)	36 (42.4%)	23(31.1%)	0.18
Prior kidney disease	157 (98.7%)	85 (100%)	72(97.3%)	0.21
with dialysis	25 (15.7%)	21 (24.7%)	4(5.4%)	0.001
without dialysis	134 (84.3%)	64 (75.3%)	70(94.6%)	0.001
Peripheral vascular disease	1 (1.2%)	1 (1.2%)	0(.0%)	0.99
Prior revascularization	40 (25.2%)	31 (36.5%)	9(12.2%)	<0.001
LVEF <40%	77 (48.4%)	41 (48.2%)	36(49.3%)	0.99
Indications for revascularization				
Stable angina	31 (19.5%)	5 (5.9%)	26(35.1%)	<0.001
Unstable angina	27 (17%)	10 (11.8%)	17(23%)	0.08
NSTEMI	69 (43.4%)	44 (51.8%)	25(33.8%)	0.02
STEMI	34 (21.4%)	26 (30.6%)	8(10.8%)	0.003
Number of diseased vessels				
1	25 (15.7%)	23 (27.1%)	2(2.7%)	<0.001
2	45 (28.3%)	28 (32.9%)	17(23.3%)	<0.001
3	88 (55.3%)	34 (40%)	54(74%)	<0.001
Length of stay(days)	7.8 ± 6.8	5.4 ± 3.9	10.6 ± 6.9	<0.001

MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; other abbreviations see Table-1.

onset MI and MACCE and died due to cardiogenic cause. Twelve (14.1%) patients in the moderate to severe CKD group underwent hemodialysis and continuous renal replacement therapy (CRRT) after coronary revascularization and all of them belonged to the PCI group. The characteristics of patients with CKD were also analyzed according to the mode of revascularization (PCI and CABG) (Table-3). A total of 85 patients underwent PCI and 74 patients underwent CABG. The baseline creatinine (2.7±1.7) and creatinine on admission (1.8±1.04) were significantly higher in the PCI group as compared to CABG group, (3.4±2.3 and 1.7±0.9 respectively). The type of revascularization among moderate to severe CKD groups was PCI while it was CABG in mild to moderate group. More patients with stable angina underwent CABG. PCI was the choice of revascularization in STEMI and NSTEMI. PCI was the choice for single or double vessel coronary disease and CABG for three vessel coronary disease. In-hospital stay was 5.4±3.9 for PCI and 10.6±6.9 days in CABG group. Table-4 shows that age, STEMI, NSTEMI, prior revascularization, complete revascularization and number of coronary artery disease predicted PCI as treatment strategy in patients with moderate to severe CKD.

Table 4: Multivariate analysis of factors predicting PCI among CKD patients.

	OR (95% CI)	*p value*
Age	1.06 (1.001-1.14)	0.04
NSTEMI	18 (3.22-100)	0.001
STEMI	8.54 (1.46-50)	0.01
Prior revascularization	21 (3.59-119.2)	0.001
Complete revascularization	0.004 (0-0.04)	<0.001
Number of disease vessels		
2	0.03(0.005-0.25)	0.001
3	0.005 (0.001-0.04)	<0.001

OR, odds ratio; CI, confidence interval; other abbreviations see Table-1.

Discussion

The primary finding of this study is that patients with moderate to severe CKD had similar rates of MI,

stroke and cardiogenic and non-cardiogenic death as compared to patients with mild CKD. It has clearly been determined that cardiovascular events are 3.5-100 folds greater in dialysis-dependent patients than in the general population[21]. It has also been determined in the previous studies that mild renal insufficiency has been associated with worse clinical outcomes as compared to patients with normal kidney function in patients undergoing PCI or CABG. Zhang Q et al[22] reported that the risk of in-hospital death and cardiogenic death were both 2.3-fold greater in mild renal insufficiency group as compared to the normal renal function group and similarly the risk of new-onset MI was 5-fold greater in mild renal insufficiency group[22]. In current study, there was one patient who sustained new onset MI in the mild CKD group. Though in this study there was no group with normal creatinine to compare with mild CKD group. It reminds us that patients with mild CKD can have worse clinical outcome. Our study is consistent with previous studies in coronary angiographic findings[6]. Our patients with CKD had multivessel, complex and chronically occluded anatomy. With regard to the mode of coronary revascularization in our study, more patients with moderate to severe CKD underwent PCI and more patients with mild to moderate CKD underwent CABG. In both these categories, clinical outcomes were similar. Similar findings were presented in the study done by Ix JH et al in which they had shown that participants with mild to moderate CKD undergoing coronary revascularization had similar rates of MI, stroke, or death whether they underwent PCI with multivessel stenting or CABG[23].

The observational studies done in the past showed conflicting results about the implications of CKD on clinical outcomes after coronary revascularization. Szczech et al found the adjusted estimated 2-year survival to be 51.9% after PCI and 77.4% after CABG in patients with renal insufficiency[24]. In the study in which there was greater utilization of stents in PCI patients, Reddan et al found a survival advantage with CABG compared with PCI which appeared to increase as renal function declined[25]. In contrast to these studies, PCI provided survival benefit in comparison to medical management in patients with mild to moderate renal insufficiency.[25] Nevertheless, Rubenstein et al found more promising short- and long-term outcomes using advances in interventional cardiology such as stents and debulking devices[26]. In retrospective analysis of 1,654 patients with a glomerular filtration rate of <60ml/min revealed that PCI yielded better results than medical therapy and CABG in renal insufficiency patients with acute coronary syndromes[27]. In more recent meta-analysis done by Chen YY et al[28], it was found that CABG had higher short-term mortality but a lower risk of long-term all-cause mortality, cardiac mortality, late myocardial infarction rate and repeated revascularization rate for CKD patients and PCI had advantages in shorter operation time and hospital stay, less invasion, few chances of anesthesia, mechanical ventilation and infection[28]. But in this study short term clinical outcomes are not different among two treatment groups. These equivalent rates of stroke, new-onset MI, or cardiogenic and non-cardiogenic death between two treatment groups among patients with CKD indicate that PCI can be acceptable and less invasive treatment option alternative to CABG, particularly in patients with moderate to severe CKD. Another of point note in our study is that there were few factors like age, STEMI, NSTEMI, and number of coronary artery disease predicted PCI as treatment strategy in patients with moderate to severe CKD. Despite the new advancements in interventional cardiology, including drug eluting stents (DES) and bioabsoable stents, distal protection devices, and use of newer antithrombotic agents and marked progress in CABG in terms of on-pump CABG, optimal treatment strategy in patients with CKD undergoing coronary revascularization is still debatable. The primary limitation of this study is that it was not a randomized study and it had shown only short term clinical outcomes. It also had relied on estimated creatinine clearance calculated through the Cockcroft- Gault formula, which is an imprecise measure of kidney function. Nevertheless gold standard is cumbersome and expensive.

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