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Effect of Various Degrees of Chronic Kidney Disease on Long-term Outcome of Patients with Percutaneous Coronary Intervention

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Abstract

Background: We aimed to identify the association of degree of renal failure in chronic kidney disease patients who underwent percutaneous coronary intervention (PCI) at our center with 5-year major adverse cardiac events (MACE).

Methods: In this cohort study, we enrolled all patients who underwent primary or elective PCI and completed their 5-year follow-up unless they developed events related to study end-points. Demographic, angiographic and clinical data of the participants were retrieved from our databank. Glomerular filtration rate (GFR) was calculated based on the Cockcroft-Gault equation for men and women, separately. Accordingly, our patients were classified into three groups: GFR ≥ 60, GFR < 60 and ≥30 and GFR < 30 mL/min. Then, the demographic and clinical data, as well as the frequency of MACE and its elements, were compared between the study groups.

Results: We included the data for 5,510 patients. MACE occurred in 891 (16.1%) of the patients. A total of 632 cases (16.7%) occurred in patients with GFR > 60 while 224 cases (18.8%) and 35 events (43.7%) occurred in patients with 30 ≤ GFR < 60 and GFR < 30 mL/min, respectively. So, GFR < 30 mL/min was significant predictor for MACE (hazard ratio [HR] = 3.74, 95% CI: 2.64–5.28; $P < 0.001$). The prediction effect of GFR < 30 remained significant after adjustment for the confounding variables (HR = 3.43, 95% CI: 2.38–4.94; $P < 0.001$).

Conclusion: GFR <30 mL/min was a strong predictor for 5-year MACE. Moreover, in patients with GFR > 30 mL/min, PCI is a more applicable approach.

Keywords: Chronic kidney disease, Glomerular filtration rate, Major adverse cardiac events, Percutaneous coronary intervention, Survival

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Introduction

Chronic kidney disease (CKD) patients and particularly those with end-stage renal disease (ESRD) and under hemodialysis are at high risk for ischemic heart disease (IHD).[1,2] Despite several studies that have compared coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) in CKD patients, selection of the proper treatment in CKD patients with IHD is still under debate.[1,3,4] It should be noted that PCI in CKD patients has its own challenges, such as complicated vascular lesions, extensive calcification and multi-vessel disease.[2,5]

CKD alone has been recognized as a potential predictor for clinical outcome and major adverse cardiac events (MACE) following PCI.[6-9] However, degree of renal failure has been studied less as a predictor for MACE. As prevention of MACE is a fundamental element in the success of PCI in CKD patients, we aimed to identify the association of degree of renal failure in CKD patients who underwent PCI at our center and the 5-year MACE. We also detected other predictors of MACE in our study group.

Materials and Methods

In this cohort study, we enrolled all patients who underwent primary or elective PCI at our center between March 2007 and March 2011 and completed their 5 year follow-up unless they developed events related to our study end-points. The exclusion criterion was an incomplete hospital file. This study conforms to the principles outlined in the Declaration of Helsinki. A written informed consent was obtained from the participants before admission stating that their clinical data would be used anonymously for research purposes.

Demographic, angiographic and clinical data of the participants were retrieved from the databank of our center. The clinical data included history of classical cardiovascular risk factors, including diabetes mellitus,

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hypertension, dyslipidemia, smoking and family history of coronary artery disease, previous CABG or PCI, presence of peripheral vascular disease or cerebrovascular accidents, ejection fraction based on the latest echocardiography before the intervention, as well as the angiographic and angioplastic data based on their reports. Definition of hypertension, diabetes mellitus and dyslipidemia at our center has been published previously.[10]

For each patient, glomerular filtration rate (GFR) was calculated based on the Cockcroft-Gault equation for men and women separately. Accordingly, our patients were classified into three groups: GFR ≥ 60 mL/min, GFR < 60 and ≥30 mL/min and GFR < 30 mL/min. Then, the demographic and clinical data as well as the frequency of MACE and its elements were compared between the study groups.

The clinical follow-up data were collected by scheduled clinic evaluations or direct telephone interviews for patients who were not able to come to our hospital. The follow-up visits are usually done at 1, 3, 6 and 12 months following PCI and annually in our center. All the events were recorded from the time of intervention. MACE was defined as the occurrence of one or more of the following items within at least 5 years after PCI: 1) Cardiac death; 2) myocardial infarction; 3) CABG; 4) rehospitalization due to unstable angina; 5) Target vessel revascularization (TVR) or target lesion revascularization (TLR).

Statistical Analysis

Continuous variables are presented as mean ± standard deviations (SDs) and compared between the three groups of GFR using the one-way analysis of variance (ANOVA) test. Categorical variables are presented as counts and percentages and were compared between GFR groups with the Chi-square test or the Fisher's exact test when appropriate. Survival curves were generated using the Kaplan-Meier method. A Cox proportional hazards model was applied for assessing the unadjusted and adjusted effect of GFR on MACE. The effects were presented through hazards ratio (HR) with 95% confidence intervals (CI).

Results

In this study, we included data from 5510 patients who underwent PCI at our center and completed at least 5 years of follow-up, unless they developed MACE. Elective PCI was performed in 96.6% of the patients and the rest underwent primary PCI. Mean age of the total study population was 57.8 ± 10.5 years and 70% were male. The patients in the GFR < 30 mL/min group were more likely to be older, female, diabetic, hypertensive and dyslipidemic and more likely to have peripheral vascular disease or history of cerebrovascular accident and a lower ejection fraction. They also had a higher body mass index but were less likely to be smokers. Details of the comparison between the study groups for the demographic and clinical characteristics are summarized in Table 1.

MACE occurred in 891 (16.1%) patients. A total 632 (16.7%) cases occurred in patients with GFR > 60 while 224 (18.8%) and 35 (43.7) events occurred in patients with 30 ≤ GFR < 60 and GFR <30 mL/min, respectively. Details of MACE and its elements in the study groups are shown in Table 2.

In the unadjusted Cox-regression model, GFR < 30 mL/min was a significant predictor for MACE (HR = 3.74, 95% CI: 2.64–5.28; $P < 0.001$). The prediction effect of GFR < 30 remained significant after adjustment for the confounding variables as shown in Table 3 (HR = 3.43, 95% CI: 2.38–4.94; $P < 0.001$). The confounding variables in this analysis included diabetes mellitus, hypertension, family history of coronary artery disease, presence of peripheral vascular disease or cerebrovascular accident, ejection fraction, involvement of left main, left anterior descending arteries and venous graft, type of intervention, history of coronary artery bypass graft surgery or PCI. Based on the Kalpan-Meier graphs, patients with GFR < 30 mL/min had the worst survival both in the non-adjusted and adjusted model (Figure 1).

Discussion

In the present study, we found that low GFR (i.e. GFR < 30) is a strong predictor for 5-year MACE in patients who underwent PCI event after adjustment for confounding variables and the highest rate of MACE occurred in these patients. Other determinants of survival were female gender, diabetes mellitus, hypertension, dyslipidemia, family history of CAD, previous PCI or CABG, ejection fraction, primary PCI, involvement of left main and/or left anterior descending arteries or a venous graft. Renal impairment has been shown as a strong predictor of MACE in previous studies.[5,11,12] As far as IHD is common among CKD patients,[13] it should be clarified which patients benefit more from coronary revascularization.

In a study with 9-month follow-up, overall mortality was higher for ESRD patients than for the control population and they were at higher risk for TLR after coronary stenting than the control group.[7] Barthelemy et al divided their study population into 4 groups based on stent type and presence of CKD (defined as GFR <60 mL/min) and studied one-year clinical outcomes following PCI. Their results showed that the survival rate was the lowest among CKD patients who received bare metal stents (BMS) while the survival rate in CKD patients who received drug eluting stents (DES) was comparable to non-CKD patients with BMS.[14] Gruberg et al showed that low left ventricular ejection fraction, low GFR, ESRD, non–Q-wave myocardial infarction, diabetes mellitus, and CKD were independent correlates of poor survival in a one-year follow-up.[6] One study has shown that restenosis following revascularization with drug-eluting stents is common in patients with ESRD on hemodialysis.[15] However, in our

Table 1. Baseline Characteristics of the Study Population According to GFR Groups

Characteristic	GFR ≥60 mL/min (n = 3769)	30≤GFR<60 mL/min (n = 1188)	GFR<30 mL/min (n = 80)	*P* Value
Age, year	54.9 ± 9.3	66.6 ± 8.3	68.2 ± 10.2	<0.001
Male gender, No. (%)	3072 (74.4)	748 (57.6)	36 (45.0)	<0.001
BMI, kg/m^2	28.3 ± 4.2	25.8 ± 3.9	24.5 ± 4.0	<0.001
Diabetes mellitus, No. (%)	1113 (26.9)	395 (30.4)	36 (45.0)	<0.001
Hypertension, No. (%)	1874 (45.4)	750 (57.7)	67 (83.8)	<0.001
Dyslipidemia, No. (%)	2750 (66.6)	809 (62.3)	50 (62.5)	0.015
Smoking, No. (%)				
Current	1205 (29.2)	202 (15.6)	7 (8.8)	<0.001
Former	711 (17.2)	190 (14.6)	7 (8.8)	
Family history of CAD, No. (%)	960 (23.2)	210 (16.2)	5 (6.3)	<0.001
Previous PCI, No. (%)	301 (7.3)	88 (6.8)	5 (6.3)	0.783
Previous CABG, No. (%)	164 (4.0)	77 (5.9)	9 (11.3)	<0.001
Peripheral Vascular Disease or CVA, No. (%)	36 (0.9)	23 (1.8)	5 (6.3)	<0.001
EF, %	50.8 ± 9.3	50.0 ± 10.4	46.5 ± 12.7	<0.001
Type of PCI, No. (%)				
Primary	148 (3.6)	34 (2.6)	3 (3.80	0.237
Elective	3983 (96.4)	1265 (97.4)	77 (96.3)	
Involvement of left main artery	12 (0.3)	5 (0.4)	0 (0)	0.668
Involvement of LAD, No. (%)	2650 (64.1)	823 (63.4)	51 (63.7)	0.873
Involvement of LCX, No. (%)	911 (22.1)	281 (21.6)	16 (20.0)	0.87
Involvement of RCA, No. (%)	1185 (28.7)	375 (28.9)	25 (31.3)	0.878
Involvement of the graft, No. (%)	62 (1.5)	35 (2.7)	0 (0)	0.008
Type of stent				
Hybrid	320 (7.7)	114 (8.8)	3 (3.8)	
Drug	2209 (53.5)	688 (53.0)	40 (50.0)	0.549
Bare	1544 (37.4)	479 (36.9)	35 (43.8)	
POBA	58 (1.4)	18 (1.4)	2 (2.5)	
Stent diameter	3.20 ± 0.43	3.15 ± 0.43	3.14 ± 0.42	0.001
Stent length	23.4 ± 7.1	23.3 ± 7.1	22.5 ± 7.4	0.422

Abbreviations: BMI, body mass index; CABG, coronary artery bypass graft; CAD, coronary artery disease; EF, ejection fraction; GFR, glomerular filtration rate; LAD, left anterior descending artery; LCX, left circumflex artery; PCI, percutaneous coronary intervention; POBA, plain old balloon angioplasty; RCA, right coronary artery.

Table 2. Incidence of Major Adverse Cardiac Events in the Total Population and Subgroups Based on Glomerular Filtration Rate

Event[a]	GFR≥60 mL/min (n = 3769)	30≤GFR<60 (n = 1188)	GFR<30 (n = 80)	Total (n = 5510)
Mortality	100 (2.6)	84 (7.0)	19 (23.7)	203 (3.6)
TLR	51 (1.3)	18 (1.5)	1 (1.2)	70 (1.2)
TVR	107 (2.8)	17 (1.4)	4 (5.0)	128 (2.3)
CABG	128 (3.3)	33 (2.7)	4 (5.0)	165 (2.9)
Non-fatal MI	246 (6.5)	72 (6.0)	7 (8.7)	325 (5.8)
Stroke	17 (0.4)	18 (1.5)	1 (1.2)	36 (0.6)
Total MACE	632 (16.7)	224 (18.8)	35 (43.7)	891 (16.1)

[a] Data are shown as frequency (percentage).
CABG, coronary artery bypass graft; GFR, glomerular filtration rate; MACE, major adverse cardiac events; MI, myocardial infarction; TLR, total lesion revascularization; TVR, total vessel revascularization.

Table 3. Unadjusted and Adjusted Predictive Value of Glomerular Filtration Rate for Major Adverse Cardiac Events

	Unadjusted			Adjusted*		
Variable	Hazard Ratio	95% CI	*P* Value	Hazard Ratio	95% CI	*P* Value
GFR≥60	Ref			Ref		
30≤GFR<60	1.13	0.96–1.32	0.121	1	0.85–1.19	0.937
GFR<30	3.74	2.64–5.28	<0.001	3.43	2.38–4.94	<0.001

*Adjusted for diabetes mellitus, hypertension, family history of coronary artery disease, presence of peripheral vascular disease or cerebrovascular accident, ejection fraction, involvement of left main, left anterior descending arteries and venous graft, type of intervention, history of coronary artery bypass graft surgery or percutaneous coronary intervention.
CI, Confidence interval; GFR, Glomerular filtration rate.

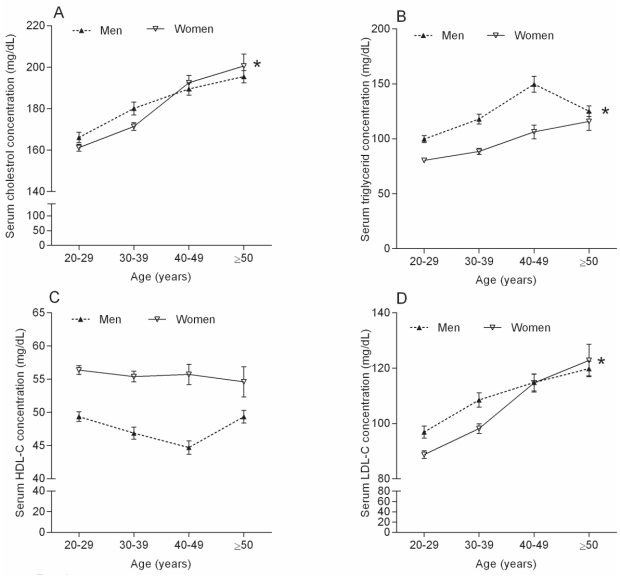

Figure 1. Survival Rate According to GFR Groups.

study, we did not find any association between the type of stent and 5-year survival. This is in line with another study that found no association between use of DES and reduction of TLR and TVR in comparison with BMS.[16] In a similar study that identified the determinants of mortality in CKD patients undergoing PCI, CKD stage 5 (GFR <15 mL/min) had the strongest association with mortality and other determinants for MACE were increasing age, deteriorating left ventricular systolic impairment, worsening renal function and urgent indication for PCI.[17] In a study that investigated the relation between GFR and in-hospital and long-term MACE in 884 ST-elevation myocardial infarction patients undergoing primary PCI, degree of renal impairment was associated with increased in-hospital and long-term MACE.[18] Another similar study on 656 patients also showed that GFR <60 was associated with a higher risk of MACE in patients undergoing PCI following STEMI.[19]

The main difference between our study with previous studies is that we showed that the rate of mortality increases by decline in GFR and patients with GFR <30 mL/min are more susceptible to occurrence of MACE. The strength of our study is its large sample size as well as a long-term follow-up period. However, there are some limitations to our study. First, it is a single-center study and as our center is a referral heart center, it is probable that the pattern of the patients may differ from the general population. On the other hand, we did not have data regarding the etiology and duration of CKD that may influence our results.

In conclusion, in this study, we investigated the association of GFR and MACE in a 5-year follow-up of PCI patients at our center. GFR <30 mL/min was a strong predictor for 5-year MACE. We can also conclude that in patients with GFR >30 mL/min, PCI is a more practical approach. Moreover, several other clinical factors were significantly associated with 5-year MACE in our study group. Our findings show that patients with CKD should not be deprived of revascularization and the decision can be made based on the GFR level. Any intervention, particularly before the severe decline in GFR, can help to increase their survival.

Authors' Contribution

YN: Supervision and final approval; AS: Study concept, proposal, drafting and final approval; SEK: Supervision and final approval; AJ: data management, statistical analysis and final approval; MR: Data gathering, revisions and final approval; HS: Data gathering, data cleaning and final approval.

Conflict of Interest Disclosures

The authors have no conflicts of interest.

Ethical Statement

The protocol of this study was approved by the committee of ethics at Tehran Heart Center, Tehran, Iran.

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