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The Impact of Advanced Chronic Kidney Disease on In-Hospital Mortality Following Percutaneous Coronary Intervention for Acute Myocardial Infarction

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Background: The impact of advanced chronic kidney disease (CKD) on the outcomes of patients undergoing percutaneous coronary intervention (PCI) in the acute phase of myocardial infarction is poorly understood. We assessed the impact of CKD (stages 3–5) on the in-hospital outcomes of patients undergoing PCI for acute myocardial infarction (AMI) in a statewide registry. Methods: This study evaluated all patients who underwent PCI in New York State between 1997 and 1999. Of the 9,015 patients, 94 (1%) had at least stage 3 CKD (serum creatinine for AMI > 2.5 mg/dL) and were not on dialysis. Patients with advanced CKD were compared with those without advanced CKD using univariate and multivariate methods. The primary outcome of interest was in-hospital mortality. Results: Patients with advanced CKD had a higher incidence of diabetes, hypertension, and peripheral vascular disease. Patients with advanced CKD presented more commonly with cardiogenic shock or heart failure. The unadjusted in-hospital mortality was 23.4% for patients with advanced CKD compared with 4.2% for patients without advanced CKD ($P < 0.001$). After adjusting for the increased comorbidity and high risk clinical features, advanced CKD remained an independent predictor of in-hospital mortality (odds ratio 2.4, 95% Confidence Interval, 1.002–5.804, $P = 0.049$). Conclusions: Patients with AMI and advanced CKD who undergo PCI have more comorbidities and significantly worse in-hospital outcomes than patients without advanced CKD. Even after adjusting for these comorbidities, advanced CKD remains an independent predictor of increased in-hospital mortality.

Key words: chronic kidney disease; angioplasty; stent; outcomes

INTRODUCTION

Among patients with acute myocardial infarction (AMI) treated with fibrinolytic therapy, impaired renal function is associated with increased mortality. The mortality risk increases with the severity of the renal dysfunction with the greatest risk observed among patients with serum creatinine levels >2.0 mg/dL which corresponds to stages 3–5 of chronic kidney disease (CKD) [1]. Furthermore, as renal function declines, the risk of intracranial hemorrhage following fibrinolytic therapy increases [1]. Thus, alternative methods of reperfusion should be considered in patients with the most advanced renal disease. However, the impact of advanced CKD on the outcomes of patients treated with percutaneous coronary intervention (PCI) for AMI remains unclear.

METHODS

Data Ascertainment

The Coronary Angioplasty Reporting System of the New York State Department of Health contains information regarding every patient who undergoes PCI in the state of New York. Data elements in the registry include patient demographic information, baseline clinical characteristics, serum creatinine >2.5 mg/dL, risk factors, angiographic characteristics, including lesion

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TABLE I. Baseline Clinical Characteristics

	No chronic kidney disease ($n = 8{,}921$)	Chronic kidney disease ($n = 94$)	P value
Mean age (years)	60	62	0.258
Body mass index (kg/m^2)	28.4	26.5	0.008
Male	71%	62.8%	0.079
White	88.3%	69.1%	<0.001
History of diabetes	17.3%	45.7%	<0.001
History of hypertension	55.5%	85.1%	<0.001
Current cigarette smoking	29%	10.6%	<0.001
Peripheral vascular disease	5.7%	20.2%	<0.001
Prior stroke	3.9%	12.8%	<0.001
Previous congestive heart failure	2.2%	10.6%	<0.001
Prior open heart surgery	6.7%	11.7%	0.058
Myocardial infarction < 6 hr	56.6%	62.8%	0.229
Myocardial infarction < 24 hr	43.4%	37.2%	0.227
Thrombolysis within 7 days	7.7%	7.4%	0.914
Congestive heart failure	10.8%	21.3%	0.001
Shock	3.8%	11.7%	<0.001
Unstable hemodynamics	5.4%	7.4%	0.393

location and morphological type, in-hospital outcomes, complications and discharge date and disposition. This information is first entered on a two-page form by the cardiologist following each intervention, which is subsequently entered into a computer database. All procedural decisions, including device selection and adjunctive pharmacotherapy are made at the discretion of the individual physician performing the procedure. For the present study, we utilized data elements obtained between 1997 and 1999 and compared patients according to serum creatinine levels on admission. A total of 98,564 patients underwent PCI of which, 9,015 patients underwent PCI for AMI within 23 hr of onset of symptoms. The primary outcome of interest was in-hospital mortality.

Definitions

The definition of advanced CKD used by this registry was as a preintervention serum creatinine >2.5 mg/dL. Hemodynamic instability was defined as the requirement for pharmacological or mechanical support to maintain blood pressure or cardiac output. Stroke was defined as a transient or permanent new focal neurological deficit occurring intraoperatively to 24 hr after the procedure. Acute occlusion at site of angioplasty was any acute occlusion, partial or complete resulting in reduction of flow through the dilated artery. Stent thrombosis was defined as the formation of a blood clot in the stented segment of the artery and/or adjacent area. Ejection fraction was that recorded closest in time to the cardiac procedure.

TABLE II. In-Hospital Outcomes

	No chronic kidney disease ($n = 8{,}921$)	Chronic kidney disease ($n = 94$)	P value
Emergency bypass surgery	1.0%	0%	0.325
Abrupt vessel closure	0.9%	1.1%	0.855
Stent thrombosis	0.9%	1.1%	0.884
Postprocedure stroke	0.6%	3.2%	0.002
Dialysis	0.5%	6.4%	<0.001
In-hospital death	4.2%	23.4%	<0.001
Major adverse cardiac events	6.7%	25.5%	<0.001

Statistical Analysis

Categorical variables were compared by χ^2 analysis. Continuous variables are presented as mean values ± standard deviation and were compared using the Student t test. All P values are two-tailed and all confidence intervals reported are 95% intervals. Statistical significance was defined as $P < 0.05$. Stepwise multiple logistic regression analysis was performed incorporating relevant clinical variables in addition to those with a univariate P value of <0.10. All analysis was performed using the SPSS 11.0 statistical analysis program.

RESULTS

Baseline Characteristics

Of the 9,015 patients who underwent PCI for AMI, 94 patients (1%) had a baseline serum creatinine >2.5 mg/dL. These patients had a significantly higher incidence of comorbidities. Diabetes, hypertension, peripheral vascular disease, and heart failure were more frequent in advanced CKD patients (Table I). The majority of patients in both groups underwent PCI within 6 hr of symptom onset. However, advanced CKD patients had a lower ejection fraction than patients without advanced CKD (39% vs. 46% $P < 0.001$), were more likely to present with cardiogenic shock (11.7% vs. 3.8%, $P < 0.001$), to be treated with intra-aortic balloon counterpulsation prior to the procedure (14.9% vs. 7.4%, $P = 0.006$) and were more likely to develop heart failure (21.3% vs. 10.8%, $P = 0.001$). A stent was deployed in the majority of patients in both groups, although ~30% of CKD patients were not treated with a stent (69.1% vs. 78.4%, $P = 0.03$).

Clinical Outcomes

There was no significant difference in the incidence of emergency bypass surgery, abrupt vessel closure, and stent thrombosis (Table II). An increased incidence of stroke after PCI was observed in the population with

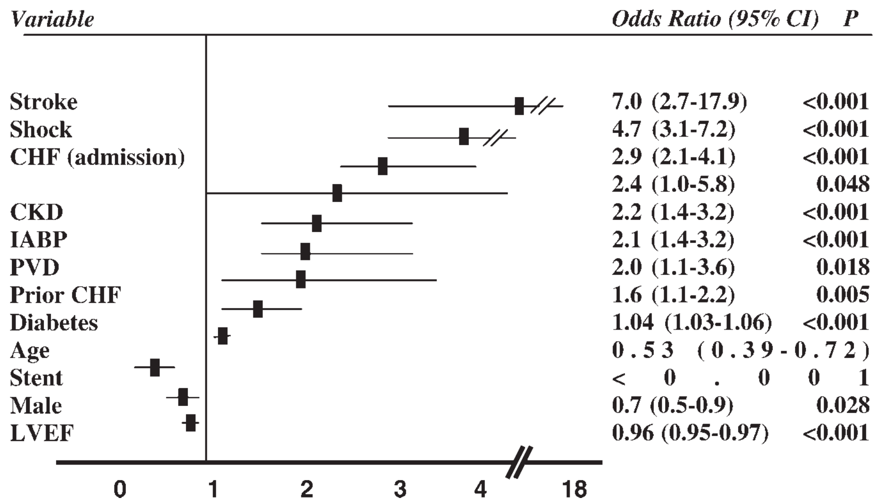

Fig. 1. Multiple logistic regression predictors of in-hospital mortality. CHF, congestive heart failure; IABP, intraaortic balloon pump; PVD, peripheral vascular disease; LVEF, left ventricular ejection fraction.

CKD (3.2% vs. 0.6% $P = 0.002$) and the in-hospital unadjusted mortality rate was significantly higher in CKD patients (23.4% vs. 4.2%, $P < 0.001$). Also, the need for in-hospital dialysis was significantly higher in these patients. The combined endpoint of death, reinfarction, and stroke (major adverse cardiac events) was significantly higher in CKD patients. Logistic regression analysis (Fig. 1) demonstrated that CKD was independently associated with an increased risk of in-hospital mortality (odds ratio 2.4, 95% Confidence Interval, 1.002–5.804, $P = 0.049$). Other significant predictors of in-hospital mortality included increased age, diabetes, vascular disease, decreased ejection fraction, heart failure during the admission, and intraaortic balloon placement. Shock and stroke following PCI were the strongest independent predictors of in-hospital mortality. Stent use and male gender were associated with a reduction in in-hospital mortality.

DISCUSSION

The major finding of the present study is that stage 3–5 CKD patients who present with an AMI are at a very high risk for a poor outcome despite early intervention with PCI. This study also clearly demonstrates the clustering of significant risk factors and comorbidities in this patient population, which likely contributes to the elevated mortality. However, even after adjusting for these comorbidities (diabetes, hypertension, prior stroke, heart failure on presentation, and cardiogenic shock), patients with advanced CKD are twice as likely to die in the hospital compared to patients with lesser degrees of or no CKD. Our observations are consistent with previous studies that have shown increased mortality in AMI patients with any CKD and not only in those patients with end-stage renal disease on dialysis [2–7]. Patients with CKD and AMI represent a sicker population who more commonly exhibit shock and heart failure on presentation and also have an increased risk of stroke following any type of reperfusion therapy.

The present study is composed of a relatively younger population when compared with previous analyses. The fact that the present registry comprises a wider array of patients, obtained during a prolonged period of time, in all community and university hospital settings makes it more representative of the general population than a clinical trial database. Clinical factors which may have contributed to the high mortality in this study are reduced left ventricular function and the presence of shock on presentation. A higher incidence of periprocedural complications such as bleeding, stroke, and the underutilization of proven therapies such as aspirin, beta-blockers, and angiotensin-converting enzyme inhibitors have all been linked to higher mortality rates in CKD patients with AMI who undergo reperfusion therapy [4,8]. Contrast-induced nephropathy could also have contributed to the high mortality as it occurs in 20–40% of patients with preexisting CKD [9–11].

In addition, this population has unique risk factors causing accelerated atherosclerosis and endothelial dysfunction such as proteinuria, increased systemic inflammation (high levels of C-reactive protein and fibrinogen), high levels of advanced oxidation protein products [12], unique vascular calcification, hyperhomocystinemia, and disruption in nitric oxide synthesis [13]. There is a different pattern of atherosclerosis in patients with CKD where there is both intimal and medial involvement as compared with the general population which has predominantly intimal involvement. The plaques in CKD patients, especially those on chronic dialysis, are frequently calcified, as opposed to fibroatheromatous, and have increased medial thickness compared with lesions in the general population [14,15]. Furthermore, CKD patients have a significant burden of atherosclerotic disease in non-cardiac organ systems as evidenced by the high rate of stroke and peripheral vascular disease seen in this and previous studies [16].

Studies that have evaluated the impact of revascularization strategies on mortality in CKD patients have shown that these patients have lower rates of long-term success following PCI due to higher restenosis rates and the increased requirement for repeat revascularization procedures. Some have suggested that surgical revascularization might be a better option in this high risk population [17–20]. However newer studies in patients with CKD have shown a reduced rate of restenosis with the advent of drug-eluting stents. Unfortunately this benefit has not been accompanied by lower mortality rates [21]. Having identified that CKD is independently associated with worse outcomes after AMI, improving the quality of care and identifying the optimal reperfusion strategies through well designed randomized clinical trials involving all degrees of renal impairment are critical to improving outcomes. Quality of care can be improved by understanding the reasons for underuse of proven therapies and providing established aggressive reperfusion strategies and adjunctive medical therapies in patients with all degrees of CKD. In addition, the American Heart Association (AHA) Council on Kidney in Cardiovascular Disease [22], National Kidney Foundation (NKF) task force [23], and the Joint National Committee (JNC-7) for the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure [24] have classified CKD patients as a group at high risk for the development of cardiovascular disease. These councils have recommended aggressive risk factor reduction such as lowering the target blood pressure and target lipid levels in patients with CKD along with tight glucose control in diabetics with CKD.

Limitations

The present study has several limitations that are inherent to all retrospective registries. There may be unidentified differences between groups that, if identified, would change the results of this analysis. The arbitrary use of a serum creatinine >2.5 mg/dL as a definition of CKD is an insensitive method to define renal dysfunction, as >50% reduction in glomerular filtration rate may occur before any increase in creatinine is observed. This binary definition results in patients with significant CKD but a serum creatinine $\leq$2.5 mg/dL being assigned to the cohort without advanced CKD and thereby reduces the apparent impact of CKD on mortality. Other limitations include the small number of advanced CKD patients and the lack of long term follow-up.

Until newer strategies for treatment of AMI in CKD patients are developed, the best way to improve outcomes is providing established therapies such as angiotensin-converting enzyme inhibitors, aspirin, β-adrenergic blockers, statins, and early reperfusion.

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