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Original Article

Higher post procedural bleeding in patients with advanced chronic kidney disease undergoing percutaneous coronary intervention

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Abstract: Background: Advanced chronic kidney disease (ACKD) is common in patients undergoing percutaneous coronary intervention (PCI). Post-PCI bleeding has been shown to increase mortality and remains an important challenge in these patients. Previous studies have shown increased post-PCI bleeding in CKD patients but often ACKD patients are excluded from these trials. The goal of this study was to evaluate if patients undergoing PCI with advanced renal disease have higher bleeding complications. Methods: We analyzed the National Inpatient Sample (NIS) database to compare the post-PCI bleeding rates for ACKD (CKD stage 3 and above) undergoing PCI between 2006 and 2011 to those without ACKD in patients over the age of 40. Specific ICD-9 CM codes were used to identify these patients. Results: A total of 49,192 patients had post-PCI bleeding during the study period of which 3,675 (7.5%) had ACKD. Patients with ACKD were older (68.7±11.7 years). During the study period, there was a decline in post-PCI bleeding rates in both ACKD and control groups. Patients with ACKD have significantly higher post-PCI bleeding rates compared to the control group. For example, in 2006, 133.9 in patients with ACKD had bleeding vs. 104.4 per 100,000 in patients without ACKD ($P<0.05$). After multivariate adjustment for bassline comorbidities, ACKD remained independently associated with post-PCI bleeding risk (OR: 1.07, CI: 1.03-1.11, $P<0.001$). Conclusion: Despite the overall decline in post-PCI bleeding in patients undergoing PCI, ACKD remains independently associated with post-procedural bleeding.

Keywords: Angioplasty, stenting, chronic renal failure, percutaneous coronary intervention, chronic renal disease, stent, coronary revascularization

Introduction

For years, the presence of kidney function disorders has been considered a risk factor for adverse outcomes in coronary patients, especially patients undergoing cardiovascular treatment procedures [1, 2]. Based on the evidence, a history of underlying kidney disease is associated with an increased risk of morbidity and even mortality in patients undergoing coronary bypass surgery or percutaneous coronary intervention (PCI) [3]. Following, evidence of increased postoperative bleeding in such patients compared to patients without kidney disorders has been published [4]. The main reason for the increased bleeding risk in renal patients appears to be multifactorial. Platelet dysfunction and impaired thrombotic pathways, which are common findings in these patients are the main reasons for the increased likelihood of postoperative bleeding [5]. In addition, requiring dual anti-platelet therapy after cardiac revascularization can impose the risk of bleeding [6]. According to the literature, major bleeding occurs at a rate of 1.7% after PCI, about half from the site of arterial access and half from non-access locations, most commonly the gastrointestinal tract, intraocular, intracranial, and retroperitoneal sites [7]. Therefore, the summary of the available evidence indicates an increased risk of bleeding events following PCI, especially in patients with severe renal dysfunction. However, there is still no conclusive evidence in this regard, and it is not clear whether the presence of underlying chronic kidney disease can be associated with an

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Table 1. Baseline characteristics of study population

Characteristics	Post-PCI bleeding (+)	Post-PCI bleeding (-)	*P* value
Mean age, year	68.66±11.69	67.51±11.84	<0.001
Male gender, %	49.55%	52.84%	0.001
Race, %			<0.001
White	48.76%	62.93%	
Black	16.49%	6.14%	
Hispanic	9.52%	5.62%	
Asian/Pacific	3.54%	1.92%	
Native American	1.01%	0.52%	
Other	20.68%	22.87%	

increased risk of bleeding after the procedures. What we discussed in the present study was evaluating the role of advanced chronic kidney disease (ACKD) as a risk factor for bleeding after PCI.

Materials and methods

Database

This retrospective study was performed on 1,826,536 patients who underwent PCI procedures between 2005 and 2011. Their clinical information was recorded in the National Inpatient Sample (NIS) data registry including all preoperative, intraoperative, and postoperative data of all patients undergoing cardiac revascularization. The collected information included demographic characteristics, underlying cardiac risk factors, and intra- and postoperative outcomes during hospitalization. Based on the definition of advanced chronic kidney disease (stages 4 and 5 of the chronic kidney disease classification defined as severe reduction in glomerular filtration rate less than 30 ml/min), the studied population was assigned into two groups with and without advanced chronic kidney disease. Inclusion criteria were patients who underwent PCI over the age of 40 and had advanced kidney disease defined as stages 4 and 5 captured in the ICD-9 coding. These patients were compared to patients who underwent PCI without stage 4 or 5 renal disease over age 40. Exclusions were patients younger than 18 and patients who did not have PCI. There were no other exclusions.

The study outcome was in-hospital post-PCI bleeding defined as any of the following occurring during hospitalization before discharge after PCI. We used ICD-9 coding for bleeding. We evaluated the rate of bleeding in PCI patients with advanced renal disease with those without advanced renal disease.

Statistical analysis

For statistical analysis, results were presented as mean ± standard deviation (SD) for quantitative variables and were summarized by frequency (percentage) for categorical variables. The normality of the data was checked by the Kolmogorov-Smirnov statistical test. For each year of study, the average annual age-adjusted in-hospital procedure rates for post-PCI bleeding were calculated by multiplying the age-specific rates by age-specific weights. The weights utilized in the age adjustment of the data were the proportion of the year 2000 standard U.S. population within each age group. The categorical parameters were compared using the Chi-Square test or Fisher's exact test if required. Multivariable logistic regression analysis was used adjusting for age gender, race, and comorbidities such as diabetes mellitus, hypertension, hyperlipidemia, prior myocardial infarction, peripheral vascular disease, atrial fibrillation, stroke, myocardial infarction, and smoking. *P* values of ≤0.05 were considered statistically significant. The statistical software SPSS version 28.0 for Windows (IBM, Armonk, New York) was used for statistical analysis.

Results

Bassline characteristics

Overall, 1,826,536 patients who underwent PCI procedures between 2005 and 2011 were included in our study. According to advanced chronic kidney disease definitive criteria, 113,018 patients (6.2%) suffered from this baseline renal co-morbidity. Baseline characteristics of study subjects in the group with and without kidney disease are summarized in **Table 1**. In this regard, patients with kidney disease were older, and mostly men, with a significantly higher prevalence rate of cardiovascular risk factors including diabetes mellitus, peripheral artery disease, cerebrovascular accidents, and also a history of atrial fibrillation as compared to those without kidney disease.

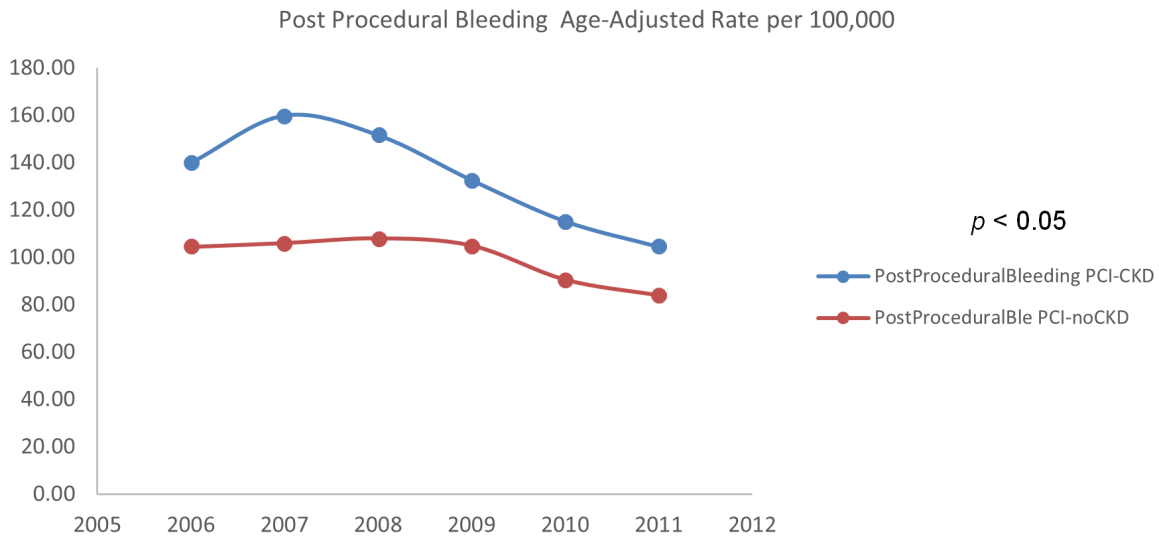

Figure 1. The trend of the changes in post-PCI bleeding during study period.

Findings

Overall, a total of 49,192 patients suffered from post-PCI bleeding, and 3,675 (7.5%) patients had a history of advanced chronic kidney disease. During the study period, there was a decline in post-PCI bleeding rates in both ACKD and control groups. Patients with ACKD have significantly higher post-PCI bleeding rates compared to the control group. For example, in the year 2006, 133.9 in patients with ACKD had bleeding vs. 104.4 per 100,000 in patients without ACKD (P<0.05). After multivariate adjustment for bassline comorbidities, ACKD remained independently associated with post-PCI bleeding risk (OR: 1.07, 95% CI: 1.03-1.11, P<0.001). Despite the higher risk of postoperative bleeding in patients with a history of ACKD, bleeding complications were trending lower over the years regardless of ACKD status. Complications in these patients during the studied years indicated a decreasing trend (**Figure 1**).

Discussion

The present study showed that the risk of bleeding is higher following PCI procedure in ACKD patients. In this regard, this study is one of the first studies that used a large volume of PCI patients, and therefore the result can be trusted due to the high power of the study. In previous studies, the role of bleeding risk in patients with chronic renal failure has been documented. As found earlier by Attallah et al, the incidence of major bleeding within the first month post-PCI was higher in the chronic kidney disease group and this event was closely associated with worsening renal impairment [8]. Saltzman and colleagues showed that patients with chronic kidney disease compared with patients without this co-morbidity had a higher rate of postoperative major bleeding (19.3% vs. 6.7%, P<0.001). They also revealed that baseline creatinine was an independent predictor of early major bleeding as well as 3-year postoperative death [9]. Even, some studies found that periprocedural complications such as in-hospital bleeding, myocardial infarction, and death are much higher in kidney disease patients, approaching an increased relative risk of two- to six-fold [10, 11], however, some authors could not confirm the association of kidney dysfunction and risk for postoperative hemorrhage. Recently, Tobe et al revealed that chronic kidney disease or dialysis was not associated with a higher risk of bleeding events after adjustment of covariates [12].

Homeostasis and hemorrhagic disturbances are the main findings in patients suffering from advanced chronic kidney diseases. The reasons for these disorders are complex and involve the imbalanced coagulation cascade regarding thrombotic activity, the fibrinolytic system, platelets, endothelium, or the vessel wall with its extracellular matrix. The relationship between these components is influenced

by uremic toxins and metabolic compounds accumulating during renal insufficiency [13-15]. Furthermore, patients with renal insufficiency suffer from a varying degree of inflammation, which also influences homeostasis [16]. Of course, it should be kept in mind that such changes can be increased due to hemodynamic and coagulability imbalances in the context of heart diseases [17, 18]. Therefore, it can be expected that in Advanced CKD due to the nature of renal dysfunction itself or the need for hemodialysis in the presence of cardiac ischemic disorders an increased risk of bleeding after cardiac procedures can be expected.

Although we are facing an increased risk of bleeding post-PCI in ACKD patients, the trend of decreasing the occurrence of this complication after the operation has been quite evident in recent years. This change can be found in several points. Firstly, due to the recognition of the bleeding nature of chronic kidney disorders, patients who are candidates for cardiac procedures are under strict monitoring in terms of bleeding or thrombotic disorders, and if any of these disorders are detected, they should be corrected or invasive heart procedure is replaced with medical therapies. Additionally, the recent progress of medicated stents as well as the modification of PCI techniques has led to a significant improvement in the outcomes of this procedure in patients with chronic renal failure even in its severe stages [19, 20]. Higher bleeding risk in patients with renal disease is multifactorial. Platelet dysfunction in renal disease patients plays a major role. Higher vascular calcifications can also increase access bleeding as vascular compression after sheath removal can be less effective in calcified arteries. Gastrointestinal bleeding secondary to platelet dysfunction certainly can contribute to higher bleeding rates in this population who were treated with high anticoagulation during PCI.

Conclusion

We found that ACKD is associated with increased bleeding risk following PCI. However, the reduction in bleeding risk over the year studied is encouraging.

Limitations

The use of ICD-9 coding has inherent limitations as administrative coding has limitations in inaccuracy. Many ACKD patients will not undergo PCI introducing a selection bias regarding ACKD patients limiting our results.

Disclosure of conflict of interest

None.

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