Editorial

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Impact of Chronic Kidney Disease in Patients Undergoing Percutaneous Coronary Intervention: Improved but Not Solved

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Chronic kidney disease (CKD) is an independent risk factor for the development of coronary artery disease, and for the progression to more severe coronary heart disease.[1] CKD is also associated with adverse outcomes in those with existing cardiovascular disease.[2] The most frequent cause of CKD is diabetic nephropathy. Nearly 45% of incident renal failure is attributed to diabetes and another 20% is attributed to chronic hypertension.[3] Nowadays it is not uncommon for interventional cardiologists to encounter diabetic patients with associated CKD in proportion to increasing numbers of patients who need percutaneous coronary intervention (PCI). The large numbers of patients with CKD treated with PCI have been found to suffer from a markedly higher mortality of about 40% within 3-4 years after PCI.[4] Patients with diabetic nephropathy undergoing PCI have increased risk of contrast-induced nephropathy (CIN), an annoying problem not to be overlooked. There is a complicated relationship between CIN, comorbidity, and mortality. Abe et al.[5] reported that CIN was significantly correlated with long-term mortality in patients with CKD but not in those without CKD. During the last decade, there have been remarkable advancements in optimal medical therapy, interventional techniques and devices, which made it possible to reduce procedure-related complications in patients undergoing PCI. It was expected that these advancements would reduce the adverse effect of CKD on clinical outcomes. However, updated data sets reflecting these changes are rare. Significantly, the study performed by Kim et al.[6] provides the latest data regarding the impact of CKD for clinical outcomes in patients undergoing PCI.

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Principal study findings

The study performed by Kim et al.[6] reported that, in contrast to previous studies, CKD was not associated with an increased risk for device-related events, including stent thrombosis and target lesion revascularization (TLR) in diabetic patients in the era of newer-generation drug eluting stents (DES), even after adjustment for other clinical factors. However, 1-year adverse clinical outcomes including bleeding complications were significantly more common in patients with CKD than patients without CKD. They also demonstrated that CKD was an independent predictor for CIN in these patients. These findings were consistent with previous studies. In this study, among 2303 patients who underwent PCI with newer generation DES, 887 consecutive patients with a history of diabetes or whose HbA1c was higher than 6.5% at admission were analyzed. CKD was associated with diabetes in 338 patients and not associated in 549 patients. The authors analyzed two kinds of composite outcome, patient-oriented composite outcome (POCO) and device-oriented composite outcome (DOCO), as well as CIN and bleeding complications. POCO included all-cause mortality, any myocardial infarction (MI), and any revascularization and DOCO included cardiac death, target vessel-related MI, and TLR at 1-year follow-up among survivors at discharge. To control for heterogeneities in the clinical and angiographic characteristics between patients with and without CKD, multivariate Cox regression models were adjusted. Multivariate analysis showed that during the index hospitalization, CKD presence was an independent predictor for bleeding complications (hazard ratio [HR]: 11.512, 95% CI: 2.726-48.618) and CIN (HR: 2.468, 95% CI: 1.389-4.385), but

not for POCO (HR: 2.769, 95% CI: 0.963-7.962) or DOCO (HR: 2.794, 95% CI: 0.889-8.781). Among survivors at discharge at 1-year follow-up, the presence of CKD was an independent predictor only for POCO (HR: 1.824, 95% CI: 1.065-3.124) but not for DOCO (HR: 2.082, 95% CI: 0.690-6.278). Two core findings of this study were as follows: 1) CKD was a powerful and independent predictor of CIN, bleeding complications and 1-year POCO. 2) CKD was not related to in-hospital and 1-year DOCO, especially stent thrombosis and target lesion revascularization in this era of newer generation DES.

Clinical impact of the study

In previous studies, it was well documented that CKD patients had an extremely high risk for developing cardiovascular disease compared with the general population. Hence, both the National Kidney Foundation and the American Heart Association already listed CKD as an independent cardiovascular risk factor. Also, CKD patients treated with PCI were found to suffer from a markedly high mortality of about 40% within 3-4 years after the procedure.[7] This adverse outcome has been observed even in patients with mild CKD, which suggests that the CKD cardiovascular risk burden might be higher than previously assumed. Therefore, advanced CKD is considered a coronary artery disease risk factor equivalent to diabetes. Most recently, Peng et al.[8] reported that CKD seemed to be the strongest predictor for adverse outcomes compared with other traditional factors in coronary bypass candidates who were treated with PCI. According to the present study, after adjustment for potential confounding factors, patient-oriented adverse effects of CKD were still maintained even in this era of newer generation DES. These results are not so different from data in the RIFT study performed by Zhu et al.,[9] which enrolled 1174 patients undergoing revascularization exclusively with sirolimus-eluting stents. Authors emphasized the fact that the incidence of device-related events was not different between patients with CKD and patients without CKD. This assertion of the present study is quite different from the RIFT study data which reported that the presence of CKD was an independent predictor for stent thrombosis (odds ratio=4.5, 95% confidence interval 1.4-15, p=0.011). This discordance seems to be derived from the improvement in interventional techniques, use of newer-generation DES and improved drug efficacy. In this study, CKD patients also showed higher rates of both ischemic and bleeding complications despite improved drug therapy and use of newer generation devices. In CKD patients, higher ischemic complications are due to platelet hyperactivity and disorders of coagulation regulatory factors, while higher bleeding complications are caused by platelet dysfunction and activation of the fibrinolytic system. Little is known so far about the reasons one patient develops bleeding problems, while another tends to excessive ischemic events.[10] Although only a small portion (3.6%) of this study's patients used more potent adenosine diphosphate (ADP) receptor inhibitors such as prasugrel and ticagrelor. These drugs are rapidly gaining popularity in the field of interventional cardiology. Interactions between CKD and new generation ADP-receptor inhibitors in terms of bleeding complications would be a helpful issue. Although the present study has inherent limitations due to its retrospective design, its core findings highlight that patients with diabetic nephropathy undergoing PCI with advanced medical devices and techniques show reduced device-related complications. However, more importantly, patient-related adverse clinical outcomes have still not improved even in this era of newer generation devices and these results urge us to make greater efforts to reduce CKD-related complications.

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