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The Optimal Revascularization Therapy for Coronary Artery Disease Patients with Chronic Kidney Disease

Chul Soo Park

Division of Cardiology, Department of Internal Medicine, Yeouido St. Mary's Hospital, The Catholic University of Korea College of Medicine, Seoul, Korea

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Coronary artery disease is the leading cause of death in patients with chronic kidney disease (CKD) [1], and the survival of patients with CKD who undergo coronary revascularization is worse than for other patients with coronary artery disease [2]. Although some studies have examined the optimal revascularization strategy in CKD patients, it is still not clear what strategy we should choose in these patients.

CABG OR PCI

In the era of bare metal stents (BMSs), coronary artery bypass grafting (CABG) had better long-term survival than percutaneous coronary intervention (PCI) in high-risk patients, including CKD patients [3]. Although the Arterial Revascularization Therapy Study II trial did not show a significant difference in the adjusted 5-year mortality rate of patients treated with CABG or PCI, the 5-year major adverse cardiovascular event rates were significantly lower after CABG than after PCI; the risk of revascularization in patients who had undergone PCI was greater [4]. However, these studies were done in the era of BMS, and subsequent observational studies have shown that PCI with drug-eluting stents (DESs) is associated with a lower risk of revascularization, lower risk of major adverse cardiovascular events, and better long-term survival than PCI with BMS [5]. Most observational studies comparing CABG and DES-PCI for treating multivessel coronary artery disease in the general population have found that CABG offers greater long-term survival [6]. There are few data on the difference in the survival benefit between CABG and DES-PCI in CKD patients. Ashrith et al. [7] reported that CABG tends to have survival benefits in non-hemodialysis CKD patients with three-vessel disease compared with DES-PCI. However, there was no significant difference in two-vessel disease and CABG more frequently results in hemodialysis dependency than PCI. The superior outcomes produced by CABG in patients with three-vessel disease can be explained by the presence of more severe diffuse disease in such patients and by the effects of disease progression. Despite medical therapy, coronary artery disease can progress in both native coronary arteries and bypass conduits; however, disease progression in the percutaneously treated vessel probably has greater adverse effects on native vessels than on vessels protected, even briefly, by bypass conduits. The apparent superiority of CABG surgery comes at the expense of a greater risk of the patient requiring permanent hemodialysis after the revascularization procedure. This is because of fluid shifts and the use of cardiopulmonary bypass during CABG predisposes patients with CKD to worsening renal function. In conclusion, there does not seem to be a significant difference in survival benefit between CABG and DES-PCI in CKD patients, so CABG can be considered in CKD patients with multivessel disease or complicated lesions where the restenosis rate is expected to be high.

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Correspondence to Chul Soo Park, M.D.
Division of Cardiology, Department of Internal Medicine, Yeouido St. Mary's Hospital, The Catholic University of Korea College of Medicine, 10 63-ro, Yeongdeungpo-gu, Seoul 150-713, Korea
Tel: 82-2-3779-1325, Fax: 82-2-3779-1374, E-mail: Charlie@catholic.ac.kr

BMS OR DES

Several studies have shown that patients with CKD who undergo revascularization with PCI and stenting consistently have worse short- and long-term outcomes relative to patients without CKD [8]. Many of these studies included patients who had PCI before the advent of DES. Studies that included patients with DES were small, single-center, observational analyses. No randomized clinical trial has investigated the efficacy of DES in patients with CKD. Shenoy et al. [9] reported that the use of DES in consecutive patients with CKD undergoing PCI was associated with improved outcomes in terms of all-cause death, target vessel revascularization, and major adverse cardiac events and was not associated with a higher risk of stent thrombosis (ST) or incidence of myocardial infarction compared to BMS during the 3-year follow-up. They reported that the use of DES is a significant independent predictor of reduced all-cause mortality, compared to BMS. This reduction in mortality with DES was not accompanied by reductions in the rates of myocardial infarction or ST, but was accompanied by lower rates of restenosis. The absolute benefits of DES compared to BMS might be greater in CKD patients given their higher restenosis risk, which can potentially contribute to the survival advantage. Patients with CKD, especially end-stage renal disease, have higher in-stent restenosis rates, irrespective of the type of stent. Exaggerated neointimal growth in CKD patients has been attributed to higher rates of co-morbidities, such as diabetes mellitus, greater atherosclerotic burden, vascular calcification, stent under expansion, chronic systemic inflammation, granulocyte activation, and oxidative stress. However, it is difficult to explain the lower mortality among DES patients solely by the reduced rates of restenosis. In the two studies of CKD patients with follow-up longer than 12 months, the use of DES compared to BMS reduced the risk of all-cause mortality at 17 months in Zhang et al. [10], but did not reduce mortality at 4 years in Appleby et al. [11]. Of note, Appleby et al. [11] found a significant survival benefit from DES compared to BMS in the first year, with catch-up at 2 years.

In the general population, DESs are associated with an increased risk of late ST compared with BMS [12]. However, several studies of the ST incidence in CKD patients showed that DES did not increase ST incidence in 12-month or 3-year follow-ups compared with BMS. This is notable, since CKD has been described as a risk factor for ST after DES implantation [13]. Two studies have compared ST at 12 months between DES and BMS in CKD patients. Halkin et al. [5], reported no differences in the rates of ST between DES and BMS at 12 months in patients with either mild CKD (creatinine clearance 60 to 89 mL/min) or at least moderate CKD (creatinine clearance 60 mL/min). Okada et al. [14] included only patients on hemodialysis and found no significant difference in the rates of ST at 12 months between DES and BMS. Shenoy et al. [9] also suggested that there was no increase in the risk of ST for at least 3 years after DES implantation. A possible explanation for this observation might be that the baseline endothelial dysfunction and inflammatory milieu in patients with CKD increases the risk of ST to similar degrees with DES and BMS. Although there are still contradictory data, DES seems to be superior in terms of the incidence of major adverse cardiac event and most of them reduce target lesion revascularization. CKD is a risk factor for ST after PCI, but DES dose not confer a higher risk of ST than BMS in CKD patients.

There are no data regarding the optimal DES selection in CKD patients with acute myocardial infarction. Bae et al. [15] reported that DES implantation has a survival benefit in CKD with myocardial infarction patients compared with BMS implantation using the Korea Acute Myocardial Infarction Registry. In this issue of the journal, using data derived from Korea Acute Myocardial Infarction Registry, Hachinohe et al. [16] reported that zotarolimus-eluting stents are less effective in terms of target lesion revascularization than sirolimus-eluting stents and paclitaxel-eluting stents (PESs) in CKD patients with acute myocardial infarction. However, neither sirolimus-eluting stents nor PES had a survival benefit compared with zotarolimus-eluting stent. Zotarolimus-eluting stent results in higher neointimal growth, but less ST compared with sirolimus-eluting stents and PES, so it is not surprising that zotarolimus-eluting stent has higher target lesion revascularization than sirolimus-eluting stents and PES. The long-term data on ST incidence in CKD patients after specific DES implantation has not been released, and Hachinohe et al. [16] did not provide this information. In conclusion, DES seems to have benefit compared with BMS in CKD patients who undergo PCI. However, it is still unclear what the long-term benefits of DES are and which DES should be the first choice for PCI in CKD patients.

Conflict of interest

No potential conflict of interest relevant to this article is reported.

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