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EDITORIAL COMMENT

Calcium-Channel Blockers

An Alternative Therapy to Beta-Blockers for Myocardial Infarction?*

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Beta-blockers (BBs), which decrease myocardial oxygen demand by lowering heart rate and myocardial contractility and improve ventricular remodeling,[1] have been a central component of secondary prevention pharmacotherapy after acute myocardial infarction (AMI), especially in patients with left ventricular systolic dysfunction.[1-3] Indeed, the current guidelines including Asian recommend long-term BB treatment as Class I for patients with MI and a reduced left ventricular ejection fraction (LVEF) (<40%) in the absence of contraindications such as acute heart failure, hemodynamic instability, or higher degree atrioventricular block. [4-6] However, most of the supporting data are based on the studies undertaken before the implementation of reperfusion and secondary prevention therapies,[1] and the effect of BBs on mortality in patients with MI and preserved LVEF is less well-established.[7] Moreover, a meta-analysis has questioned the benefit of long-term BB therapy in patients with prior MI.[8]

Meanwhile, calcium channel blockers (CCBs) are alternative anti-ischemic drugs and their pharmacological effects are different between subclasses.[9-11] Dihydropyridine (DHP) CCBs tend to be more potent vasodilators, and non-DHP CCBs such as verapamil and diltiazem have more negative inotropic effects. A randomized controlled trial in the pre-reperfusion era has demonstrated that, during a 18-month follow-up, treatment with verapamil after AMI reduced overall mortality and major cardiac events, especially in those without heart failure.[9] In contrast, another randomized trial showed that the treatment with diltiazem after thrombolysis for AMI patients did not reduce the occurrence of cardiac death, nonfatal reinfarction, or refractory ischemia during a 6-month follow-up.[10] Furthermore, a randomized trial in the preintervention era demonstrated that cardiovascular events were comparable between BB therapy and DHP-CCB therapy after AMI.[11] However, there are no randomized trials comparing the prognostic impact of CCB therapy and BB therapy after AMI in the modern reperfusion era; therefore, the role of CCBs in patients with MI remains to be elucidated.

In this issue of the *JACC: Asia*, a paper by Kim et al[12] provides an important information from the Korean Acute Myocardial Infarction Registry-V, is a nation-wide multicenter registry of patients with AMI from 43 centers, between January 2016 and June 2020. Briefly, the study was aimed to compare the prognostic impact of CCB therapy and BB therapy on cardiovascular outcomes after AMI. In a total of 10,650 AMI patients treated with either CCBs or BBs at discharge, 2,665 patients were involved in a 1:4 propensity score-matched population. Among CCB groups, approximately two-thirds received non-DHP CCBs. Over 12 months of follow-up, there were no significant differences in the incidence of all-cause death (2.8% vs 2.2%), cardiac death (1.9% vs 1.3%), MI (1.3% vs 1.7%), revascularization (3.4% vs 3.6%), heart failure (1.7% vs 1.8%), stroke (0.9% vs 1.0%), or major adverse cardiac and cerebrovascular events (7.1% vs 7.3%) between the CCB group and the BB group. Interestingly, the prognostic impact of CCB therapy compared with BB therapy after AMI varied by LVEF. As compared with the BB group, the CCB group had a higher incidence of cardiac death and major adverse cardiac and cerebrovascular events in those with an LVEF of <50% (4.7% vs 1.2% and 9.3% vs 5.3%, respectively), whereas a reverse trend was noted in those with an LVEF of ≥50% (1.8% vs 2.8%

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and 5.9% vs 8.3%, respectively). Meanwhile, those trends were not evident in the non-DHP CCB group, and the prognostic differences between the DHP and the non-DHP-CCB groups was not demonstrated.

The findings from Kim et al[12] are of clinical importance. First, they reconfirmed the beneficial effect of BB therapy for AMI patients with reduced LVEF, as previous studies had reported.[1-3] Second, they demonstrated that CCB therapy does not increase adverse cardiovascular events for AMI patients with preserved LVEF, compared with BB therapy. The beneficial effect of CCB therapy for AMI might be due to suppressing vasospasm. Indeed, vasospastic angina has been shown to be more prevalent in East Asia as compared to Western countries,[11] and it has been demonstrated that cardiovascular events were comparable between DHP-CCB and BB therapies after AMI in Japan,[11] which was consistent to the findings by Kim et al[12] in Korea. Therefore, CCB therapy can be considered as an alternative to BB therapy for those patients, especially in East Asia.

Despite the potentially important clinical implication of the findings by Kim et al,[12] there are some limitations that should be considered. Indeed, this study was nonrandomized and observational data, and the reason why physicians had prescribed CCB instead of BB at discharge as well as the dosages were not available. Therefore, unmeasured potential confounders, residual variables, and selection bias could not be fully controlled, even after adjustment by propensity matching. Moreover, it was possible that the sample size, especially in the DHP CCB group, or the duration of follow-up might be not enough to evaluate the prognostic impact of CCB therapy compared with BB therapy.

Another limitation is the uncertainness of the prognostic impact of BB therapy for AMI patients with preserved LVEF. A meta-analysis found that the use of BB for ≥1 year does not decrease mortality in patients with patients without heart failure in the reperfusion era.[13] Moreover, another Korean registry study demonstrated that BB therapy at discharge was associated with lower 1-year major adverse cardiac and cerebrovascular events in patients with a reduced LVEF (<40%) and mid-range LVEF (40%-50%), but not in patients with a preserved LVEF (>50%).[14] Based on these findings, BB therapy may not yield beneficial effects on AMI patients with an EF of >50%, and CCB may not be also influential in these patients.

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