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ORIGINAL RESEARCH

Clinical Outcomes of Calcium-Channel Blocker vs Beta-Blocker

From the Korean Acute Myocardial Infarction Registry

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ABSTRACT

BACKGROUND Although current guidelines recommend beta-blockers (BBs) after acute myocardial infarction (AMI), the role of calcium-channel blockers (CCBs) has not been well investigated, especially nondihydropyridine.

OBJECTIVES This study aimed to compare the effects of CCBs on cardiovascular outcomes compared with BBs in AMI because patients from East Asia have a higher incidence of a vasospastic angina component compared with Western countries.

METHODS Among 15,628 patients enrolled in the KAMIR-V (Korean Acute Myocardial Infarction Registry-V), we evaluated 10,650 in-hospital survivors who were treated with either CCBs or BBs. We applied a propensity score for 1:4 pair matching of baseline covariates and Cox regression to compare CCBs and BBs. The primary endpoint was all-cause death at 1 year. The secondary endpoints were 1-year major adverse cardiac and cerebrovascular events, which was the composite of cardiac death, myocardial infarction, revascularization, and readmission due to heart failure and stroke.

RESULTS There was a significant interaction with the treatment arm with left ventricular ejection fraction (LVEF) (P for interaction = 0.011). CCB groups at discharge had higher 1-year cardiac death and major adverse cardiac and cerebrovascular events for patients with LVEF <50% (HR: 4.950; 95% CI: 1.329-18.435; $P = 0.017$; and HR: 1.810; 95% CI: 1.038-3.158; $P = 0.037$, respectively) but not for patients with LVEF ≥50% (HR: 0.699; 95% CI: 0.435-1.124; $P = 0.140$).

CONCLUSIONS CCB therapy did not increase adverse cardiovascular events for patients after AMI with preserved LVEF. CCBs can be considered as an alternative for BBs in East Asian patients after AMI with preserved LVEF.
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Calcium-channel blockers (CCBs) and beta-blockers (BBs) are used to prevent angina attack or reduce angina symptoms. However, in patients with suspected/confirmed vasospastic angina, CCBs and nitrates should be considered, and BBs should be avoided (Class IIa, Level of Evidence: B).[1] The current American College of Cardiology Foundation/American Heart Association guideline for ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation acute

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coronary syndromes states that BBs are a Class I indication.[2,3] The evidence for beneficial effects is based on early studies in the prereperfusion era. The European Society of Cardiology guideline recommends BBs for patients without contraindications and with systolic left ventricular dysfunction or heart failure (HF) with reduced left ventricular ejection fraction (LVEF) (Class I, Level of Evidence: A).[4,5]

In the reperfusion era, the use of CCBs among post-acute myocardial infarction (AMI) patients has not been well described, especially for non-dihydropyridine (DHP). The incidence of variant angina in Korea and Japan is higher than in Western countries,[6,7] including acute coronary syndrome.[8,9] We sought to assess the efficacy of CCB therapy in AMI in the modern reperfusion era and compare it with that of BB therapy.

METHODS

STUDY POPULATION AND STUDY DESIGN. This study analyzed data from the KAMIR-V (Korean Acute Myocardial Infarction Registry-V), which is a nation-wide multicenter registry of patients with AMI in Korea from 43 centers that has been previously described.[10] From January 2016 to June 2020, a total of 15,628 consecutive patients with AMI were enrolled in this registry. CCB therapy included amlodipine (n = 186), amlodipine plus diltiazem (n = 9), benidipine (n = 8), cilnidipine (n = 7), diltiazem (n = 489), lacidipine plus diltiazem (n = 1), efonidipine (n = 4), felodipine (n = 1), lacidipine (n = 3), lercanidipine (n = 2), manidipine (n = 4), nifedipine (n = 22), nifedipine plus diltiazem (n = 1), and nisoldipine (n = 2). Reasons for exclusion for the analysis were: 1) in-hospital death (n = 510); 2) no follow-up after hospital discharge (n = 1,369); 3) those who were prescribed CCB and BB therapy (n = 649) at discharge; and 4) those who were not prescribed CCB and BB therapy (n = 2,450). In total, 10,650 patients were included in this study (Figure 1). Furthermore,

ABBREVIATIONS AND ACRONYMS

AMI = acute myocardial infarction

BB = beta-blocker

CCB = calcium-channel blocker

DHP = dihydropyridine

EF = ejection fraction

HF = heart failure

LVEF = left ventricular ejection fraction

MACCE = major adverse cardiovascular and cerebrovascular event(s)

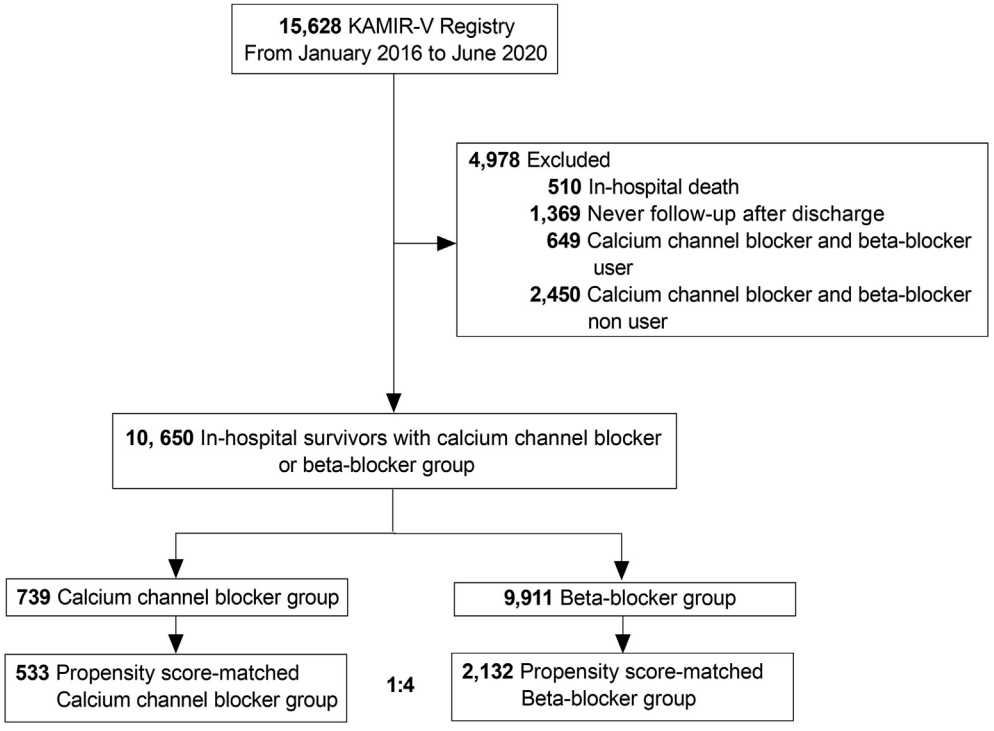
MI = myocardial infarction

PCI = percutaneous coronary intervention

PS = propensity score

STEMI = ST-segment elevation myocardial infarction

FIGURE 1 Flow Chart of Group Distribution for Analysis



From the KAMIR-V (Korean Acute Myocardial Infarction Registry-V), a total of 15,628 patients were evaluated. After excluding the patients who died in hospital, did not revisit the hospital, were prescribed calcium-channel blocker (CCB) and beta-blocker (BB) therapy, and were not prescribed CCB and BB therapy, the data from 10,650 patients were included in the analysis. Among them, 739 and 9,911 patients were further classified into the CCB and BB groups, respectively. The propensity score matching was presented with all parameters shown in Table 1.

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TABLE 1 Baseline Characteristics of CCB and BB Therapy Groups

	Before PSM				After PSM			
	CCB (n = 739)	BB (n = 9,911)	*P* Value	SMD	CCB (n = 533)	BB (n = 2,132)	*P* Value	SMD
Age, y	62.9 ± 11.9	63.1 ± 12.2	0.632	0.018	62.6 ± 11.6	62.9 ± 12.3	0.558	0.018
Male	550 (74.4)	7,788 (78.6)	0.008	0.098	402 (75.4)	1,623 (76.1)	0.734	0.016
Hypertension	403 (54.5)	4,767 (48.1)	0.001	0.129	295 (55.3)	1,134 (53.2)	0.372	0.043
Diabetes mellitus	184 (24.9)	2,631 (26.5)	0.327	0.038	146 (27.4)	522 (24.5)	0.166	0.066
Dyslipidemia	124 (16.8)	1,430 (14.4)	0.081	0.065	90 (16.9)	343 (16.1)	0.655	0.021
Prior angina pectoris	133 (18.0)	623 (6.3)	<0.001	0.364	67 (12.6)	251 (11.8)	0.612	0.024
Prior myocardial infarction	80 (10.8)	576 (5.8)	<0.001	0.182	54 (10.1)	184 (8.6)	0.277	0.051
Prior heart failure	5 (0.7)	99 (1.0)	0.390	0.035	4 (0.8)	16 (0.8)	>0.999	0.000
Prior stroke	45 (6.1)	570 (5.8)	0.704	0.014	35 (6.6)	137 (6.4)	0.906	0.006
Current smoker	246 (33.3)	3,907 (39.4)	0.001	0.128	184 (34.5)	790 (37.1)	0.277	0.053
Killip class ≥II	60 (8.1)	1,629 (16.4)	<0.001	0.255	52 (9.8)	209 (9.8)	0.974	0.002
Creatinine, mg/dL	1.1 ± 1.1	1.1 ± 1.1	0.681	0.016	1.1 ± 1.1	1.1 ± 1.0	0.582	0.016
LVEF	53.5 ± 10.7	52.6 ± 10.8	0.027	0.088	53.3 ± 10.7	53.1 ± 10.9	0.702	0.088
STEMI	171 (23.1)	5,037 (50.8)	<0.001	0.599	146 (27.4)	608 (28.5)	0.576	0.025
Thrombolysis and/or PCI	574 (77.7)	8,982 (90.6)	<0.001	0.360	450 (84.4)	1,790 (84.0)	>0.999	0.013
Medications at discharge								
Aspirin	701 (94.9)	9,872 (99.6)	<0.001	0.293	530 (99.4)	2,120 (99.4)	>0.999	0.000
$P2Y_{12}$ inhibitor	698 (94.5)	9,856 (99.4)	<0.001	0.293	529 (99.2)	2,111 (99.0)	0.615	0.025
RAS inhibitor	405 (54.9)	8,075 (81.5)	<0.001	0.596	361 (67.7)	1,420 (66.6)	0.622	0.024
Statin	650 (88.0)	9,579 (96.7)	<0.001	0.331	499 (93.6)	2,010 (94.3)	0.564	0.028

Values are mean ± SD or n (%).

BB = beta-blocker; CCB = calcium-channel blocker; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention; PSM = propensity score matching; RAS = renin-angiotensin system; STEMI = ST-segment elevation myocardial infarction; SMD = standardized mean difference.

subjects were divided into CCB (n = 739) and BB (n = 9,911) groups in this registry. The BBs administered included atenolol (n = 11), betaxolol (n = 1), bisoprolol (n = 2,985), carvedilol (n = 4,440), celiprolol (n = 1), metoprolol (n = 30), nadolol (n = 1), nebivolol (n = 2,432), and propranolol (n = 10). After excluding 5,228 patients, 10,400 patients were included in non-DHP or BB group (Supplemental Figure 1). Our study was conducted according to principles outlined in the Declaration of Helsinki. The local Institutional Review Board at each hospital approved the study protocol, and written informed consent was obtained from all patients (DAUHIRB-16098).

CLINICAL ENDPOINT AND DEFINITION. The primary endpoint was 1-year all-cause death. The secondary endpoints were 1-year major adverse cardiac and cerebrovascular events (MACCE), which was the composite of cardiac death, myocardial infarction (MI), revascularization, readmission due to HF, and stroke. All deaths were considered to be cardiac, unless a definite noncardiac cause was established. MI included reinfarction or recurrent MI. Revascularization included either target or nontarget vessels with percutaneous coronary intervention (PCI) or coronary artery bypass grafting. Staged or scheduled PCI was not classified as revascularization. Follow-up was routinely performed at 6 and 12 months with clinic visits and whenever any clinical event occurred. Clinical events were adjudicated by the principal investigator at each hospital.

STATISTICAL ANALYSIS. Data are expressed as mean ± SD for continuous variables and as number (percentage) for categorical variables. Data were compared using an unpaired *t*-test for continuous variables and a chi-square test for categorical variables. Survival curves for clinical endpoints and cumulative event rates with incidence rates were generated using the Kaplan-Meier estimates. HRs and their 95% CIs for each clinical endpoint were calculated using Cox proportional hazards analysis. The Cox proportional hazards model was used to compare the HR for each endpoint in use of CCBs or non-DHP CCBs and use of BBs.

We used propensity score (PS) matching to account for confounding by indication. Because CCB and BB therapy were not randomized, a PS was used to adjust for selection or predisposition bias. The PS was estimated using multiple logistic regression analysis with all variables in Tables 1 and 2. Each CCB user was

TABLE 2 Baseline Characteristics of Non-DHP CCB and BB Therapy Groups

	Before PSM				After PSM			
	Non-DHP CCB (n = 489)	BB (n = 9,911)	*P* Value	SMD	Non-DHP CCB (n = 365)	BB (n = 1,460)	*P* Value	SMD
Age, y	61.6 ± 11.7	63.1 ± 12.2	0.005	0.128	62.0 ± 11.7	61.6 ± 12.2	0.565	0.018
Male	367 (75.1)	7,788 (78.6)	0.064	0.084	280 (76.7)	1,121 (76.8)	0.978	0.002
Hypertension	224 (45.8)	4,767 (48.1)	0.322	0.046	169 (46.3)	654 (44.8)	0.605	0.030
Diabetes mellitus	98 (20.0)	2,631 (26.5)	0.001	0.154	79 (21.6)	280 (19.2)	0.289	0.061
Dyslipidemia	68 (13.9)	1,430 (14.4)	0.748	0.015	56 (15.3)	217 (14.9)	0.818	0.013
Prior angina pectoris	91 (18.6)	623 (6.3)	<0.001	0.380	50 (13.7)	170 (11.6)	0.281	0.062
Prior myocardial infarction	48 (9.8)	576 (5.8)	<0.001	0.150	34 (9.3)	127 (8.7)	0.710	0.022
Prior heart failure	3 (0.6)	99 (1.0)	0.399	0.043	3 (0.8)	11 (0.8)	0.893	0.008
Prior stroke	12 (2.5)	570 (5.8)	0.002	0.167	11 (3.0)	40 (2.7)	0.776	0.016
Current smoker	174 (35.6)	3,907 (39.4)	0.090	0.079	137 (37.5)	577 (39.5)	0.487	0.041
Killip class ≥II	39 (8.0)	1,629 (16.4)	<0.001	0.261	37 (10.1)	125 (8.6)	0.344	0.016
Creatinine, mg/dL	1.0 ± 1.0	1.1 ± 1.1	0.063	0.089	1.1 ± 1.1	1.0 ± 0.8	0.088	0.088
LVEF	51.4 ± 10.4	52.6 ± 10.8	0.020	0.114	51.4 ± 10.6	51.4 ± 10.9	0.544	0.054
STEMI	123 (25.2)	5,037 (50.8)	<0.001	0.548	111 (30.4)	460 (31.5)	0.668	0.024
Thrombolysis or/and PCI	389 (79.6)	8,982 (90.6)	<0.001	0.315	305 (83.6)	1,220 (83.6)	>0.999	0.000
Medications at discharge								
Aspirin	456 (93.3)	9,872 (99.6)	<0.001	0.348	362 (99.2)	1,445 (99.0)	0.722	0.021
$P2Y_{12}$ inhibitor	454 (92.8)	9,856 (99.4)	<0.001	0.348	361 (98.9)	1,444 (98.9)	>0.999	0.000
RAS inhibitor	228 (46.7)	8,075 (81.5)	<0.001	0.777	209 (57.3)	823 (56.4)	0.759	0.018
Statin	422 (86.3)	9,579 (96.7)	<0.001	0.377	337 (92.3)	1,368 (93.7)	0.345	0.054

Values are mean ± SD or n (%).
Abbreviations as in Table 1.

matched 1:4 without replacement with a BB user to the nearest based on a PS with 0.1 SD. The efficacy of the PS model was assessed by estimating standardized differences for each covariate between the 2 groups. Data manipulation and statistical analyses were conducted using SAS version 9.3 (SAS Institute) and R software version 4.1.1 (R Foundation for Statistical Computing). Statistical significance was set at *P* value <0.05.

RESULTS

Tables 1 and 2 summarize the characteristics of the 10,650 and 10,400 AMI patients. Patients in the BB group had lower ejection fraction (EF), less hypertension, less prior angina, less prior MI, more men, more STEMI, more Killip class ≥II, more current smokers, and thrombolysis and/or PCI. They were taking more aspirin, $P2Y_{12}$ inhibitors, RAS inhibitors, and statins (Table 1). Compared with the non-DHP group, patients with BBs were older and had higher EF, less prior angina, less prior MI, more diabetes mellitus, more prior stroke, more Killip class ≥II, more STEMI, and thrombolysis or/and PCI. Aspirin, $P2Y_{12}$ inhibitor, RAS inhibitor, and statin treatment was less frequently used in the non-DHP group (Table 2).

After PS matching, baseline characteristics of the 2 groups became balanced (Tables 1 and 2).

CLINICAL OUTCOMES. The follow-up duration was 12 months. In a 1:4 PS-matched population, there were no significant differences in the incidence of all-cause death (2.8% vs 2.2%; HR: 1.284; 95% CI: 0.718-2.296; $P = 0.400$), cardiac death (1.9% vs 1.3%; HR: 1.488; 95% CI: 0.720-3.074; $P = 0.283$), MI (1.3% vs 1.7%; HR: 0.755; 95% CI: 0.337-1.694; $P = 0.496$), revascularization (3.4% vs 3.6%; HR: 0.935; 95% CI: 0.559-1.561; $P = 0.796$), HF (1.7% vs 1.8%; HR: 0.927; 95% CI: 0.449-1.914; $P = 0.838$), stroke (0.9% vs 1.0%; HR: 0.909; 95% CI: 0.344-2.400; $P = 0.847$), and MACCE (7.1% vs 7.3%; HR: 0.986; 95% CI: 0.692-1.406; $P = 0.939$) between the CCB and BB groups (Table 3, Central Illustration). In addition, the difference between the non-DHP CCB and BB therapy groups was not statistically significant in the incidences of all-cause death (1.9% vs 2.0%; HR: 0.965; 95% CI: 0.423-2.203; $P = 0.933$), cardiac death (0.5% vs 0.8%; HR: 0.666; 95% CI: 0.149-2.975; $P = 0.594$), MI (0.5% vs 1.2%; HR: 0.444; 95% CI: 0.103-1.913; $P = 0.276$), revascularization (2.2% vs 3.0%; HR: 0.725; 95% CI: 0.341-1.540; $P = 0.403$), HF (1.4% vs 1.9%; HR: 0.714; 95% CI: 0.276-1.850; $P = 0.488$), stroke (1.1% vs 1.0%; HR: 1.069; 95% CI: 0.355-3.220; $P = 0.906$), and MACCE

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TABLE 3 Clinical Outcomes in the PSM Population Comparing the CCB and BB Groups

	CCB (n = 533)	BB (n = 2,132)	HR (95% CI)	*P* Value
All-cause death	15 (2.8)	47 (2.2)	1.284 (0.718-2.296)	0.400
Cardiac death	10 (1.9)	27 (1.3)	1.488 (0.720-3.074)	0.283
Myocardial infarction	7 (1.3)	37 (1.7)	0.755 (0.337-1.694)	0.496
Revascularization	18 (3.4)	77 (3.6)	0.935 (0.559-1.561)	0.796
Heart failure[a]	9 (1.7)	39 (1.8)	0.927 (0.449-1.914)	0.838
Stroke	5 (0.9)	22 (1.0)	0.909 (0.344-2.400)	0.847
MACCE	38 (7.1)	155 (7.3)	0.986 (0.692-1.406)	0.939

Values are n (%). The primary endpoint was 1-year all cause death. The secondary endpoints were 1-year MACCE, which was a composite of cardiac death, myocardial infarction, revascularization, and readmission due to heart failure and stroke. [a]Rehospitalization due to heart failure.

MACCE = major adverse cardiac and cerebrovascular event(s); other abbreviations as in Table 1.

(4.7% vs 6.6%; HR: 0.696; 95% CI: 0.416-1.166; P = 0.169) (Table 4, Central Illustration).

SUBGROUP ANALYSIS OF PS-MATCHED POPULATION. There was a significant interaction between the treatment arm and EF with regard to the clinical endpoint of cardiac death and MACCE (P for interaction = 0.038 and 0.011, respectively). The incidences of 1-year cardiac death and MACCE were significantly higher in patients who were treated with CCBs in the EF <50% group (Supplemental Table 1). However, the CCB group tended to be associated with a lower risk of clinical outcomes compared with the BB group with EF ≥50% (Supplemental Table 1).

Similarly, this trend was consistent in non-DHP CCBs with respect to each clinical outcome, without a significant interaction between the treatment arms (non-DHP CCBs vs BBs). No significant interaction was identified between the treatment arms and EF with regard to the clinical endpoint (Supplemental Table 2). Also, there was no significant difference in clinical outcomes between DHP CCB group and non-DHP CCB group (Supplemental Table 3).

The CCB group showed an interaction with prior MI and EF (P for interaction = 0.017 and 0.039, respectively). The other subgroup did not interact significantly between the treatment arms and had comparable rates of MACCE (Figure 2). There was no significant interaction between the treatment arms with regard to the second endpoint of MACCE, except for prior MI status (Supplemental Figure 2).

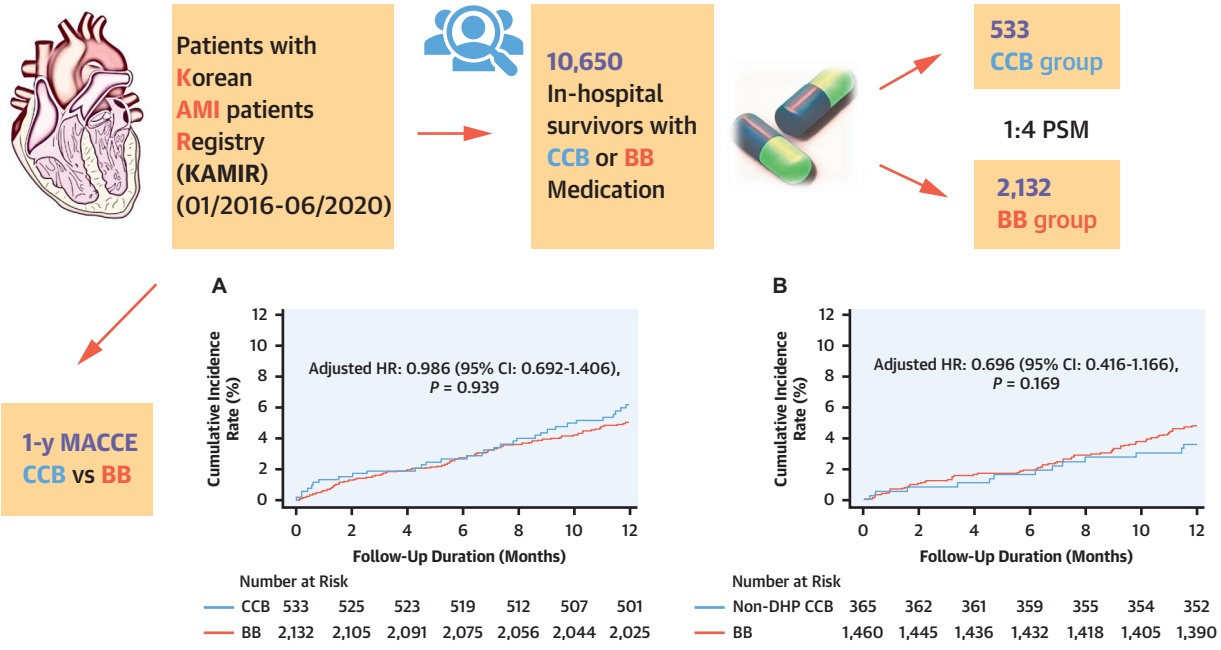
DISCUSSION

This study, which was based on a nationwide multicenter registry, showed that there was no significant difference between CCB and BB therapy in the incidences of cardiovascular outcomes among patients who experienced AMI with preserved LVEF. Of note, non-DHP therapy (diltiazem) also showed a comparable and tendency to have lower 1-year clinical outcomes (MACCE) compared with the BB therapy group after AMI. To the best of our knowledge, these are the first registry-based data to explore the usefulness of CCB (especially diltiazem) usage after AMI.

CCBs are a heterogeneous group of drugs used in different cardiovascular disorders such as angina pectoris, hypertension, hypertrophic cardiomyopathy, and supraventricular arrhythmias.[11] A multiple randomized trial showed that amlodipine decreased the number of angina attacks, reduced the consumption of nitroglycerin, and increased exercise capacity.[12] The ACTION (A Coronary disease Trial Investigating Outcome with Nifedipine gastrointestinal therapeutic system) demonstrated that treatment with nifedipine had no effect on major cardiovascular event-free survival.[13] In the preperfusion era, a randomized trial showed that diltiazem was safe and effective in preventing early reinfarction and severe angina after non-Q-wave infarction for up to 14 days.[14] However, another randomized trial demonstrated that diltiazem only reduced all composite endpoints of nonfatal cardiac events, especially the need for myocardial revascularization, which mentioned that approximately 90% of patients received thrombolysis.[15]

BBs decrease myocardial oxygen demand, decreasing the incidence of fatal arrhythmias and improving ventricular remodeling.[16] It has long been considered the standard of care for patients with AMI. However, this concept is largely based on prereperfusion studies. Several large randomized controlled trials have convincingly demonstrated the efficacy and safety of BBs in the management of patients after AMI. A randomized trial in Norway showed that long-term treatment with timolol in patients surviving AMI reduces mortality and the incidence of reinfarction.[17] The BHAT (Beta-Blocker Heart Attack Trial) showed that cardiovascular mortality was reduced in the propranolol therapy group when compared with placebo group.[18] A meta-analysis that mostly included trials demonstrated that long-term BB therapy for more than 6 months was associated with a reduction in mortality.[19] However, those studies were conducted in the prereperfusion era. In the reperfusion era, few randomized trials have focused on this issue. The CAPRICORN (Carvedilol Post-Infarct Survival Control in LV Dysfunction) trial included predominantly Caucasian patients.[20] However, half of the 1,959 patients underwent thrombolysis or primary angioplasty. Carvedilol therapy was associated with a 23% and 41% reduction in incidences of all-cause death and nonfatal MI,

CENTRAL ILLUSTRATION **1-Year MACCE of CCB vs BB Therapy**



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Kaplan-Meier curves and adjusted HR for major adverse cardiac and cerebrovascular events (MACCE) at 1 year. **(A)** Calcium-channel blocker (CCB) vs beta-blocker (BB). **(B)** Non-DHP CCB vs BB. PSM = propensity score matching.

respectively, at a median follow-up of 1.3 years. The COMMIT (Clopidogrel and Metoprolol in Myocardial Infarction Trial) showed that more than half of all patients who received fibrinolysis and early intravenous BB treatment had a reduced risk of acute malignant ventricular arrhythmias, but there was no difference in death between the metoprolol and placebo groups.[21] A meta-analysis of 48 randomized trials showed a reduction in mortality with BBs in the prereperfusion era. However, the analysis of 12 randomized trials in the reperfusion era, each of which had a small sample size (except for the COMMIT trial), showed no difference in mortality with BB therapy. In contrast, BBs increased the risk of HF or cardiogenic shock in the reperfusion era.[22] Korean registry data showed that BB therapy decreased all-cause or cardiac death at a median 1-year follow up in STEMI patients undergoing primary PCI.[23] However, an interaction with LVEF was not observed in these patients. Another Korean registry dataset demonstrated that BB therapy at discharge was associated with lower 1-year MACE in patients with reduced LVEF (≤40%) and midrange LVEF (>40%, <50%) but not in patients with preserved LVEF (≥50%).[24] These data suggest that long-term BB therapy may be guided by LVEF. A meta-analysis found that the use of oral BBs for 1 year or more does not reduce the mortality of MI patients without HF in the modern reperfusion era.[25]

The role of CCBs in patients with AMI is even more unclear in the modern reperfusion era, especially for non-DHP CCBs. There are no randomized trials

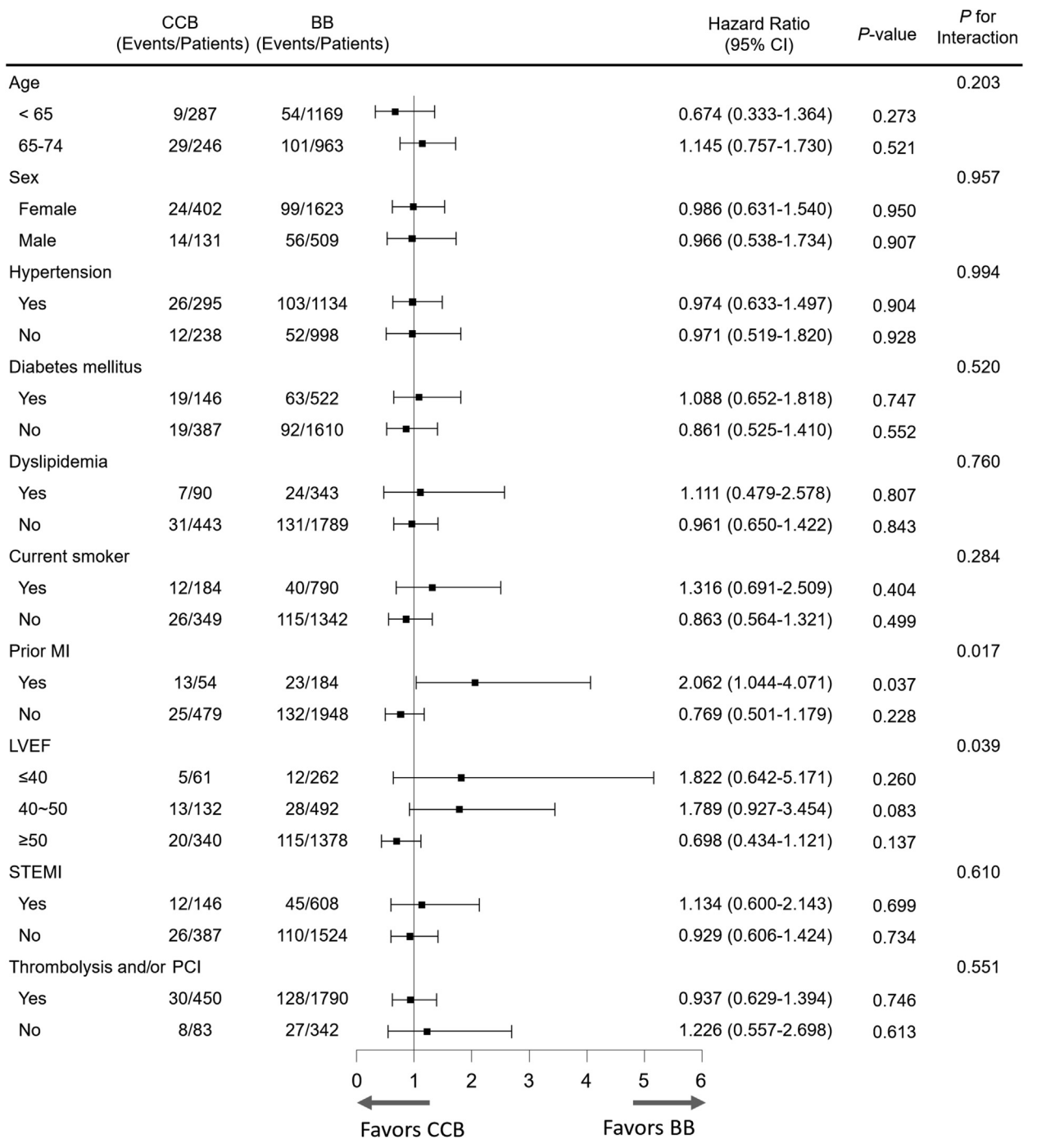
TABLE 4 **Clinical Outcomes in the PSM Population Comparing the Non-DHP CCB and BB Groups**

	Non-DHP CCB (n = 365)	BB (n = 1,460)	HR (95% CI)	*P* Value
All-cause death	7 (1.9)	29 (2.0)	0.965 (0.423-2.203)	0.933
Cardiac death	2 (0.5)	12 (0.8)	0.666 (0.149-2.975)	0.594
Myocardial infarction	2 (0.5)	18 (1.2)	0.444 (0.103-1.913)	0.276
Revascularization	8 (2.2)	44 (3.0)	0.725 (0.341-1.540)	0.403
Heart failure[a]	5 (1.4)	28 (1.9)	0.714 (0.276-1.850)	0.488
Stroke	4 (1.1)	15 (1.0)	1.069 (0.355-3.220)	0.906
MACCE	17 (4.7)	97 (6.6)	0.696 (0.416-1.166)	0.169

Values are n (%). The primary endpoint was 1-year all cause death. The secondary endpoints were 1-year MACCE, which was a composite of cardiac death, myocardial infarction, revascularization, and readmission due to heart failure and stroke. [a]Rehospitalization due to heart failure.

Abbreviations as in Tables 1 and 3.

FIGURE 2 **1-Year Major Adverse Cardiac and Cerebrovascular Events for Propensity Score-Matched Populations With the Treatment Arms**



HRs of 1-year major adverse cardiac and cerebrovascular events for subgroups in propensity score matching using the CCB and BB groups. LVEF = left ventricular ejection fraction; MI = myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction; other abbreviations as in Figure 1.

comparing the safety and efficacy between non-DHP and BB therapy after AMI in the modern reperfusion era. In our study, CCB therapy showed similar cardiovascular outcomes compared with BB therapy in the modern reperfusion era, which was in agreement with a previous study, which did not include non-DHP.[26]

CCBs inhibit L-type calcium flow into arterial smooth cells, which causes coronary vasodilation and control angina and coronary spasm. The afterload reduction, and in the case of non-DHP CCBs, the suppressant effects on the sinoatrial node and myocardium, also contribute to antianginal effects.[27] The primary mechanism whereby BBs reduce ischemia is the reduction of myocardial oxygen demand by lowering heart rate and myocardial wall stress and contractility.[11] Based on these beneficial mechanisms, non-DHP CCBs may decrease revascularization as well as BBs. Patients with preserved LVEF had small infarcts, and the clinical benefit of BB therapy was inevitably reduced in these patients.[28] Thus, CCBs or non-DHP had the same effect as BBs.

STUDY LIMITATIONS. First, this study analyzed nonrandomized, observational registry data. Second, data on why physicians prescribed CCBs instead of BBs at discharge as well as the dosages were not available. Third, patient compliance was not confirmed. Fourth, we attempted to adjust for potential confounders through the PS-matched analysis, but other unmeasured, residual variables, and selection bias could not be fully controlled. Fifth, this study could not examine the precise beneficial effect of CCBs for AMI patients. Sixth, subgroup analysis was limited due to the small sample size of the non-DHP CCB group based on EF. Seventh, the duration of follow-up was short (1 year) and may not have been long enough to demonstrate differences in efficacy between CCB and BB therapy. Last, cardioprotective diabetic drugs (especially sodium-glucose cotransporter-2 inhibitors) were not fully evaluated due to a low prescription rate.

CONCLUSIONS

Our study demonstrates that CCB therapy does not increase adverse cardiovascular events after AMI with preserved LVEF. CCBs can be considered as an alternative for BBs in East Asian patients after AMI with preserved LVEF.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: CCB therapy did not increase adverse cardiovascular events after AMI with preserved LVEF. CCBs can be considered as an alternative for BBs in East Asians after AMI with preserved LVEF.

TRANSLATIONAL OUTLOOK: Longer-term follow-up and large-scale studies are needed to evaluate clinical outcomes, especially based on EF. Furthermore, randomized trials are needed to clarify the safety and efficacy of CCB and BB therapy with preserved EF, especially for non-DHP CCBs.

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KEY WORDS acute myocardial infarction, beta-blocker, calcium-channel blocker, clinical outcomes

APPENDIX For supplemental tables and figures, please see the online version of this paper.