Beta-blockers in Patients with Mid-range Left Ventricular Ejection Fraction after AMI Improved Clinical Outcomes

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Disclosure of Interest

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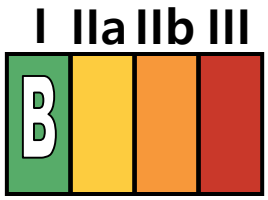
- All investigators; Nothing to disclose

Recommendations of Beta-Blockers in AMI

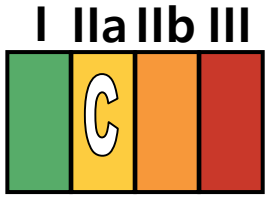
ACC/AHA STEMI guideline (*Circulation.* 2013;127:529-555)

Beta blockers should be continued during and after hospitalization for all patients with STEMI and with no contraindications to their use.

ACC/AHA NSTEMI guideline (*Circulation.* 2014;130:2354-94)



In patients with concomitant NSTE-ACS, *stabilized* HF, and reduced systolic function, it is recommended to continue beta-blocker therapy with 1 of the 3 drugs proven to reduce mortality in patients with HF: sustained-release metoprolol succinate, carvedilol, or bisoprolol.



It is reasonable to continue beta-blocker therapy in patients with normal LV function with NSTE-ACS.

Recommendations of Beta-Blockers in AMI

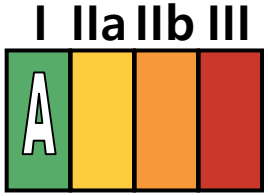
ESC NSTEMI guideline (*Eur Heart J.* 2016;37, 267-315)

Beta-blocker therapy is recommended in patients with LVEF ≤40%, unless contraindicated.

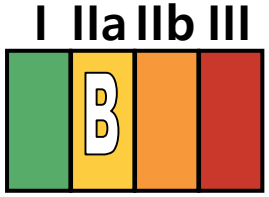
c.f) Beta-blocker after NSTE-ACS and no reduced LV function or HF

In a large-scale observational study, beta-blocker use was not associated with a lower risk of CV events or mortality.

ESC STEMI guideline (*Eur Heart J.* 2017)



Oral treatment with beta-blockers is indicated in patients with heart failure and/or LVEF ≤ 40% unless contraindicated.



Routine oral treatment with beta-blockers should be considered during hospital stay and continued thereafter in all patients without contraindications

Recent Observational Studies and Meta-Analysis about Beta-Blockers in AMI

- β-Blocker use and clinical outcomes in stable outpatients with and without coronary artery disease (*Bangalore S et al. JAMA.* 2012;308:1340-9)

  In this observational study of patients with either CAD risk factors only, known prior MI, or known CAD without MI, the use of β-blockers was not associated with a lower risk of composite cardiovascular events.

- Clinical outcomes with β-blockers for myocardial infarction: a meta-analysis of randomized trials (*Bangalore S et al. Am J Med.* 2014;127:939-53)

  In the reperfusion era, β-blockers were associated with no mortality benefit at most time points except MI and angina at 30 days, a significant increase in HF, cardiogenic shock at 30 days and between 30 days and 1 year.

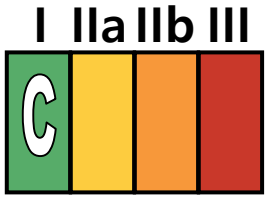
Definition of Heart Failure with Preserved (HFpEF), Mid-range (HFmrEF) and Reduced Ejection Fraction (HFrEF)

Type of HF		HFrEF	HFmrEF	HFpEF
Criteria	1	Symptoms ± Signs	Symptoms ± Signs	Symptoms ± Signs
	2	LVEF <40%	LVEF 40-49%	LVEF ≥50%
	3	-	1. Elevated levels of natriuretic peptides* 2. At least, one additional criterion; a. relevant structural heart disease (LVH and/or LAE) b. diastolic dysfunction	1. Elevated levels of natriuretic peptides* 2. At least, one additional criterion; a. relevant structural heart disease (LVH and/or LAE) b. diastolic dysfunction

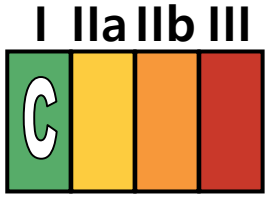
*BNP >35 pg/mL and/or NT-proBNP >125 pg/mL

2016 ESC Guideline. Eur Heart J 2016;37:2129

Recommendations for Treatment of Patients with HFpEF and HFmrEF



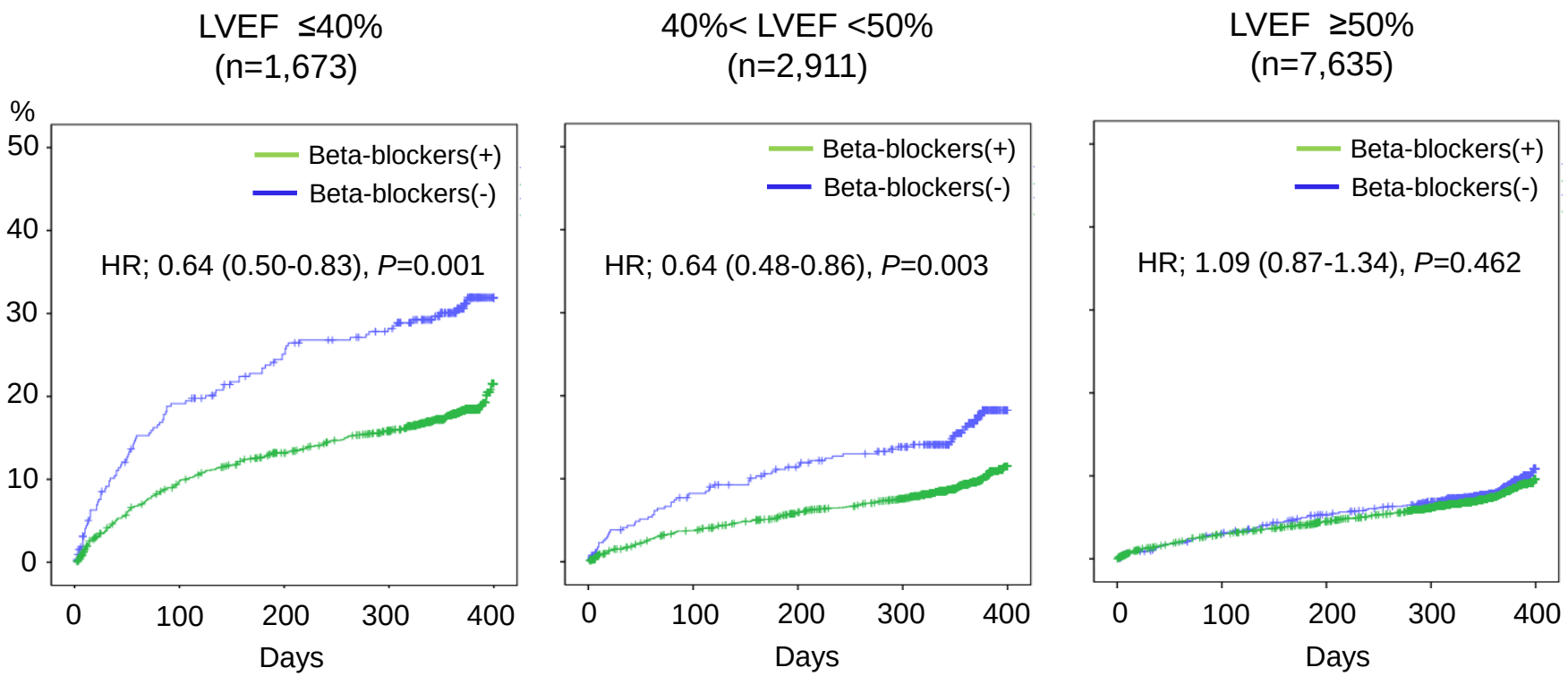
It is recommended to screen patients with HFpEF or HFmrEF for both cardiovascular and non-cardiovascular comorbidities, which, if present, should be treated provided safe and effective interventions exist to improve symptoms, well-being and/or prognosis.



Diuretics are recommended in congested patients with HFpEF or HFmrEF in order to alleviate symptoms and signs.

2016 ESC Guideline. Eur Heart J 2016;37:2129

Beta-blockers reduced MACE in patients with mid-range LVEF after AMI



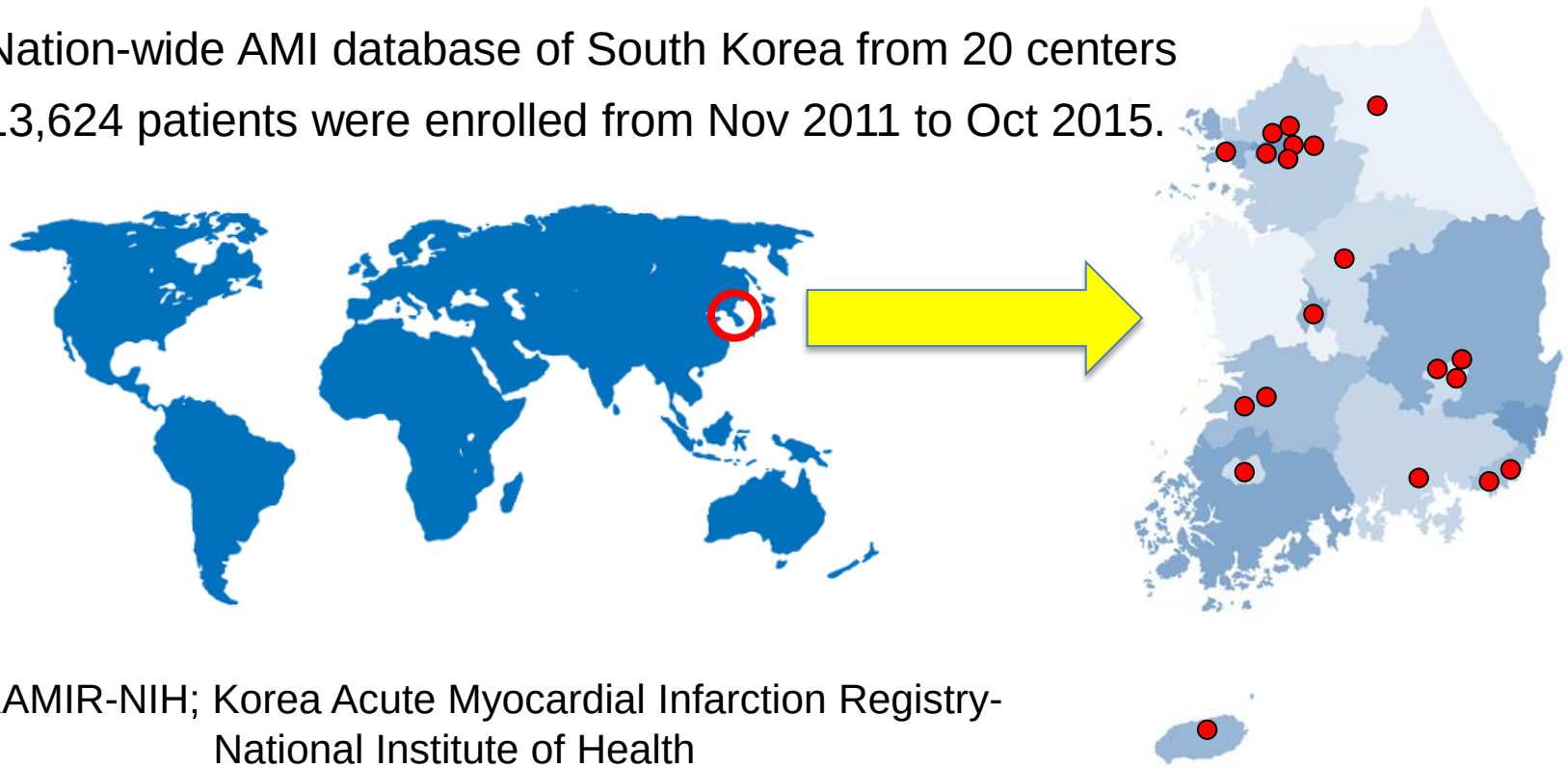
JCR 2017 Presentation

Background and Purposes

- The benefit of oral beta-blockers has been shown only in patients with left ventricular ejection fraction (LVEF) ≤40% after AMI in the era of current evidence-based interventional or medical therapies.
- The role of beta-blockers in patients with mid-range LVEF (40<LVEF<50%) after AMI has been rarely studied.
- This study aimed to investigate the long-term clinical effects of beta-blockers in patients with AMI, especially who survived the initial attack and had mid-range LVEF.

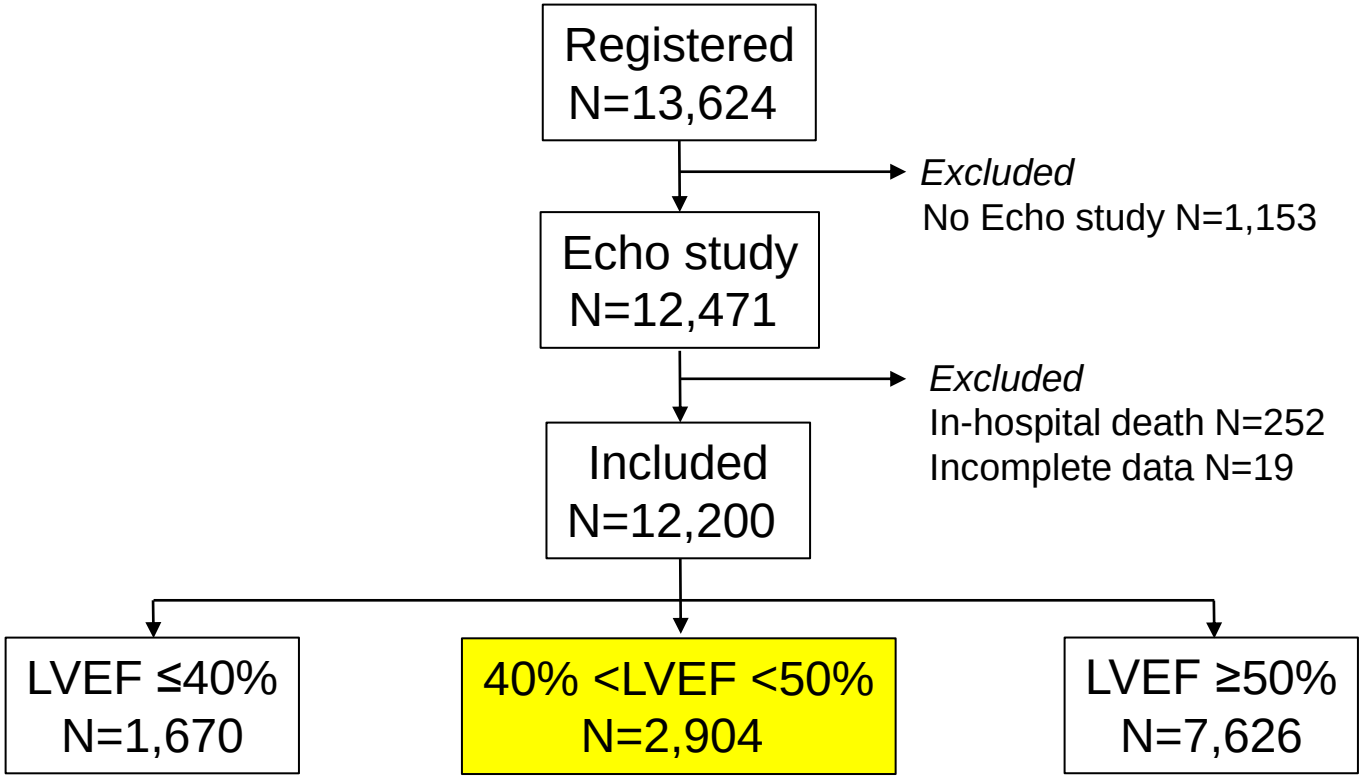
The KAMIR-NIH Registry

- Nation-wide AMI database of South Korea from 20 centers
- 13,624 patients were enrolled from Nov 2011 to Oct 2015.



*KAMIR-NIH; Korea Acute Myocardial Infarction Registry-National Institute of Health

Inclusion of Patients



*LVEF; left ventricular ejection fraction

Primary End-points

- 13-month major adverse cardiac events (MACE)

  A composite of

  - Cardiac death,
  - Myocardial infarction,
  - Revascularization,
  - Re-admission due to heart failure
  - Stent thrombosis

Baseline Characteristics of Patients

	With β-blocker (N=2,508)	Without β-blocker (N=396)	SD	P value
Age (years)	63.8±12.4	67.4±13.1	0.275	<0.001
Male	1,859 (74.1)	271 (68.4)	-0.122	0.020
Body mass index (kg/m^2)	23.98±3.26	23.14±3.18		<0.001
Hypertension	1,208 (48.2)	196 (49.5)	0.027	0.627
Diabetes mellitus	703 (28.0)	107 (27.0)	-0.023	0.718
Hyperlipidemia	243 (9.7)	45 (11.4)		0.319
Prior angina pectoris	201 (8.0)	46 (11.6)	0.112	0.020
Prior myocardial infarction	216 (8.6)	36 (9.1)	0.017	0.773
Prior heart failure	27 (1.1)	4 (1.0)	-0.007	1.000
Prior stroke	170 (6.8)	29 (7.3)	0.021	0.669
Current smoker	1,024 (40.8)	143 (36.1)	-0.098	0.078
Killip class ≥II	550 (21.9)	110 (27.8)	0.162	0.012
eGFR <60 (mL/min/1.73m^2)	450 (17.9)	96 (24.2)	0.150	0.004
Left ventricular EF (%)	45.6±2.5	45.5±2.5	-0.051	0.341
STEMI	1,579 (63.0)	203 (51.3)	-0.234	<0.001
Successful PCI	2,365 (94.3)	336 (84.8)	-0.263	<0.001

Values are mean±standard deviation or number (%).

EF; ejection fraction, eGFR; estimated glomerular filtration rate by Modification of Diet in Renal Disease (MDRD) equation, PCI; percutaneous coronary intervention, SD; standardized difference, STEMI; ST elevation myocardial infarction

Medications Other Than Beta-blockers

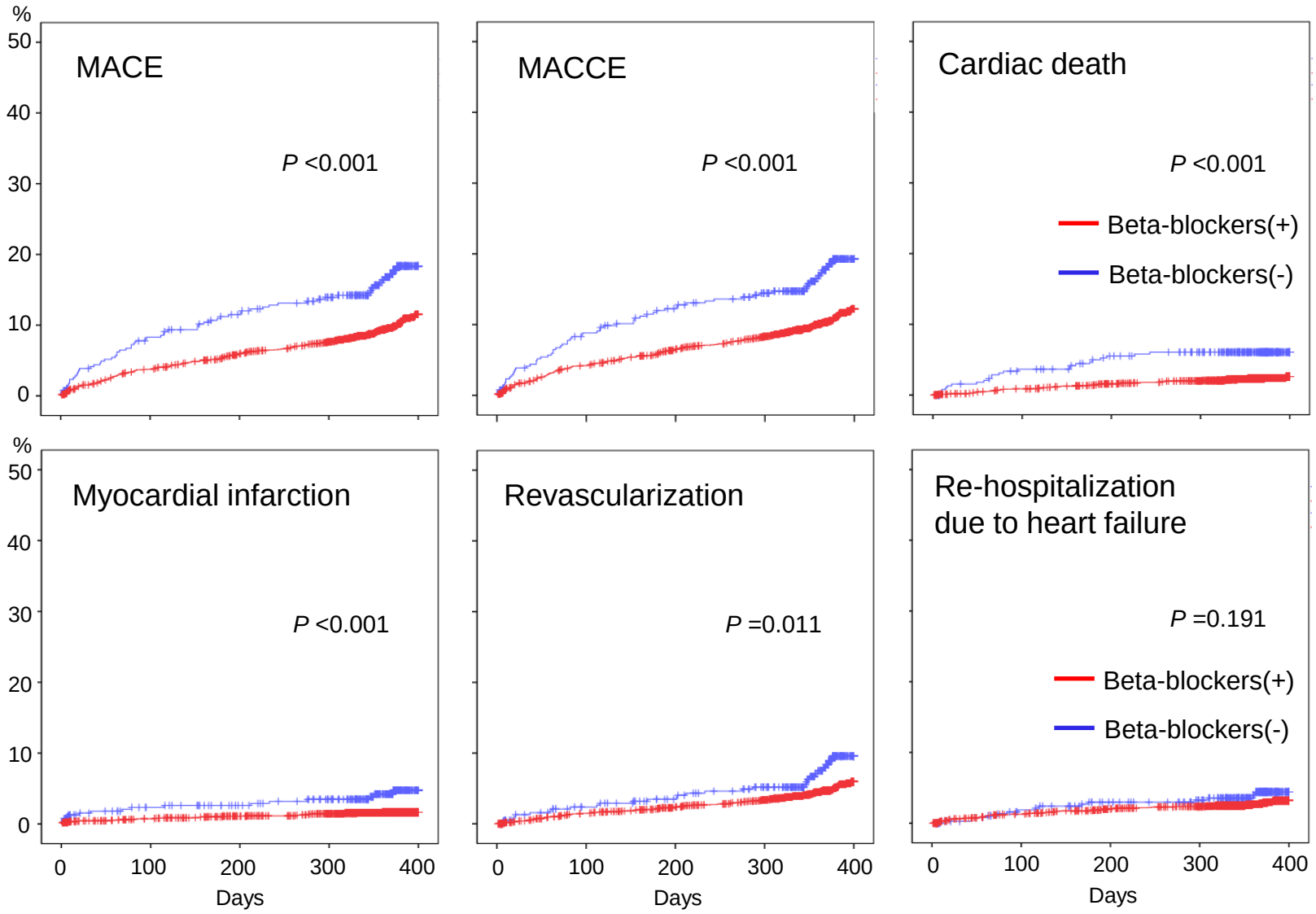
	With β-blocker (N=2,508)	Without β-blocker (N=396)	SD	P value
Aspirin	2,505 (99.9)	394 (99.5)	-0.054	0.140
Clopidogrel	1,972 (78.6)	320 (80.8)		0.353
Prasugrel	312 (12.4)	47 (11.9)		0.806
Ticagrelor	562 (22.4)	91 (23.0)		0.796
P2Y12 inhibitors	2,452 (97.8)	365 (92.2)	-0.208	<0.001
RAS inhibitors	2,103 (83.9)	213 (53.8)	-0.602	<0.001
Statins	2,378 (94.8)	344 (86.9)	-0.235	<0.001
Oral anticoagulants	101 (4.0)	18 (4.5)		0.587

RAS; renin-angiotensin system

Discontinuation of Beta-Blockers

- 13-month follow-up rate
  - Patients with beta-blockers; 96.5%
  - Patients without beta-blockers; 93.9%
- Discontinuation in patients with beta-blockers at discharge
  - 316/2,275 patients (13.9%) **data availability 90.7%*
- New-start in patients without beta-blockers at discharge
  - 129/329 patients (39.2%) **data availability 83.1%*

Kaplan-Meier Survival Curve before PSM



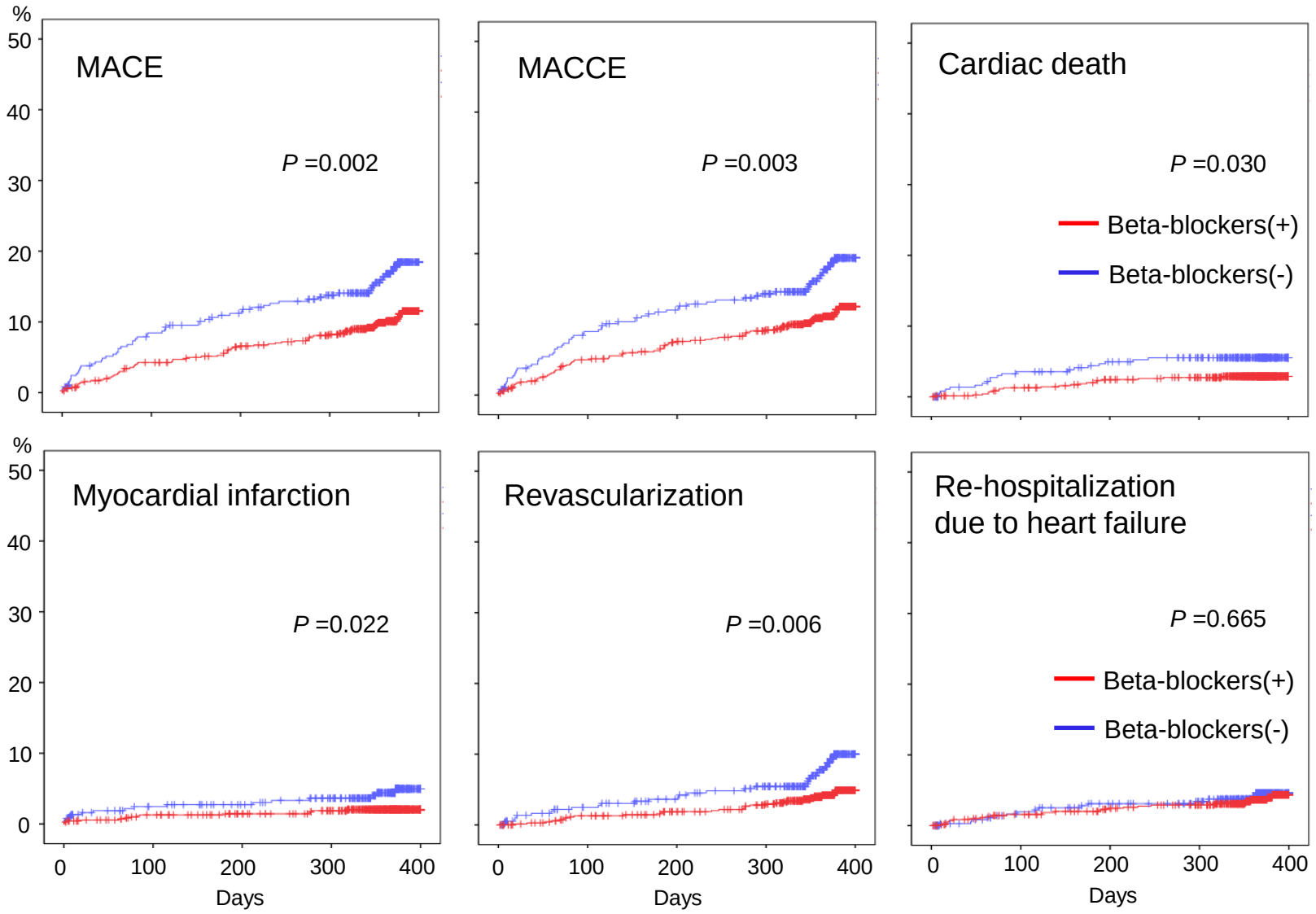
Baseline Characteristics after PSM

	With β-blocker (N=713)	Without β-blocker (N=377)	SD	P value
Age (years)	66.9±11.9	67.3±13.0	-0.007	0.667
Male	481 (67.5)	260 (69.0)	0.040	0.633
Body mass index (kg/m^2)	23.58±3.21	23.20±3.22		0.068
Hypertension	346 (48.5)	185 (49.1)	0.003	0.899
Diabetes mellitus	191 (26.8)	99 (26.3)	-0.024	0.886
Hyperlipidemia	66 (9.3)	44 (11.7)		0.207
Prior angina pectoris	74 (10.4)	40 (10.6)	-0.017	0.917
Prior myocardial infarction	65 (9.1)	32 (8.5)	-0.014	0.823
Prior heart failure	11 (1.5)	4 (1.1)	-0.040	0.596
Prior stroke	47 (6.6)	28 (7.4)	0.015	0.616
Current smoker	247 (34.6)	138 (36.6)	0.047	0.549
Killip class ≥II	174 (24.4)	101 (27.6)	0.065	0.273
eGFR <60 (mL/min/1.73m^2)	161 (22.6)	91 (24.1)	-0.014	0.597
Left ventricular EF (%)	45.6±2.5	45.5±2.5	-0.028	0.708
STEMI	376 (52.7)	201 (53.3)	0.050	0.898
Successful PCI	429 (67.6)	231 (69.4)	0.026	0.611
Aspirin	711 (99.7)	376 (99.7)	0.019	1.000
P2Y12 inhibitors	576 (94.8)	359 (95.2)	0.039	0.885
RAS inhibitors	431 (60.4)	213 (56.5)	-0.016	0.219
Statins	648 (90.9)	335 (88.9)	-0.008	0.285

Values are mean±standard deviation or number (%).

EF; ejection fraction, eGFR; estimated glomerular filtration rate by Modification of Diet in Renal Disease (MDRD) equation, PCI; percutaneous coronary intervention, RAS; renin-angiotensin system, SD; standardized difference, STEMI; ST elevation myocardial infarction,

Kaplan-Meier Survival Curve after PSM



Beta-blockers reduced MACE, MACCE, and Revascularization

	HR	95% CI	*P* value
MACE	0.569	0.400-0.810	0.002
MACCE	0.614	0.437-0.862	0.005
Cardiac death	0.568	0.290-1.112	0.099
Myocardial infarction	0.480	0.229-1.003	0.051
Revascularization	0.482	0.284-0.819	0.007
Re-hospitalization due to HF	0.771	0.400-1.484	0.436
Stent thrombosis	0.671	0.101-4.461	0.680

CI; confidence interval, HF; heart failure, HR; hazard ratio, MACE; major adverse cardiac events, MACCE; major adverse cardiocerebral events

* Multivariate Cox-proportional hazard analysis including age, sex, Killip class, body mass index, hypertension, diabetes mellitus, prior myocardial infarction, prior angina, prior heart failure, smoker, eGFR <60 mL/min/1.73m^2, left ventricular ejection fraction, uses of aspirin, P2Y12 inhibitors, renin-angiotensin system inhibitors, and statins, type of myocardial infarction, and successful percutaneous coronary intervention

Summaries

- Beta-blockers were prescribed in 86%
- Beta-blockers reduced 13-month MACE, MACCE, cardiac death, myocardial infarction, and revascularization on Kaplan-Meier analysis, even in propensity score matched groups
- On Cox-proportional hazard analysis, beta-blockers decreased MACE, MACCE, and revascularization.

Conclusions and Clinical Implications

- Beta-blockers reduced the clinical events in patients with mid-range LVEF after AMI who survived the initial attack.
- Beta-blockers need to be prescribed in patients with mid-range LVEF after AMI.