

Supplemental Material

Supplementary Table 1 Trial Quality and Risk of Bias

	Trial centers	Intention to treat principle	Random sequence generation (risk of selection bias)	Allocation concealment (risk of selection bias)	Blinding (risk of performance bias)	Blinding (risk of detection bias)	Incomplete outcome data (risk of attrition bias)	Selective reporting (risk of reporting bias)
BEAT-AMI ⁵	1	yes	low	low	low	unclear risk	low	low
EARLY-BAMI ⁶	14	yes	low	low	low	low	low	low
Hanada et al. ⁷	1	yes	low	high	high	unclear risk	low	low
METOCARD-CNIC ⁸	7	yes	low	high	high	low	low	low

Supplemetnary Table 2

Baseline characteristics

	BEAT-AMI		EARLY-BAMI		Hanada et al.		METOCARD-CINC	
	Beta-blocker	Control	Beta-blocker	Control	Beta-blocker	Control	Beta-blocker	Control
	(n = 50)	(n = 51)	(n = 336)	(n = 347)	(n = 47)	(n = 49)	(n = 139)	(n = 131)
<i>Baseline characteristics</i>								
Age, year, mean \pm SD	58 \pm 11	62 \pm 12	62 \pm 12	62 \pm 13	63 \pm 11	61 \pm 14	59 \pm 13	58 \pm 11
Male, %	41/50 (82%)	36/51 (71%)	251/336 (75%)	259/347 (75%)	40/47 (85%)	40/49 (82%)	119/139 (86%)	114/131 (87%)
BMI, mean \pm SD	27 \pm 4	26 \pm 4	27 \pm 4	27 \pm 4	25 \pm 3	25 \pm 3	28 \pm 4	28 \pm 4
Hypertension, %	27/50 (54%)	26/51 (51%)	135/335 (40%)	133/344 (39%)	33/47 (70%)	35/49 (71%)	54/134 (40%)	54/128 (42%)
Diabetes, %	6/50 (12%)	6/51 (12%)	48/335 (14%)	62/347 (18%)	20/47 (43%)	21/49 (43%)	31/133 (23%)	24/128 (19%)
Smoking, %	29/50 (58%)	24/51 (47%)	132/316 (42%)	137/320 (43%)	28/47 (60%)	26/49 (53%)	71/134 (53%)	69/128 (54%)
Hyperlipidemia, %	13/50 (26%)	16/51 (31%)	93/329 (28%)	82/338 (24%)	38/47 (81%)	38/49 (78%)	53/133 (40%)	51/127 (40%)
Previous MI, %	1/50 (2%)	4/51 (8%)	10/332 (3%)	11/345 (3%)	4/47 (9%)	2/49 (4%)	NA	NA
Previous PCI, %	1/50 (2%)	5/51 (10%)	21/333 (6%)	16/346 (5%)	8/47 (17%)	3/49 (6%)	NA	NA
Previous CABG, %	1/50 (2%)	0/51 (0%)	1/333 (0%)	6/346 (2%)	2/47 (4%)	0/49 (0%)	NA	NA
Prior beta-blocker use, %	NA	NA	54/329 (16%)	60/343 (18%)	NA	NA	NA	NA
<i>Clinical presentation</i>								
Killip class I, %	NA	NA	275/290 (95%)	290/308 (94%)	46/47 (98%)	45/49 (92%)	124/135 (92%)	112/128 (88%)
Killip class II, %	NA	NA	12/290 (4%)	13/308 (4%)	1/47 (2%)	4/49 (8%)	11/135 (8%)	14/128 (11%)

Baseline SBP, mmHg, mean \pm SD	138 \pm 21	138 \pm 22	147 \pm 25	147 \pm 25	126 \pm 18	131 \pm 18	143 \pm 19	142 \pm 19
Baseline DBP, mmHg, mean \pm SD	83 \pm 12	84 \pm 12	90 \pm 16	90 \pm 17	74 \pm 12	74 \pm 12	89 \pm 16	88 \pm 16
Baseline HR, beat/min, mean \pm SD	79 \pm 15	79 \pm 14	79 \pm 15	80 \pm 16	80 \pm 16	79 \pm 12	82 \pm 14	82 \pm 14
SBP after intervention, mmHg, mean \pm SD	116 \pm 13	120 \pm 16	136 \pm 23	139 \pm 26	117 \pm 16	119 \pm 14	129 \pm 20	NA
DBP after intervention, mmHg, mean \pm SD	68 \pm 8	72 \pm 10	82 \pm 15	83 \pm 16	67 \pm 11	68 \pm 12	82 \pm 15	NA
HR after intervention, beat/min, mean \pm SD	68 \pm 9	74 \pm 12	74 \pm 14	79 \pm 16	70 \pm 12	77 \pm 13	69 \pm 12	NA
<i>Hospitalization</i>								
Reperfusion time, minutes, median (IQR)	162 (117-248)	157 (115-238)	171 (129-263)	171 (120-272)	270 (198-270)	270 (191-387)	186 (145-230)	180 (143-224)
Infarct related artery								
LAD, %	17/50 (34%)	28/51 (55%)	154/312 (49%)	165/318 (52%)	25/47 (53%)	29/49 (59%)	120/126 (95%)	115/122 (94%)
LCX, %	5/50 (10%)	4/51 (8%)	44/312 (14%)	44/318 (14%)	11/47 (23%)	6/49 (12%)	2/126 (2%)	2/122 (2%)
RCA, %	28/50 (56%)	19/51 (37%)	113/312 (36%)	105/318 (33%)	11/47 (23%)	14/49 (29%)	3/126 (2%)	4/122 (3%)
No. Diseased coronary vessels								
1, %	26/50 (52%)	27/51 (53%)	175/330 (53%)	201/339 (59%)	24/47 (51%)	26/49 (53%)	NA	NA
2, %	16/50 (32%)	10/51 (20%)	100/330 (30%)	71/339 (21%)	8/47 (17%)	10/49 (20%)	NA	NA
3, %	8/50 (16%)	14/51 (28%)	39/330 (12%)	46/339 (14%)	15/47 (32%)	13/49 (27%)	NA	NA
Primary PCI during admission, %	50/50 (100%)	51/51 (100%)	306/335 (91%)	308/346 (89%)	47/47 (100%)	49/49 (100%)	126/129 (98%)	120/123 (98%)
CABG during admission, %	0/50 (0%)	0/51 (0%)	12/336 (4%)	22/347 (6%)	0/47 (0%)	0/49 (0%)	0/139 (0%)	0/131 (0%)
Beta-blocker at discharge, %	NA	NA	260/333 (78%)	249/341 (73%)	45/47 (96%)	46/49 (94%)	115/135 (85%)	118/129 (92%)

Admission length, days, median (IQR) NA NA 2 (1-5) 2 (1-4) NA NA 5 (4-7) 5 (4-6)

BMI: body mass index, CABG: coronary artery bypass grafting, DBP: diastolic blood pressure, IQR: interquartile range, MI: myocardial infarction, PCI: percutaneous coronary intervention, SBP: systolic blood pressure, SD: standard deviation

Supplementary table 3 **Biomarker-based** infarct size

	BEAT-AMI		EARLY-BAMI		Hanada et al.		METOCARD-CINC	
	Beta-blocker	Control	Beta-blocker	Control	Beta-blocker	Control	Beta-blocker	Control
	(n = 50)	(n = 51)	(n = 336)	(n = 347)	(n = 47)	(n = 49)	(n = 139)	(n = 131)
CK peak, U/l, median (IQR)	619 (252-1720) (n = 50)	1413 (644-2647) (n = 50)	1277 (355-2890) (n = 324)	1079 (327-2685) (n = 334)	1277 (355-2890) (n = 47)	1079 (327-2685) (n = 49)	2217 (877-4152) (n = 137)	3559 (1118-5593) (n = 128)
CK-MB, U/l, median (IQR)	74 (30-200) (n = 50)	157 (74-313) (n = 50)	141 (59-325) (n = 217)	134 (47-284) (n = 218)	241 (85-352) (n = 47)	212 (104-338) (n = 49)	NA	NA
CK-MB, µg/l, median (IQR)	NA	NA	155 (65-440) (n = 63)	114 (41-324) (n = 70)	NA	NA	NA	NA
CK-MB AUC, (U*h/l), median (IQR)	NA	NA	2610 (926-5885) (n = 204)	2561 (929-5498) (n = 202)	NA	NA	NA	NA

Troponin T peak, ng/l, median (IQR)	1290 (528-4843) (n = 50)	3175 (1403-5390) (n = 50)	1780 (257-5890) (n = 291)	1600 (187-5802) (n = 304)	NA	NA	NA	NA
Troponin I peak, µg/l, median (IQR)	NA	NA	45 (11-211) (n = 29)	63 (20-133) (n = 34)	NA	NA	NA	NA
Troponin T AUC, (ng*h/l), median (IQR)	NA	NA	51230 (8653-153825) (n = 226)	52826 (13580-133547) (n = 228)	NA	NA	NA	NA

AUC : area under the curve, CK: creatine-kinase, CK-MB: creatine-kinase isoenzyme brain/muscle, IQR: interquartile range

Supplementary table 4 Clinical outcomes

	BEAT-AMI		EARLY-BAMI		Hanada et al.		METOCARD-CINC	
	Beta-blocker (n = 50)	Control (n = 51)	Beta-blocker (n = 336)	Control (n = 347)	Beta-blocker (n = 47)	Control (n = 49)	Beta-blocker (n = 139)	Control (n = 131)
<i>Left ventricular ejection fraction</i>								
1 month, mean ± SD	63 ± 9 (n = 49)	59 ± 9 (n = 49)	51 ± 11 (n = 162)	52 ± 11 (n = 169)	NA	NA	46 ± 9 (n = 105)	43 ± 10 (n = 114)
6 months , mean ± SD	62 ± 10 (n = 50)	60 ± 10 (n = 48)	NA	NA	52 ± 9 (n = 41)	50 ± 9 (n = 42)	48 ± 10 (n = 98)	45 ± 12 (n = 101)
<i>Seven days clinical outcomes</i>								

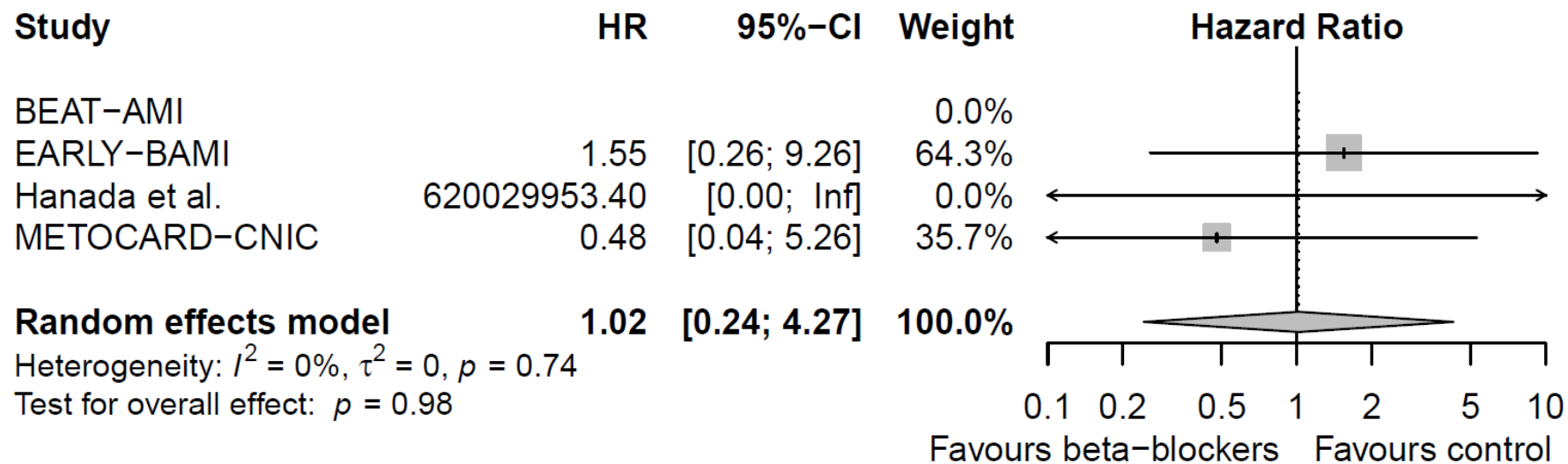
Death or myocardial infarction	NA	NA	7/335 (2.1%)	7/345 (2.1%)	0/47 (0.0%)	0/49 (0.0%)	3/139 (2.2%)	2/131 (1.5%)
All-cause mortality	0/50 (0.0%)	0/51 (0.0%)	4/335 (1.2%)	5/345 (1.5%)	0/47 (0.0%)	0/49 (0.0%)	2/139 (1.5%)	2/131 (1.5%)
Cardiac death	0/50 (0.0%)	0/51 (0.0%)	3/335 (0.9%)	5/345 (1.5%)	0/47 (0.0%)	0/49 (0.0%)	2/139 (1.5%)	2/131 (1.5%)
Myocardial infarction	NA	NA	3/335 (0.9%)	2/345 (0.6%)	0/47 (0.0%)	0/49 (0.0%)	1/139 (0.7%)	0/131 (0.0%)
<i>One-year clinical outcomes</i>								
Death or MI	NA	NA	14/335 (4.4%)	13/345 (4.0%)	1/47 (2.1%)	2/49 (4.1%)	6/139 (4.5%)	7/131 (5.5%)
All-cause mortality	0/50 (0.0%)	1/51 (2.0%)	11/335 (4.4%)	11/345 (3.5%)	0/47 (0.0%)	2/49 (4.1%)	5/139 (3.7%)	5/131 (3.9%)
Cardiac death	0/50 (0.0%)	1/51 (2.0%)	7/335 (2.2%)	8/345 (2.4%)	0/47 (0.0%)	0/49 (0.0%)	4/139 (3.0%)	5/131 (3.9%)
MI	NA	NA	3/335 (0.9%)	2/345 (0.6%)	1/47 (2.1%)	0/49 (0.0%)	1/139 (0.7%)	2/131 (1.6%)
<i>Safety outcomes during hospitalization</i>								
Composite safety outcome	NA	NA	15/334 (4.5%)	10/345 (2.9%)	1/47 (2.1%)	0/49 (0.0%)	6/139 (4.3%)	9/131 (6.9%)
Ventricular tachycardia	NA	NA	10/336 (3.0%)	10/347 (3.0%)	21/47 (44.7%)	12/49 (24.5%)	5/139 (3.6%)	10/131 (7.6%)

MI: myocardial infarction, NA: not available, SD: standard deviation

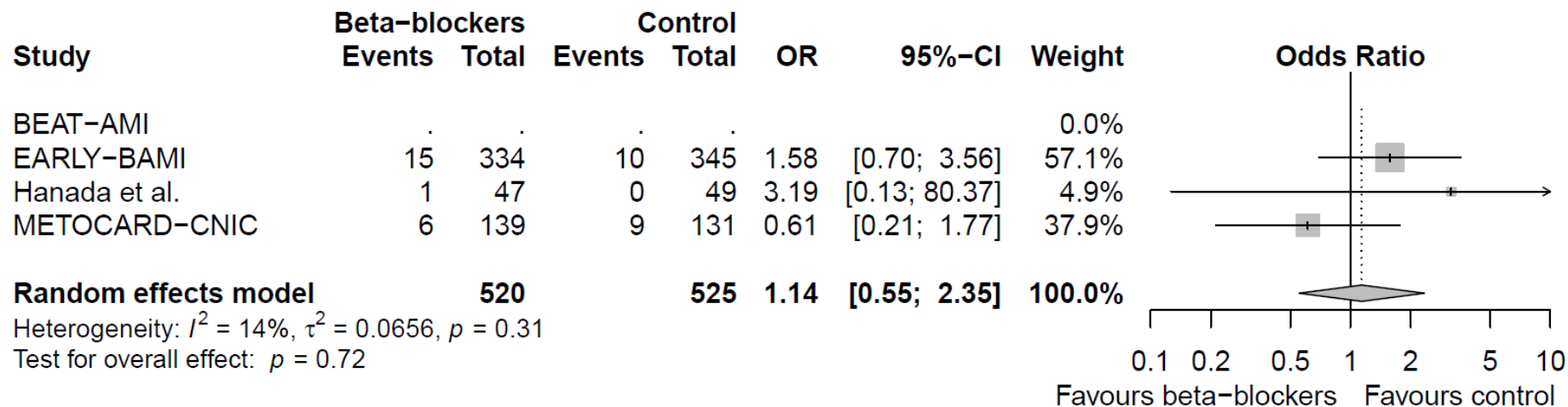
Safety outcome is the composite of cardiogenic shock, symptomatic bradycardia or hypotension

One-year efficacy outcomes are Kaplan-Meier estimates, compared with a log-rank test. Safety outcome and ventricular tachycardia are percentages, compared with a Chi-square test.

Supplemental Figure S2



Supplemental Figure S3



Supplemental Figure S4

