



Figure 4. Cumulative incidences of MACEs (all-cause death, recurrent MI, and heart failure hospitalization) in patients with preserved LVEF (A) and in patients with low LVEF (B) were compared according to use of β blockers.

Table 5
Frequency of events during clinical follow-up in patients with low left ventricular ejection fraction

Event	All Patients (n = 125)	β -Blocker Group (n = 62)	No- β -Blocker Group (n = 63)	Log-Rank p Value
Death	15 (12.0%)	4 (6.5%)	11 (17.5%)	0.04
Cardiac death	8 (6.4%)	1 (1.6%)	7 (11.1%)	0.02
Sudden death	3 (2.4%)	0 (0%)	3 (4.8%)	0.07
Reinfarction	3 (2.4%)	0 (0%)	3 (4.8%)	0.08
Stent thrombosis (definite)	1 (0.8%)	0 (0%)	1 (1.6%)	0.31
Stroke	5 (4.0%)	2 (3.2%)	3 (4.8%)	0.59
Heart failure hospitalization	21 (16.8%)	8 (12.9%)	13 (20.6%)	0.12
Target lesion revascularization	25 (20.0%)	11 (17.7%)	14 (22.2%)	0.41
Any revascularization	37 (29.6%)	18 (29.0%)	19 (30.2%)	0.66
Major adverse cardiac events	29 (23.2%)	9 (14.5%)	20 (31.8%)	0.009

Values are numbers of events (incidences).

Table 6
Frequency of events during clinical follow-up in patients with preserved left ventricular ejection fraction

Event	All Patients (n = 567)	β -Blocker Group (n = 217)	No- β -Blocker Group (n = 350)	Log-Rank p Value
Death	24 (4.2%)	13 (6.0%)	11 (3.1%)	0.15
Cardiac death	9 (1.6%)	4 (1.8%)	5 (1.4%)	0.75
Sudden death	3 (0.5%)	2 (0.9%)	1 (0.3%)	0.33
Reinfarction	16 (2.8%)	7 (3.2%)	9 (2.6%)	0.77
Stent thrombosis (definite)	10 (1.8%)	5 (2.3%)	5 (1.4%)	0.50
Stroke	19 (3.4%)	9 (4.2%)	10 (2.9%)	0.47
Heart failure hospitalization	29 (5.1%)	13 (6.0%)	16 (4.6%)	0.54
Target lesion revascularization	69 (12.2%)	26 (12.0%)	43 (12.2%)	0.83
Any revascularization	140 (24.7%)	51 (23.5%)	89 (25.4%)	0.45
Major adverse cardiac events	58 (10.2%)	29 (13.4%)	29 (8.3%)	0.10

Values are numbers of events (incidences).

to re-examine the role of β -blocker therapy for secondary prevention in addition to primary PCI and other currently available medications. Appropriate stratification of patients with STEMI who receive benefits from β -blocker therapy would decrease health care costs and prevent the occurrence of adverse effects by β blockers.

Our study has several important limitations. First, selection bias for use of β blockers is unavoidable in observational studies. Although we used a propensity score for adjusting baseline β -blocker use, we could not exclude influences of unmeasured confounders on clinical outcomes. Second, we did not have data on types and doses of β blockers used, which might affect clinical outcomes. Beta blockers are quite heterogeneous as a group in properties and outcomes.^{21,24,25} Administration of less sufficient β blockers may have decreased their benefit in the present study. Third, we do not know how long β blockers continued to be taken after discharge. Previous studies have report that >80% of patients continued to receive β blockers 6 months after MI hospitalization.^{26,27} Other study reports have a much higher (45% at 6 months) discontinuation rate.²⁸ Prescription of β blockers at discharge might not be representative of long-term use of β blockers after STEMI.

Acknowledgment: We thank the members of the cardiac catheterization laboratories of the participating centers and the clinical research coordinators. Lists of participating centers, investigators, clinical research coordinators, and contributing members of the clinical events committee are listed in an online-only data supplement (Appendixes A, B and C).

Supplementary Data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.amjcard.2010.06.048.

1. A randomized trial of propranolol in patients with acute myocardial infarction. I. Mortality results. *JAMA* 1982;247:1707-1714.
2. Timolol-induced reduction in mortality and reinfarction in patients surviving acute myocardial infarction. *N Engl J Med* 1981;304:801-807.
3. The MIAMI Trial Research Group. Metoprolol in acute myocardial infarction. Patient population. *Am J Cardiol* 1985;56(suppl):10G-14G.
4. First International Study of Infarct Survival Collaborative Group. Randomised trial of intravenous atenolol among 16 027 cases of suspected acute myocardial infarction: ISIS-1. *Lancet* 1986;2:57-66.
5. Freemantle N, Cleland J, Young P, Mason J, Harrison J. Beta blockade after myocardial infarction: systematic review and meta regression analysis. *BMJ* 1999;318:1730-1737.
6. Hjalmarson A, Herlitz J, Holmberg S, Ryden L, Swedberg K, Vedin A, Waagstein F, Waldenström A, Waldenström J, Wedel H, Wilhelmsson L, Wilhelmsson C. The Goteborg Metoprolol Trial. Effects on mortality and morbidity in acute myocardial infarction. *Circulation* 1983; 67(suppl):I26-I32.
7. Antman EM, Anbe DT, Armstrong PW, Bates ER, Green LA, Hand M, Hochman JS, Krumholz HM, Kushner FG, Lamas GA, Mullany CJ, Ornato JP, Pearle DL, Sloan MA, Smith SC Jr, Alpert JS, Anderson JL, Faxon DP, Fuster V, Gibbons RJ, Gregoratos G, Halperin JL, Hiratzka LF, Hunt SA, Jacobs AK. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of Patients with Acute Myocardial Infarction). *Circulation* 2004;110(suppl):e82-c292.
8. Campbell-Scherer DL, Green LA. ACC/AHA guideline update for the management of ST-segment elevation myocardial infarction. *Am Fam Phys* 2009;79:1080-1086.
9. Kimura T, Morimoto T, Nakagawa Y, Tamura T, Kadota K, Yasumoto H, Nishikawa H, Hiasa Y, Muramatsu T, Meguro T, Inoue N, Honda H, Hayashi Y, Miyazaki S, Oshima S, Honda T, Shiode N, Namura M, Sone T, Nobuyoshi M, Kita T, Mitsudo K. Antiplatelet therapy and stent thrombosis after sirolimus-cluting stent implantation. *Circulation* 2009;119:987-995.
10. Serruys PW, Unger F, Sousa JE, Jatene A, Bonnier HJ, Schonberger JP, Buller N, Bonser R, van den Brand MJ, van Herwerden LA, Morel MA, van Hout BA. Comparison of coronary-artery bypass surgery and stenting for the treatment of multivessel disease. *N Engl J Med* 2001; 344:1117-1124.
11. Mauri L, Hsieh WH, Massaro JM, Ho KK, D'Agostino R, Cutlip DE. Stent thrombosis in randomized clinical trials of drug-eluting stents. *N Engl J Med* 2007;356:1020-1029.
12. Imai E, Horio M, Nitta K, Yamagata K, Iseki K, Hara S, Ura N, Kiyohara Y, Hirakata H, Watanabe T, Moriyama T, Ando Y, Inaguma D, Narita I, Iso H, Wakai K, Yasuda Y, Tsukamoto Y, Ito S, Makino H, Hishida A, Matsuo S. Estimation of glomerular filtration rate by the MDRD study equation modified for Japanese patients with chronic kidney disease. *Clin Exp Nephrol* 2007;11:41-50.
13. Kopecky SL. Effect of beta blockers, particularly carvedilol, on reducing the risk of events after acute myocardial infarction. *Am J Cardiol* 2006;98:1115-1119.
14. Roberts R, Rogers WJ, Mueller HS, Lambrew CT, Diver DJ, Smith HC, Willerson JT, Knatterud GL, Forman S, Passamani E. Immediate versus deferred beta-blockade following thrombolytic therapy in patients with acute myocardial infarction. Results of the Thrombolysis In Myocardial Infarction (TIMI) II-B Study. *Circulation* 1991;83:422-437.
15. Chen ZM, Pan HC, Chen YP, Peto R, Collins R, Jiang LX, Xie JX, Liu LS. Early intravenous then oral metoprolol in 45,852 patients with acute myocardial infarction: randomised placebo-controlled trial. *Lancet* 2005;366:1622-1632.
16. Chen J, Radford MJ, Wang Y, Marciniak TA, Krumholz HM. Are beta-blockers effective in elderly patients who undergo coronary revascularization after acute myocardial infarction? *Arch Intern Med* 2000;160:947-952.
17. Bramlage P, Messer C, Bitterlich N, Pohlmann C, Cuneo A, Stammwitz E, Tebbenjohanns J, Gohlke H, Senges J, Tebbe U. The effect of optimal medical therapy on 1-year mortality after acute myocardial infarction. *Heart* 2010;96:604-609.
18. Packer M, Bristow MR, Cohn JN, Colucci WS, Fowler MB, Gilbert EM, Shusterman NH. The effect of carvedilol on morbidity and mortality in patients with chronic heart failure. U.S. Carvedilol Heart Failure Study Group. *N Engl J Med* 1996;334:1349-1355.
19. Hori M, Sasayama S, Kitabatake A, Toyooka T, Handa S, Yokoyama M, Matsuzaki M, Takeshita A, Origasa H, Matsui K, Hosoda S. Low-dose carvedilol improves left ventricular function and reduces cardiovascular hospitalization in Japanese patients with chronic heart failure: the Multicenter Carvedilol Heart Failure Dose Assessment (MUCHA) trial. *Am Heart J* 2004;147:324-330.
20. Kernis SJ, Harjai KJ, Stone GW, Grines LL, Boura JA, O'Neill WW, Grines CL. Does beta-blocker therapy improve clinical outcomes of acute myocardial infarction after successful primary angioplasty? *J Am Coll Cardiol* 2004;43:1773-1779.
21. Dargie HJ. Effect of carvedilol on outcome after myocardial infarction in patients with left-ventricular dysfunction: the CAPRICORN randomised trial. *Lancet* 2001;357:1385-1390.
22. Infarction TJ-baCAM Investigators J. Comparison of the effects of beta blockers and calcium antagonists on cardiovascular events after acute myocardial infarction in Japanese subjects. *Am J Cardiol* 2004; 93:969-973.
23. Bedell SE, Jabbar S, Goldberg R, Glaser H, Gobbe S, Young-Xu Y, Graboys TB, Ravid S. Discrepancies in the use of medications: their extent and predictors in an outpatient practice. *Arch Intern Med* 2000; 160:2129-2134.
24. Poole-Wilson PA, Swedberg K, Cleland JG, Di Lenarda A, Hanrath P, Komajda M, Lubsen J, Lutiger B, Metra M, Remme WJ, Torp-

- Pedersen C, Scherhag A, Skene A. Comparison of carvedilol and metoprolol on clinical outcomes in patients with chronic heart failure in the Carvedilol Or Metoprolol European Trial (COMET): randomised controlled trial. *Lancet* 2003;362:7-13.
25. Asanuma H, Minamino T, Sanada S, Takashima S, Ogita H, Ogai A, Asakura M, Liao Y, Asano Y, Shintani Y, Kim J, Shinozaki Y, Mori H, Node K, Kitamura S, Tomoike H, Hori M, Kitakaze M. Beta-adrenoceptor blocker carvedilol provides cardioprotection via an adenosine-dependent mechanism in ischemic canine hearts. *Circulation* 2004;109:2773-2779.
26. Eagle KA, Kline-Rogers E, Goodman SG, Gurfinkel EP, Avezum A, Flather MD, Granger CB, Erickson S, White K, Steg PG. Adherence to evidence-based therapies after discharge for acute coronary syndromes: an ongoing prospective, observational study. *Am J Med* 2004;117:73-81.
27. Ho PM, Spertus JA, Masoudi FA, Reid KJ, Peterson ED, Magid DJ, Krumholz HM, Rumsfeld JS. Impact of medication therapy discontinuation on mortality after myocardial infarction. *Arch Intern Med* 2006;166:1842-1847.
28. Kramer JM, Hammill B, Anstrom KJ, Fetterolf D, Snyder R, Charde JP, Hoffman BS, Allen LaPointe N, Peterson E. National evaluation of adherence to beta-blocker therapy for 1 year after acute myocardial infarction in patients with commercial health insurance. *Am Heart J* 2006;152:e1-e8.

