Impact of Beta Blockade Therapy on Long-Term Mortality After ST-Segment Elevation Acute Myocardial Infarction in the Percutaneous Coronary Intervention Era

Daisaku Nakatani, MD, PhD[a], Yasuhiko Sakata, MD, PhD[a,b,d,e,*], Shinichiro Suna, MD, PhD[a], Masaya Usami, MD[a], Sen Matsumoto, MD[a], Masahiko Shimizu, MD, PhD[a], Masahiko Hara, MD[a], Masaaki Uematsu, MD, PhD[f], Masatake Fukunami, MD, PhD[g], Toshimitsu Hamasaki, PhD[c], Hiroshi Sato, MD, PhD[h], Masatsugu Hori, MD, PhD[i], and Issei Komuro, MD, PhD[a], on behalf of the Osaka Acute Coronary Insufficiency Study (OACIS) Investigators[†]

Although clinical guidelines recommend long-term β-blocker (BB) therapy to decrease mortality after acute myocardial infarction, these recommendations are based predominantly on evidence from before the reperfusion and thrombolytic eras. To investigate the effects of BB therapy for patients with acute myocardial infarctions on mortality in the percutaneous coronary intervention era, a total of 5,628 consecutive patients who were admitted <24 hours after the onset of ST-segment elevation myocardial infarction, treated with emergent percutaneous coronary intervention, and discharged alive were studied. During a median follow-up period of 1,430 days, mortality rates did not differ between patients with and without BB therapy (5.2% vs 6.2%, p = 0.786). Multivariate analysis revealed that BB treatment was not associated with a reduced risk for mortality (hazard ratio 0.935, 95% confidence interval 0.711 to 1.230, p = 0.534). The results of propensity score matching also indicated that the mortality rates did not differ between the 2 groups. However, subgroup analyses among matched populations revealed that BB treatment was associated with a significantly lower mortality risk for high-risk patients, who were defined as those with Global Registry of Acute Coronary Events (GRACE) risk scores ≥121 (hazard ratio 0.596, 95% confidence interval 0.416 to 0.854, p = 0.005) or those administered diuretics (hazard ratio 0.602, 95% confidence interval 0.398 to 0.910, p = 0.016), but not for lower risk patients. In conclusion, BB treatment was associated with reduced long-term mortality in patients after ST-segment elevation myocardial infarction at higher risk, but not in those at lower risk. Although randomized controlled studies are warranted to confirm these results, the implementation of BB therapy for discharged patients with ST-segment elevation myocardial infarction may need to be assessed on the basis of individual mortality risk in the percutaneous coronary intervention era. **(Am J Cardiol 2013;111:457−464)**

Under current clinical guidelines, oral β-blocker (BB) therapy is widely recommended for indefinite long-term use in all patients who recover from ST-segment elevation myocardial infarction (STEMI) and do not have contraindications.[1−4] However, these recommendations are based predominantly on evidences obtained before the reperfusion and thrombolytic eras,[5−9] and few data have been collected in the percutaneous coronary intervention (PCI) era. Recent advances in the management of STEMI, particularly the use of primary PCI, have significantly reduced long-term mortality.[10,11] Because these treatment advances potentially mask the mortality benefits of BB therapy, reassessing the efficacy of BB exposure for patients who survive STEMI is warranted. In this study, we investigated the relation

[a]Department of Cardiovascular Medicine, [b]Department of Advanced Cardiovascular Therapeutics, and [c]Department of Biomedical Statistics, Osaka University Graduate School of Medicine, Suita, Japan; [d]Department of Evidence-Based Cardiovascular Medicine, and [e]Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine, Sendai, Japan; [f]Cardiovascular Center, Kansai Rosai Hospital, Amagasaki, Japan; [g]Division of Cardiology, Osaka General Medical Center, Osaka, Japan; [h]School of Human Welfare Studies Health Care Center and Clinic, Kwansei Gakuin University, Nishinomiya, Japan; and [i]Osaka Prefectural Hospital Organization, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, Japan. Manuscript received June 27, 2012; revised manuscript received and accepted October 30, 2012.

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*Corresponding author: Tel: 81-6-6879-6612; fax: 81-6-6879-6613.
E-mail address: sakatayk@cardiology.med.osaka-u.ac.jp (Y. Sakata).

[†] A list of the Osaka Acute Coronary Insufficiency Study (OACIS) Investigators appears in the Appendix.

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Table 1
Patient baseline characteristics stratified by prescription of β blockers at discharge before and after propensity matching

Variable	Before Matching				After Matching			
	Without BBs	With BBs	Overall	p Value	Without BBs	With BBs	Overall	p Value
	(n = 2,748)	(n = 2,880)	(n = 5,628)		(n = 1,923)	(n = 1,923)	(n = 3,846)	
Year				<0.001				<0.001
1998−2001	41.8%	20.7%	31.0%		27.2%	30.9%	29.1%	
2002−2005	38.9%	32.7%	35.7%		45.9%	45.4%	45.6%	
2006−2009	17.1%	37.6%	27.6%		23.8%	22.4%	23.1%	
2010−2011	2.2%	9.1%	5.7%		3.1%	1.3%	2.2%	
High-volume hospital	60.7%	68.0%	64.4%	<0.001	65.3%	65%	65.2%	0.839
Age (yrs)	64.7 ± 12	64.7 ± 11.6	64.7 ± 11.8	0.923	65.1 ± 12	64.4 ± 11.4	64.7 ± 11.8	0.092
Men	75.7%	79.0%	77.3%	0.003	76.4%	77.8%	77.1%	0.300
Body mass index (kg/m^2)	23.6 ± 3.5	24 ± 3.5	23.8 ± 3.5	<0.001	23.7 ± 3.5	23.9 ± 3.5	23.8 ± 3.5	0.078
Diabetes mellitus	33.0%	32.6%	32.8%	0.716	32.9%	32.4%	32.7%	0.756
Hypertension	53.9%	64.8%	59.5%	<0.001	59.0%	61.0%	60.0%	0.222
Dyslipidemia	44.0%	47.6%	45.8%	0.008	45.6%	47.7%	46.7%	0.207
Smokers	67.2%	64.7%	65.9%	0.050	66.4%	64.9%	65.6%	0.340
Previous myocardial infarction	11.1%	10.7%	10.9%	0.574	11.5%	11.2%	11.3%	0.784
Angina pectoris	22.6%	19.1%	20.8%	0.001	21.6%	22.0%	21.8%	0.789
Onset to admission time (h)	2.4 (1.2−5.8)	2.4 (1.1−5.3)	2.4 (1.1−5.5)	0.194	2.5 (1.2−6.0)	2.5 (1.2−5.4)	2.4 (1.1−5.5)	0.205
Cardiopulmonary arrest on arrival	1.0%	1.7%	1.3%	0.024	1.4%	0.9%	1.2%	0.134
Killip class ≥II	12.7%	16.5%	14.6%	<0.001	14.4%	15.4%	14.9%	0.400
TIMI risk score	5.3 ± 2.5	5.8 ± 2.3	5.6 ± 2.4	<0.001	5.7 ± 2.4	5.5 ± 2.4	5.6 ± 2.4	0.124
GRACE risk score	100.6 ± 27.4	102.5 ± 26.9	101.6 ± 27.2	0.008	101.8 ± 28.1	101.6 ± 26.7	101.6 ± 27.2	0.838
Initial TIMI grade 3 flow	12.4%	11.8%	12.1%	0.466	12.7%	11.5%	12.1%	0.260
Collateral circulation	34.2%	34.3%	34.3%	0.924	35.7%	36.2%	36.0%	0.703
Multivessel coronary disease	33.6%	38.0%	35.8%	0.001	36.3%	35.7%	36.0%	0.714
Left anterior descending coronary artery culprit lesion	42.5%	51.6%	47.2%	<0.001	44.8%	48.6%	46.7%	0.019
Stent deployment	71.9%	82.5%	77.3%	<0.001	78.1%	77.9%	78.0%	0.869
Thrombectomy	38.0%	55.7%	47.1%	<0.001	46.6%	44.5%	45.6%	0.200
Emergent coronary-aorta bypass graft surgery	1.3%	0.6%	1.0%	0.010	1.0%	0.8%	0.9%	0.461
Final TIMI grade 3 flow	88.4%	89.6%	89.0%	0.174	89.2%	88.8%	89.0%	0.693
Peak creatinine phosphokinase >3,000 IU/L	36.8%	44.7%	40.9%	<0.001	40.4%	43.0%	41.7%	0.106
Peak creatinine phosphokinase (IU/L)	2,220 (1,145−3,865)	2,709 (1,329−4,766)	2,439 (1,235−4,328)	<0.001	2,394 (1,158−4,065)	2,631 (1,311−4,562)	2,439 (1,235−4,328)	0.002
Q-wave myocardial infarction	75.1%	76.3%	75.7%	0.334	75.3%	76.2%	75.7%	0.532
Statins	36.1%	52.2%	44.3%	<0.001	42.4%	42.6%	42.5%	0.896
Aspirin	92.8%	96.3%	94.6%	<0.001	94.2%	95.5%	94.8%	0.057
Dual-antiplatelet therapy	64.0%	76.5%	70.4%	<0.001	70.5%	70.3%	70.4%	0.896
Angiotensin-converting enzyme inhibitors	52.7%	52.0%	52.3%	0.610	52.7%	56.3%	54.5%	0.025
Angiotensin receptor blockers	19.5%	33.9%	26.8%	<0.001	25.0%	25.9%	25.5%	0.505
Angiotensin-converting enzyme inhibitors or angiotensin receptor blockers	70.7%	83.2%	77.1%	<0.001	75.8%	79.9%	77.8%	0.002
Calcium blockers	20.3%	15.9%	18.1%	<0.001	17.2%	17.9%	17.6%	0.525
Diuretics	21.5%	30.5%	26.1%	<0.001	25.1%	27.5%	26.3%	0.092
Nitrate	35.7%	26.6%	31.1%	<0.001	30.2%	31.8%	31.0%	0.280
Nicorandil	24.9%	25.4%	25.2%	0.650	24.9%	25.3%	25.1%	0.795
Propensity score	0.426 ± 0.176	0.579 ± 0.189	0.504 ± 0.198	<0.001	0.491 ± 0.165	0.492 ± 0.165	0.491 ± 0.165	0.873

Data are expressed as percentages, as mean ± SD, or as median (IQR).

between BB treatment at discharge and long-term mortality for consecutive patients with STEMI enrolled in the Osaka Acute Coronary Insufficiency Study (OACIS).

Methods

The OACIS is a prospective, multicenter observational study of consecutive patients with acute myocardial infarctions (AMIs) at 25 collaborating hospitals located in the Osaka region of Japan and is registered with the University Hospital Medical Information Network Clinical Trials Registry in Japan (UMIN000004575). One of the main aims of the OACIS is to examine the effects of cardiovascular prevention drugs on secondary prevention after AMI in the contemporary clinical setting. A detailed description of the OACIS has been published elsewhere.[12] The study protocol was approved by the ethics committee of each participating hospital, and each patient provided written informed consent.

Among the 10,074 patients registered in the OACIS registry from April 1998 to April 2011, we identified 5,628 consecutive patients who were admitted <24 hours of the onset of STEMI, treated with emergent PCI, and discharged alive.

Investigative cardiologists and research coordinators recorded demographic and clinical data for patients during the period of hospitalization. After discharge, further data were obtained at 3 and 12 months after AMI and annually thereafter for up to 5 years. Thrombolysis In Myocardial Infarction (TIMI) and Global Registry of Acute Coronary Events (GRACE) risk scores were calculated with multiple imputation for each patient as described elsewhere.[13–15] The left ventricular ejection fraction was assessed using echocardiography before discharge using the Teichholz method. The primary end point of this study was all-cause death, which was categorized as cardiac, noncardiac, or unknown.

Categorical variables were compared using chi-square tests with continuity correction or Fisher's exact tests. Continuous variables are presented as medians (interquartile range [IQR]) or as mean ± SD and were compared using unpaired Student's *t* tests or 2-tailed Wilcoxon's rank-sum tests between patients with and those without oral BB treatment at discharge. To minimize differences in baseline characteristics between the 2 groups, patients were matched in a 1-to-1 manner on the basis of propensity scores, which were calculated for each patient using a logistic regression model[16] that included a total of 32 variables (baseline demographics, angiographic parameters, and medication at discharge), as listed in Table 1. The variables inserted into the multivariate models to calculate propensity scores were determined after screening for multicollinearity. According to the propensity score, patients were selected using a 5-to-1 digit-matching technique using the nearest neighbor method.[17,18] The area under the receiver-operating characteristic curve and the Hosmer-Lemeshow goodness-of-fit statistic were calculated to assess the performance and calibration of the model, respectively. Mortality rates were determined using Kaplan-Meier curves and were compared using log-rank tests. Cox regression analyses were performed to assess whether BB therapy was associated with a reduced risk for mortality. Variables with p values <0.20 before matching in univariate analyses were included in the multivariate Cox regression models.[19] Propensity score was incorporated as a variable into the models before matching. To identify high-risk populations according to GRACE scores, classification and regression trees for survival data (survival CART) were used.[20] Survival CART analysis revealed that the first split point to partition the mortality risk for patients without BB treatment among the matched populations was a GRACE risk score of 121 and that the second and third split points for each subgroup were risk scores of 100 and 141, respectively. Therefore, the mortality benefits of BB therapy at discharge were initially compared between patients with GRACE risk scores <121 and ≥121 and then among those with scores of <100, 100 to 120, 121 to 140, and ≥141. Subgroup analysis was performed in patients after propensity score matching to identify patients having a mortality benefit of BB treatment. All analyses were performed using PASW Statistics version 18 (SPSS, Inc., Chicago, Illinois) or SAS version 9.1.3 (SAS Institute Inc., Cary, North Carolina). Statistical significance was defined as p <0.05. For the subgroup analyses, p values <0.05 and p values for interactions <0.10 were considered as statistically significant.

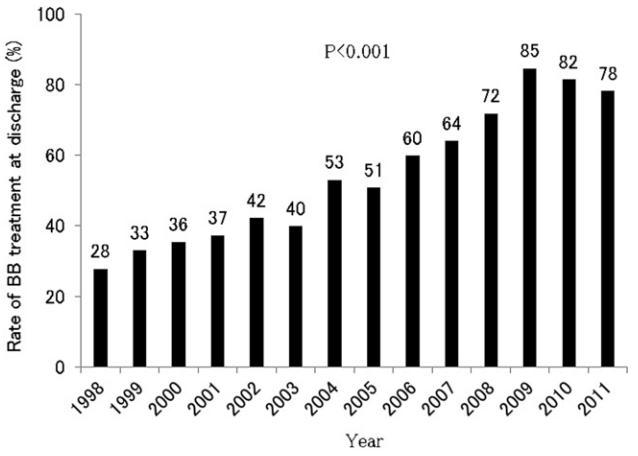

Figure 1. Trend in the annual prescription rate (1999 to 2011) of BBs at discharge in post-AMI patients.

Results

Among the 5,628 study patients, 2,880 (51.2%) were prescribed oral BB therapy at discharge after STEMI. In the BB group, 2,075 (72.0%), 559 (19.4%), 135 (4.7%), 33 (1.1%), and 78 (2.7%) patients received carvedilol, metoprolol, bisoprolol, atenolol, and other BBs, respectively. A trend of increased prescription of BB at discharge by year was clearly evident until 2009, as shown in Figure 1 (p <0.0001). After 2009, approximately 80% of patients received BB treatment. In addition, several significant differences in the baseline characteristics between patients in the BB and non-BB groups were detected (Table 1). Notably, patients in the BB group were more often men, had higher body mass indexes and TIMI and GRACE risk scores, and displayed higher frequencies of hypertension, dyslipidemia, cardiopulmonary arrest on arrival, and Killip class ≥II. With regard to angiographic findings, a greater number of BB group patients had multivessel disease and culprit lesions

Table 2
Incidence of death stratified by prescription of β blockers at discharge before and after propensity score matching

Outcome	Before Matching				After Matching			
	Without BBs (n = 2,748)	With BBs (n = 2,880)	Overall (n = 5,628)	p Value	Without BBs (n = 1,923)	With BBs (n = 1,923)	Overall (n = 3,846)	p Value
All-cause death	170 (6.2%)	149 (5.2%)	319 (5.7%)	0.786	120 (6.2%)	108 (5.6%)	228 (5.9%)	0.171
Cardiac death	45 (1.6%)	31 (1.1%)	76 (1.4%)	0.208	34 (1.8%)	27 (1.4%)	61 (1.6%)	0.248
Reinfarction	19 (0.7%)	15 (0.5%)	34 (0.6%)	0.702	16 (0.8%)	12 (0.6%)	28 (0.7%)	0.348
Heart failure	15 (0.5%)	7 (0.2%)	22 (0.4%)	0.117	11 (0.6%)	6 (0.3%)	17 (0.4%)	0.176
Arrhythmia or sudden death	5 (0.2%)	5 (0.2%)	10 (0.2%)	0.937	4 (0.2%)	5 (0.3%)	9 (0.2%)	0.802
Mechanical complication	4 (0.1%)	1 (0%)	5 (0.1%)	0.189	2 (0.1%)	1 (0.1%)	3 (0.1%)	0.530
Others	2 (0.1%)	3 (0.1%)	5 (0.1%)	0.558	1 (0.1%)	3 (0.2%)	4 (0.1%)	0.353
Noncardiac death	74 (2.7%)	81 (2.8%)	155 (2.8%)	0.222	52 (2.7%)	54 (2.8%)	106 (2.8%)	0.822
Malignant tumor	11 (0.4%)	11 (0.4%)	22 (0.4%)	0.840	4 (0.2%)	6 (0.3%)	10 (0.3%)	0.656
Unknown cause	51 (1.9%)	37 (1.3%)	88 (1.6%)	0.332	34 (1.8%)	27 (1.4%)	61 (1.6%)	0.232

Table 3
Hazard ratios of β blockers for mortality in patients before matching by propensity score

Outcome	Model 1*			Model 2†		
	HR	95% CI	p Value	HR	95% CI	p Value
All-cause death	0.929	0.707−1.222	0.599	0.935	0.711−1.230	0.534
Cardiac death	0.958	0.540−1.698	0.882	0.983	0.552−1.748	0.952
Noncardiac death	1.044	0.705−1.546	0.831	1.044	0.705−1.548	0.829

CI = confidence interval; HR = hazard ratio.
* Adjusted for variables with p values <0.20 between the BB and non-BB groups before matching, as listed in Table 1.
† Adjusted for variables in model 1 plus propensity score.

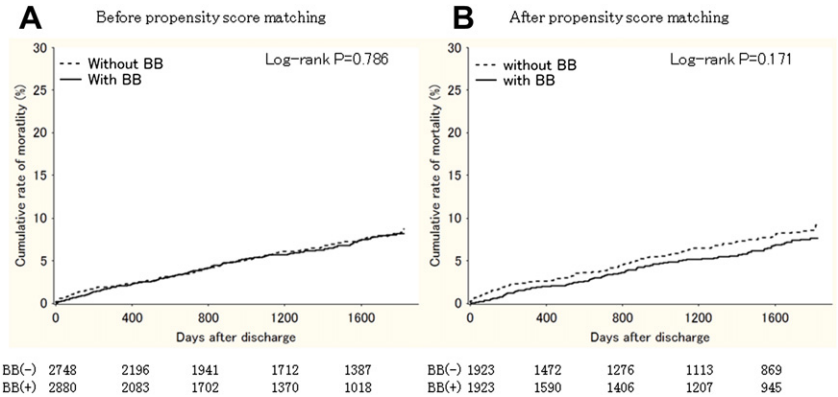

Figure 2. Cumulative incidence of mortality in patients with STEMIs who underwent PCI and were discharged with or without BB therapy before *(A)* and after *(B)* propensity score matching. *Solid and dashed lines* indicate BB and non-BB treatment, respectively. Numbers below the x axis indicate the number of patients in each group at risk at the indicated time.

involving the left anterior descending coronary artery compared to those in the non-BB group. Furthermore, BB group patients had a higher frequency of thrombectomy and stent deployment in the acute stage. Although the success rate of PCI, which was defined as final TIMI grade 3 flow, was similar in the 2 groups, peak creatinine phosphokinase was significantly higher in BB group patients, reflecting the increased severity of myocardial damage in these patients. At discharge, the prescription of dual-antiplatelet therapy, angiotensin receptor blockers, and diuretics was also more common in BB group patients, whereas calcium channel blockers and nitrate were less frequent (Table 1). During a median follow-up period of 1,430 days (IQR 454 to 1,794), no significant difference was detected in the rate of all-cause death between the BB and non-BB groups (Tables 2 and 3, Figure 2). Similarly, there were no significant differences in the cause of death (Table 2). Multivariate Cox regression analyses revealed that BB therapy was not associated with a decreased risk for all-cause, cardiac, or noncardiac death (Table 3). To minimize differences in the baseline characteristics between the BB and non-BB groups, patients were matched using the propensity score method. The area under the receiver-operating characteristic curve was 0.725 (95% confidence

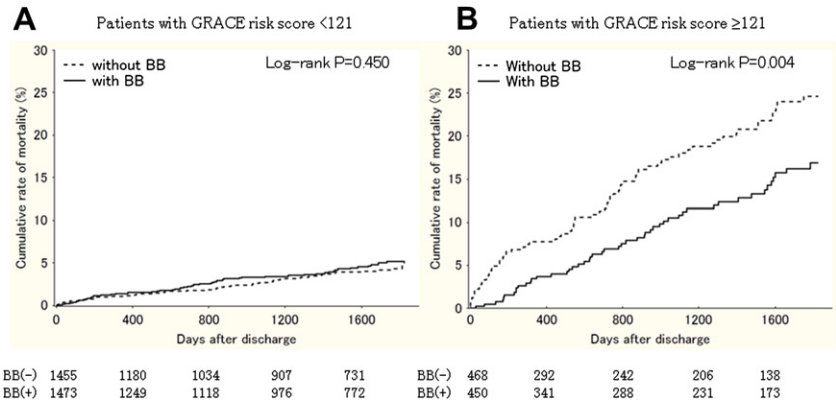

Figure 3. Cumulative incidence of mortality in patients with STEMIs who underwent PCI and were discharged alive with GRACE risk scores <121 *(A)* and ≥121 *(B)*. *Solid and dashed lines* indicate BB and non-BB treatment, respectively. Numbers below the x axis indicate the number of patients in each group at risk at the indicated time.

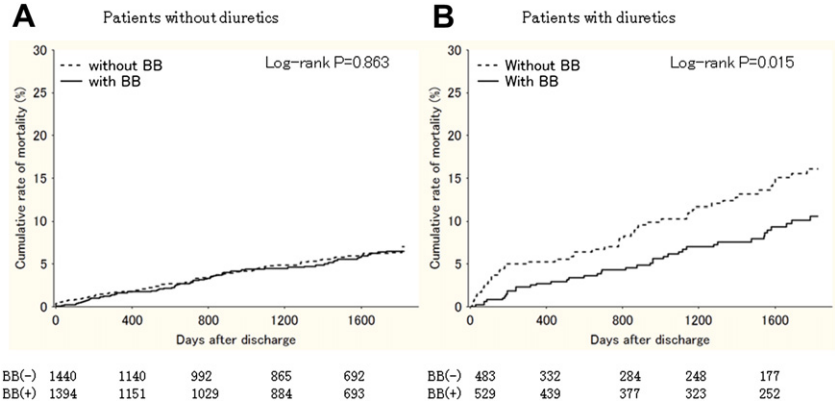

Figure 4. Cumulative incidence of mortality in patients with STEMIs who underwent PCI and were discharged alive treated without *(A)* or with *(B)* diuretics after propensity score matching. *Solid and dashed lines* indicate BB and non-BB treatment, respectively. Numbers below the x axis indicate the number of patients in each group at risk at the indicated time.

interval 0.711 to 0.739), and the p value of the Hosmer-Lemeshow test was 1.000. A total of 3,846 patients with well-matched baseline characteristics, with the exception of year, culprit lesion involving the left anterior descending coronary artery, peak creatine kinase, and prescription of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, were identified between the 2 groups, (Table 1). However, no marked differences in mortality rates were detected between the groups (Table 2, Figure 2). Among patients after propensity score matching, the prescription of BBs at discharge was associated with lower long-term mortality in high-risk patients, who were defined as those with GRACE risk scores ≥121 (Figure 3) or those who were prescribed diuretics (Figure 4), with significant p values for interaction ($p = 0.013$ and $p = 0.077$, respectively; Figure 5). Patients with GRACE risk scores ≥121 or those administrated diuretics were more likely to have histories of myocardial infarction (22.2% vs 7.9%, p <0.001, for GRACE score ≥121 vs <121; 17.8% vs 9.2%, p <0.001, for diuretics vs no diuretics), Killip class ≥II on admission (45.6% vs 5.3%, p <0.001, for GRACE score; 31.1% vs 9.1%, p <0.001, for diuretics), and greater peak creatine phosphokinase values (2,709 IU/L [IQR 1,442 to 4,518] vs 2,431 IU/L [IQR 1,192 to 4,261], p <0.001, for GRACE score; 3,549 IU/L [IQR 1,995 to 5,964] vs 2,206 IU/L [IQR 1,080 to 3,809], p <0.001, for diuretics). Kaplan-Meier estimates and Cox regression analysis for the subgroups partitioned by CART analysis suggested that an association existed between BB treatment and reduced mortality for patients with GRACE risk scores ≥121 (Figure 5), particularly for those with scores of 121 to 140 (Table 4).

Discussion

In the present study, we examined the relation between BB therapy and long-term mortality after STEMI in a real-world population of the contemporary PCI era. The results revealed that BB treatment at discharge was associated with decreased mortality in post-STEMI patients at higher risk, but not in those at lower risk. Although further randomized controlled studies are warranted, our findings may suggest reevaluation of the current guidelines, which generally recommend implementing BB therapy for all post-STEMI patients.[1–4,21]

The findings of large clinical trials conducted before the reperfusion and thrombolytic eras confirmed that BB treatment at discharge improved survival in post-AMI patients.[5–9] In the Beta-Blocker Heart Attack Trial (BHAT),

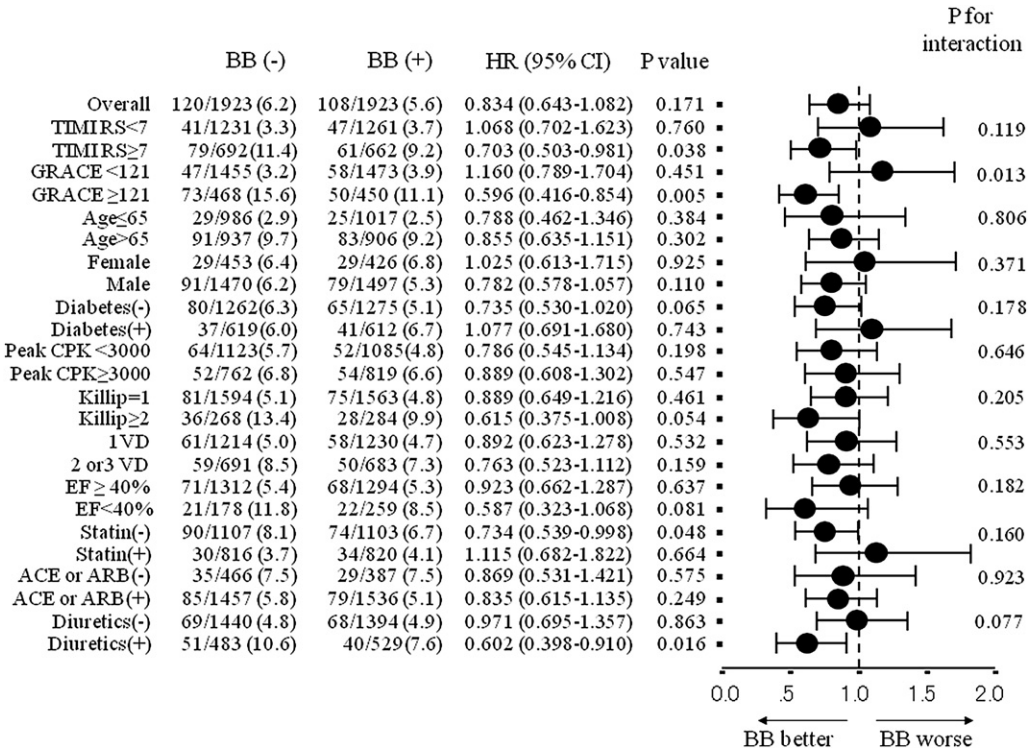

Figure 5. Subgroup analyses after propensity score matching of long-term mortality stratified according to the prescription of BB therapy at discharge. ACE = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; CI = confidence interval; CPK = creatine phosphokinase; EF = ejection fraction; HR = hazard ratio; TIMIRS = TIMI risk score; VD = vessel disease.

Table 4
Hazard ratios of β blockers for mortality according to Global Registry of Acute Coronary Events risk scores for matched populations

GRACE Risk Score	Number			Mortality Rate			HR	95% CI	p Value
	Without BBs	With BBs	Overall	Without BBs	With BBs	Overall			
<100	929	902	1,831	15 (1.6%)	21 (2.3%)	36 (2.0%)	1.393	0.718−2.703	0.327
100−120	526	571	1,097	32 (6.1%)	37 (6.5%)	69 (6.3%)	0.986	0.614−1.583	0.954
121−140	305	328	633	49 (16.1%)	26 (7.9%)	75 (11.8%)	0.438	0.272−0.704	0.001
≥141	163	122	285	24 (14.7%)	24 (19.7%)	48 (16.8%)	0.991	0.563−1.747	0.976

Abbreviations as in Table 3.

in which patients were randomized to receive either propranolol or placebo 5 to 21 days after AMI, mortality was reduced by 25% during a mean follow-up period of 2 years (7% vs 9.5%, respectively).[5,6] Similarly, a Norwegian trial in which patients were randomly assigned to receive either timolol or placebo 6 to 27 days after AMI revealed that mortality at 33 months was reduced by nearly 40% (from 21.9% to 13.3%).[7] Furthermore, previous meta-analyses showed that BB therapy significantly reduced the risk for long-term mortality by 25% and 23% before the reperfusion[8] and thrombolytic[9] eras, respectively. Caution is warranted, however, when we apply evidence from these previous eras to clinical practice in the contemporary PCI era, as recent advances in the management of STEMI have greatly reduced long-term morality, thereby possibly limiting the mortality benefits provided by BBs. Specifically, the increased implementation of evidence-based treatments, including primary PCI, cardiac rehabilitation, and the administration of cardiovascular protective drugs such as antiplatelet agents, renin-angiotensin system inhibitors, and statins, has reduced the incidence of cardiac death due to heart failure, severe cardiac remodeling, recurrent ischemia, reinfarction, and fatal arrhythmia, for which BBs are prescribed to prevent.[22−24]

An important finding of our study is that the mortality rate did not differ between post-STEMI patients on the basis of the prescription of BB agents in all patients treated with PCI during a median follow-up period of 1,430 days. Although the exact reasons for this were unclear, a possible explanation for this may be a substantial decrease in mortality risk associated with contemporary treatment strategies for STEMI. The overall mortality rates in the present study were only 5.2% and 6.2% in the BB and non-BB groups (Table 2 and Figure 2), respectively, which are markedly lower than those reported previously.[22−24] In contrast, the 2-year mortality rates in the Cooperative

Cardiovascular Project, a retrospective analysis published in 1998 that included >200,000 post-AMI patients, were 14.4% and 23.9% for BB and non-BB patients, respectively, even in low-risk patients.[25] Therefore, it is likely that the recent decrease in long-term mortality may have masked the beneficial effects of BB therapy rather than indicating a change in the efficacy of BB therapy. Indeed, in non-BB group patients at low risk (GRACE score <121) or without diuretics, mortality rates during a median follow-up period of 3.9 years were only 3.2% and 4.8%, respectively (Figures 3 and 4).

Importantly, the present findings also indicate that BB therapy at discharge has beneficial effects for high-risk patients, whose mortality rates remained relatively high throughout the follow-up period. Among patients with GRACE risk scores ≥121, or those taking diuretics, BB group patients had a significantly lower mortality risk than non-BB group patients. Together, these results indicate that in high-risk patients, the beneficial effects of BB therapy may outweigh the risks, even in the contemporary PCI era. For patients taking diuretics, BB therapy resulted in a lower risk for mortality than for patients not taking diuretics. One possible reason may be that patients taking diuretics had more severe conditions. Indeed, patients taking diuretics have had higher rates of history of myocardial infarction, Killip class ≥II on admission, and greater peak creatine phosphokinase compared to those not taking diuretics. Another possibility may be that there could have been an interaction between BBs and diuretics on reduced risk for mortality, although there is no evidence for this. Despite the observed benefits of BB therapy in high-risk patients, it is disputable whether BBs should be prescribed to those at extremely high risk. Through the application of survival CART analysis,[26,27] we identified that patients with GRACE risk scores of 121 to 140 experienced the greatest benefit from BB treatment. In this subgroup of patients, the mortality rate in a matched population was approximately 56% lower for those treated with BBs than those without, whereas no significant mortality benefit was detected in patients with GRACE risk scores ≥141 (Table 4). Accordingly, these results also suggest that the prescription of BBs should be considered with caution, particularly for patients at extremely high risk.

Several limitations of the present study warrant mention. First, our study was not a randomized controlled study, and thus, potential biases in measured and unmeasured variables may have existed. For example, we lacked information on contraindications to BB treatment, such as bronchial asthma, arteriosclerosis obliterans, and severe bradycardia. Second, no data were available for the timing of BB therapy initiation during hospitalization. Third, we lacked data on several factors, including the daily doses, adherence, and discontinuation of BB treatment after discharge in the BB group and on the initiation of BB treatment in the non-BB group after discharge, which may have modified the actual clinical impact of BB therapy on mortality. However, it has been reported that adherence to BB treatment, unlike other cardiovascular secondary prevention medications, is not associated with reduced 30-month outcomes for post-AMI patients in the overall population as well as patients stratified by various concomitant medication use,[28] suggesting that the influence of adherence on treatment outcomes was minimal. Forth, the left ventricular ejection fraction was assessed by echocardiography using the Teichholz method, an M-mode technique widely used in large trials with limited reliance on geometric assumptions. Therefore, caution is needed when interpreting the data compared to those obtained from other methods of assessing of the left ventricular ejection fraction, such as 3- or 2-dimensional echocardiography, radionuclide ventriculography, and magnetic resonance ventriculography.[29]

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Disclosures

The authors have no conflicts of interest to disclose.

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Appendix: The OACIS Investigators

Chair: Issei Komuro, Department of Cardiovascular Medicine, Osaka University Graduate School of Medicine, 2-2 Yamada-oka, Suita 565-0871, Japan.

Secretariats: Yasuhiko Sakata (chief), Daisaku Nakatani, Shinichiro Suna, Masaya Usami, Sen Matsumoto, Mariko Kishida, Rie Nagai: Department of Cardiovascular Medicine, Osaka University Graduate School of Medicine, Suita, Japan.

Investigators (institutions in alphabetical order): Yoshiyuki Kijima, Yusuke Nakagawa, Minoru Ichikawa, Higashi-Osaka City General Hospital, Higashi-Osaka, Japan; Young-Jae Lim, Shigeo Kawano, Kawachi General Hospital, Higashi-Osaka, Japan; Hiroshi Sato, Kwasnsei Gakuin University, Nishinomiya, Japan; Takashi Shimazu, Hisakazu Fuji, Kazuhiro Aoki, Kobe Ekisaikai Hospital, Kobe, Japan; Seiki Nagata, Yoshio Ishida, Masaaki Uematsu, Tetsuya Watanabe, Masashi Fujita, Masaki Awata, Kansai Rosai Hospital, Amagasaki, Japan; Michio Sugii, Meiwa Hospital, Nishinomiya, Japan; Masatake Fukunami, Takahisa Yamada, Takashi Morita, Osaka General Medical Center, Osaka, Japan; Shinji Hasegawa, Nobuyuki Ogasawara, Osaka Kosei Nenkin Hospital, Osaka, Japan; Tatsuya Sasaki, Yoshinori Yasuoka, Osaka Minami Medical Center, National Hospital Organization, Kawachinagano, Japan; Hideo Kusuoka, Yukihiro Koretsune, Yoshio Yasumura Y, Keiji Hirooka, Osaka Medical Center, National Hospital Organization, Osaka, Japan; Masatsugu Hori (previous Chair), Osaka Prefectural Hospital Organization Osaka Medical Center for Cancer and Cardiovascular Diseases; Kazuhisa Kodama, Yasunori Ueda, Kazunori Kashiwase, Akio Hirata, Mayu Nishio, Mitsutoshi Asai, Osaka Police Hospital, Osaka, Japan; Yoshio Yamada, Jun Tanouchi, Masami Nishino, Hiroyasu Kato, Ryu Shutta, Osaka Rosai Hospital, Sakai, Japan; Shintaro Beppu, Akio Kohama, Hiroyoshi Yamamoto, Osaka Seamens Insurance Hospital, Osaka, Japan; Issei Komuro, Shinsuke Nanto, Kinya Otsu, Yasushi Matsumura, Kazuhiro Yamamoto, Tetsuo Minamino, Satoru Sumitsuji, Yasuhiko Sakata, Shungo Hikoso, Daisaku Nakatani, Osaka University Graduate School of Medicine, Suita, Japan; Toru Hayashi, Yasuji Doi, Ken-ichiro Okada, Noritoshi Ito, Saiseikai Senri Hospital, Suita, Japan; Kenshi Fujii, Katsuomi Iwakura, Atsushi Okamura, Motoo Date, Yoshiharu Higuchi, Sakurabashi Watanabe Hospital, Osaka, Japan; Noriyuki Akehi, Settsu Iseikai Hospital, Settsu, Japan; Eiji Hishida, Teramoto Memorial Hospital, Kawachinagano, Japan; and Shiro Hoshida, Kazuhiko Hashimura, Takayoshi Adachi, Yao Municipal Hospital, Yao, Japan.