

Supplemental Material

Efficacy of Chronic β -Blocker Therapy for Secondary Prevention on Long-term Outcomes After Coronary Artery Bypass Grafting Surgery

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Abbreviations as in Figure S1.

Figure S5. Kaplan-Meier curves of outcomes associated with β -blocker use after CABG in propensity score-matched cohort analysis. Rates of all-cause death and MACCE in the matched cohort are shown among always users and inconsistent users (Panel A and B), and among always users and never users (Panel C and D). The *P* values were calculated by means of the log-rank test on the basis of all available follow-up data with always users as reference.

MACCE indicates major adverse cardiac and cerebrovascular events.

Supplemental Methods

Revascularization procedures

As part of standard institutional requirements, all surgeons had to have specialized in congenital or valve heart surgery for more than 3 years before undertaking any CABG procedures. With respect to off-pump CABG, the surgeon had to perform at least 100 on-pump CABG procedures before being considered qualified to carry out the off-pump procedure. Once qualified, the choice of off-pump CABG as opposed to on-pump CABG for a particular patient was generally at the discretion of the individual surgeons.

Anesthesia was managed by inhalation of isoflurane with the addition of fentanyl or sufentanil, and propofol was administered continuously until the end of the procedure if necessary. Surgical revascularization was performed using standard bypass techniques. For on-pump CABG, a standard cardiopulmonary bypass was established, and moderate systemic hypothermia (28°C to 32°C) and perfusion with antegrade intermittent cold crystalloid cardioplegia were used. Heparin was given to achieve activated clotting times of 480 seconds or above before institution of cardiopulmonary bypass. For off-pump CABG, stabilization devices were used to provide a motionless anastomosis site, and heparin was administered before the start of the first distal anastomosis to achieve an activated clotting time of 300 to 350 seconds. On-pump CABG involved aortic cross-clamping and cardioplegic arrest, while off-pump CABG was performed with a partial occlusion clamp. Whenever possible, complete revascularization was attempted, and the internal thoracic artery was used preferentially for revascularization of the left anterior descending artery. The remaining vessels were to be bypassed either using another arterial conduit or the saphenous vein in the configuration decided by the surgeon. During reperfusion, the

bypass grafting was completed with proximal anastomoses to the ascending aorta. The decision to switch to cardiopulmonary bypass during the procedure was based on significant hemodynamic instability or ventricular arrhythmia. After separation from cardiopulmonary bypass or on completion of all anastomoses, protamine was given to reverse the effects of heparin. Postoperatively, starting within the first 24 hours, aspirin therapy (100 mg/d) is recommended and should be continued indefinitely.

Definitions

Death was defined as death from any cause.

Myocardial infarction occurred when there were clinical signs and symptoms of ischemia that were distinct from the presenting ischemic event and meeting at least 1 of the following criteria:

1. Spontaneous (before or without revascularization, >48 h after CABG):

A. New, significant Q waves in at least 2 contiguous leads of an ECG that were not present with the presenting ischemic event;

B. Patients whose most recent cardiac markers measured before reinfarction, which were normal, require an increase in CK-MB or troponin that is above the 99th percentile upper limit of normal and at least $\geq 20\%$ above the most recent value.

2. Within 48 h after CABG:

A CABG-related MI was defined by elevation of cardiac biomarker values >10 times the 99th percentile upper reference limit in patients with normal baseline cardiac troponin values ($\leq 99^{\text{th}}$ percentile upper reference limit) plus either new pathological Q waves; new left bundle-branch block, angiographically documented new graft, or native coronary artery occlusion; or imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.

Stroke was confirmed by a neurologist on the basis of imaging studies and was defined as follows:

1. A focal neurologic deficit of central origin lasting >72 hours, or

2. A focal neurologic deficit of central origin lasting >24 hours, with imaging evidence of cerebral infarction or intracerebral hemorrhage, or

3. A non-focal encephalopathy lasting >24 hours with imaging evidence of cerebral infarction or hemorrhage adequate to account for the clinical state.

Retinal arterial ischemia or hemorrhage was included in the definition of stroke.

Repeat revascularization was defined as any repeat CABG or percutaneous coronary intervention.

Contraindications to β -blocker therapy

1. Allergic to β -blockers, or
2. Left ventricular ejection fraction $<35\%$, pulmonary edema, or congestive heart failure, or
3. Bradycardia (heart rate <50 bpm) on admission without taking a β -blocker, or
4. Hypotension or cardiogenic shock during hospitalization or systolic BP <100 mm Hg, or
5. Conduction disorder including second and third degree heart block, bifascicular block, or trifascicular block, and with no pacemaker implanted, or
6. History of asthma or chronic obstructive pulmonary disease, or
7. Metastatic cancer or other terminal illness, or
8. Other reasons documented by a physician for not giving β -blockers.

Supplemental Tables

Supplemental Table S1. Candidate Risk Factors

Risk Factors		
1. Age	12. CHF	23. LIMA-to-LAD graft
2. Sex	13. Previous PCI	24. Complete revascularization‡
3. BMI*	14. Previous cardiac surgery	25. Year of procedure§
4. Smoker	15. LVEF	26. No. of surgeries performed by surgeons¶
5. Diabetes mellitus	16. Three-vessel disease	27. β -Blocker use pattern
6. Dyslipidemia	17. Left main CAD	28. Use of aspirin at 1 year
7. Hypertension	18. Previous MI†	29. Use of ACEI or ARB at 1 year
8. COPD	19. Preoperative intravenous nitrates	30. Use of statins at 1 year
9. PVD	20. Preoperative IABP	31. Use of CCB at 1 year
10. Previous CVA	21. Status of surgery	32. Use of diuretics at 1 year
11. Chronic renal failure	22. Cardiopulmonary bypass	33. Use of nitrates at 1 year

BMI indicates body mass index; COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular disease; CVA, cerebrovascular accident; CHF, chronic heart failure; PCI, percutaneous coronary intervention; LVEF, left ventricular ejection fraction; CAD, coronary artery disease; MI, myocardial infarction; IABP, intra-aortic balloon pump; LIMA, left internal mammary artery; LAD, left anterior descending; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker.

*Calculated as weight in kilograms divided by height in meters squared.

†Previous MI was included in the overall cohorts and in the propensity score calculation as a covariate in the matched cohorts.

‡An index of completeness of revascularization (ICOR) was defined as the ratio of the total number of distal vessels bypassed to the number of diseased territories reported on the preoperative coronary angiographic results. A revascularization with an ICOR ≥ 1 was considered complete revascularization.

§Year of surgery was included in the multivariable regression model as each class indicating a calendar of year.

¶Surgeons were grouped into tertiles according to the surgical volume (<250 cases, 250–500 cases, and >500 cases).

Supplemental Table S2. Baseline Demographic, Biochemical and Procedural Characteristics of the Patients According to their Pattern of β -Blocker Use*

Variable	Always Users n=2922	Inconsistent Users n=1681	Never Users n=1323
Demographics			
Age, mean (SD), y	60.5 (8.9)	60.5 (9.3)	61.9 (9.0)
Male sex	2376 (81)	1379 (82)	1076 (81)
BMI, mean (SD), kg/m ²	24.7 (2.8)	24.6 (2.9)	25.3 (2.8)
Medical history			
Smoker	1564 (54)	915 (54)	673 (51)
Diabetes mellitus	950 (33)	503 (30)	379 (29)
Insulin-treated diabetes	221 (8)	109 (7)	69 (5)
Hypertension	1952 (67)	955 (57)	915 (69)
Dyslipidemia	1936 (66)	991 (59)	560 (42)
Peripheral vascular disease	51 (2)	73 (4)	174 (13)
Previous CVA	230 (8)	146 (9)	85 (6)
COPD	15 (1)	62 (4)	167 (13)
Chronic renal failure	24 (1)	17 (1)	12 (1)
Prior myocardial infarction	1280 (44)	690 (41)	544 (41)
Prior PCI	312 (11)	167 (10)	108 (8)
Prior cardiac surgery	12 (1)	7 (1)	5 (1)
Congestive heart failure	180 (6)	85 (5)	31 (2)
Recent atrial fibrillation	58 (2)	43 (3)	35 (3)
Unstable angina	451 (15)	157 (9)	99 (8)
NYHA class IV	68 (2)	46 (3)	29 (3)
LVEF, mean (SD), %	60 (9)	60 (9)	60 (9)
No. of diseased vessels			
2	290 (10)	184 (11)	165 (13)
3	2571 (88)	1454 (87)	1112 (84)
Left main CAD	1005 (34)	526 (31)	441 (33)
Status			
Elective	2883 (99)	1660 (99)	1296 (98)
Urgent	39 (1)	21 (1)	27 (2)
EuroSCORE, mean (SD)	2.8 (2.0)	2.8 (2.1)	3.1 (2.2)

Biochemical characteristics			
Creatinine, $\mu\text{mol/L}$	84.2 (20.4)	85.7 (22.1)	86.5 (20.5)
Triglycerides, mg/dL	1.7 (1.0)	1.8 (1.1)	1.7 (0.9)
Total cholesterol, mg/dL	4.5 (1.1)	4.5 (1.1)	4.6 (1.3)
HDL cholesterol, mg/dL	1.1 (0.4)	1.1 (0.3)	1.1 (0.3)
LDL cholesterol, mg/dL	2.5 (0.9)	2.5 (0.9)	2.5 (1.1)
Total albumin, g/L*	41.0 (4.4)	40.9 (4.5)	40.7 (4.8)
hsCRP, mg/L*	3.1 (3.6)	3.4 (3.8)	3.1 (3.7)
Procedural characteristics			
Grafts per patient, mean (SD), n	3.4 (0.9)	3.3 (0.9)	3.1 (0.9)
Off-pump procedure	1426 (49)	1083 (64)	1133 (86)
LIMA-to-LAD graft	2788 (95)	1590 (95)	1244 (94)
Complete revascularization	2708 (93)	1535 (91)	1160 (88)

HDL indicates high density lipoprotein; LDL, low density lipoprotein; hsCRP, high-sensitivity C-reactive protein. Other abbreviations as in Table S1.

Values expressed as number (percentage) unless otherwise indicated.

*Data are available only for participants recruited since 2006.

Supplemental Table S3. Concomitant Medication Use at Hospital Discharge and at 1 Year after CABG

Medications	Hospital Discharge			1 Year after Procedure		
	All patients n=5973	No prior MI n=3431	Prior MI n=2542	All patients n=5926	No prior MI n=3412	Prior MI n=2514
β-Blocker	69	69	69	61	59	63
Aspirin	76	75	77	86	88	85
ACEI or ARB	11	11	11	28	27	30
CCB*	20	22	18	55	54	56
Statins†	-	-	-	31	32	28
Diuretics†	-	-	-	5	4	7
Nitrates†	-	-	-	66	65	67

Abbreviations as in Table S1.

Values expressed as percentage.

*Data at hospital discharge are available only for participants recruited since 2006.

†Data at hospital discharge are not available for the years from 2004 to 2008.

Supplemental Table S4. Influence of Prior MI on Long-term Outcomes after CABG

	No. (%) of Events		Unadjusted HR* (95% CI)	P Value	Adjusted HR* (95% CI)	P Value
	No Prior MI n=3431	Prior MI n=2542				
All-cause death	192 (5.6)	170 (6.7)	1.22 (0.99–1.50)	0.06	0.89 (0.65–1.21)	0.45
Cardiac death	100 (2.9)	106 (4.2)	1.45 (1.10–1.91)	0.01	0.88 (0.59–1.31)	0.53
Myocardial infarction	47 (1.4)	51 (2.0)	1.49 (1.00–2.22)	0.05	1.41 (0.91–2.18)	0.12
Stroke	363 (10.6)	258(10.1)	0.97 (0.83–1.14)	0.74	1.00 (0.79–1.26)	0.97
Repeat revascularization	142 (4.1)	96 (3.8)	0.93 (0.72–1.21)	0.58	0.95 (0.65–1.39)	0.79
MACCE	677 (19.7)	520 (20.5)	1.06 (0.94–1.18)	0.36	0.94 (0.80–1.12)	0.49

HR indicates hazard ratio; CI, confidence interval; MI, myocardial infarction; MACCE, major adverse cardiac and cerebrovascular events.

The clinical outcomes were ascertained after hospital discharge until the most recent date for which follow-up data were available.

*The HRs were reported for patients having prior MI with those not having prior MI as reference. Multivariable Cox proportional-hazards regression was used with adjustment for all patient-level variables in Supplemental Table S1.

Supplemental Table S5. Unadjusted Long-term Outcomes According to Pattern of β -Blocker Use in the Overall Population, Patients with, and Patients without Prior Myocardial Infarction

	Always Users	Inconsistent Users			Never Users		
	No. of Patients/ n (%)	No. of Patients/ n (%)	Unadjusted HR (95% CI)	P Value	No. of Patients/ n (%)	Unadjusted HR (95% CI)	P Value
All Patients	2922	1681			1323		
All-cause death	114 (3.9)	111 (6.6)	1.89 (1.46–2.46)	<0.001	90 (6.8)	1.32 (1.00–1.75)	0.05
Cardiac death	59 (2.0)	64 (3.8)	2.27 (1.64–3.14)	<0.001	47 (3.6)	1.27 (0.86–1.88)	0.22
Myocardial infarction	37 (1.3)	16 (1.0)	0.83 (0.46–1.50)	0.54	23 (1.7)	1.07 (0.63–1.81)	0.81
Stroke	235 (8.0)	141 (8.4)	1.14 (0.92–1.40)	0.23	157 (11.9)	1.23 (1.00–1.50)	0.05
Repeat revascularization	100 (3.4)	41 (2.4)	0.77 (0.53–1.10)	0.15	58 (4.4)	1.06 (0.77–1.47)	0.73
MACCE	436 (14.9)	288 (17.1)	1.20 (1.04–1.40)	0.02	292 (22.1)	1.26 (1.08–1.46)	0.003
Patients without Prior MI	1642	991			779		
All-cause death	63 (3.8)	60 (6.1)	1.72 (1.21–2.45)	0.003	50 (6.4)	1.17 (0.80–1.71)	0.41
Cardiac death	33 (2.0)	31 (3.1)	1.71 (1.05–2.79)	0.03	20 (2.6)	0.84 (0.48–1.48)	0.55
Myocardial infarction	15 (0.9)	10 (1.0)	1.21 (0.54–2.69)	0.65	15 (1.9)	1.55 (0.75–3.20)	0.24
Stroke	132 (8.0)	84 (8.5)	1.13 (0.86–1.49)	0.37	88 (11.3)	1.16 (0.88–1.52)	0.30
Repeat revascularization	53 (3.2)	26 (2.6)	0.86 (0.54–1.38)	0.54	43 (5.5)	1.39 (0.93–2.09)	0.11
MACCE	240 (14.6)	167 (16.9)	1.20 (0.98–1.46)	0.08	171 (22.0)	1.24 (1.02–1.51)	0.04
Patients with Prior MI	1280	690			544		
All-cause death	51 (4.0)	51 (7.4)	2.14 (1.45–3.15)	<0.001	40 (7.4)	1.51 (1.00–2.29)	0.05

Cardiac death	26 (2.0)	33 (4.8)	1.93 (1.12–3.32)	0.02	27 (5.0)	2.71 (1.62–4.54)	<0.001
Myocardial infarction	22 (1.7)	6 (0.9)	0.57 (0.23–1.42)	0.23	8 (1.5)	0.71 (0.32–1.61)	0.42
Stroke	103 (8.0)	57 (8.3)	1.15 (0.83–1.59)	0.41	69 (12.7)	1.35 (0.99–1.83)	0.06
Repeat revascularization	47 (3.7)	15 (2.2)	0.65 (0.36–1.16)	0.14	15 (2.8)	0.64 (0.36–1.14)	0.13
MACCE	196 (15.3)	121 (17.5)	1.22 (0.97–1.53)	0.09	121 (22.2)	1.29 (1.03–1.62)	0.03

Abbreviations as in Table S4.

Supplemental Table S6. Outcomes in Pre-specified Subgroups

	Always Users		Inconsistent Users			<i>P</i> Value for Interaction	Never Users			<i>P</i> Value for Interaction
	No. of Patients	Events, n (%)	No. of Patients	Events, n (%)	Adjusted HR* (95% CI)		No. of Patients	Events, n (%)	Adjusted HR* (95% CI)	
All-cause death										
<65 years	1909	45 (2.4)	1093	48 (4.4)	1.76 (1.02–3.05)	<0.001	763	41 (5.4)	2.31 (1.51–3.53)	0.39
≥65 years	1013	69 (6.8)	588	63 (10.7)	1.73 (1.22–2.47)		560	49 (8.8)	1.15 (0.73–1.80)	
No heart failure	2742	105 (3.8)	1615	101 (6.3)	1.38 (0.97–1.97)	0.38	1292	86 (6.7)	1.89 (1.43–2.50)	0.04
Heart failure	180	9 (5.0)	85	10 (11.8)	2.03 (0.48–8.63)		31	4 (12.9)	1.57 (0.28–8.90)	
LVEF ≥50%	2615	90 (3.4)	1508	93 (6.2)	2.06 (1.53–2.78)	0.001	1196	77 (6.4)	1.54 (1.06–2.24)	0.15
LVEF <50%	307	24 (7.8)	173	18 (10.4)	1.95 (0.96–3.97)		127	13 (10.2)	1.16 (0.47–2.87)	
No COPD	2907	113 (3.9)	1619	106 (6.5)	1.96 (1.49–2.57)	0.61	1156	78 (6.7)	1.39 (0.98–1.97)	0.68
COPD	15	1 (6.7)	62	5 (8.1)	1.57 (0.04–57.06)		167	12 (7.2)	1.98 (0.04–43.70)	
No unstable angina	2471	91 (3.7)	1524	99 (6.5)	1.30 (0.89–1.91)	0.54	1224	83 (6.8)	1.87 (1.40–2.52)	0.56
Unstable angina	451	23 (5.1)	157	12 (7.6)	2.04 (0.94–4.42)		99	7 (7.1)	1.00 (0.33–3.06)	
MACCE										
<65 years	1909	263 (13.8)	1093	153 (14.0)	1.13 (0.91–1.39)	0.11	763	151 (19.8)	1.15 (0.88–1.51)	<0.001
≥65 years	1013	173 (17.1)	588	135 (23.0)	1.23 (0.93–1.62)		560	141 (25.2)	1.58 (1.25–2.00)	
No heart failure	2742	404 (14.7)	1615	272 (17.0)	1.20 (0.98–1.46)	0.71	1292	281 (21.7)	1.31 (1.12–1.54)	0.26
Heart failure	180	32 (17.8)	85	16 (18.8)	1.40 (0.69–2.84)		31	11 (35.5)	1.33 (0.55–3.22)	

LVEF \geq50%	2615	387 (14.8)	1508	258 (17.1)	1.23 (1.00–1.50)	0.24	1196	269 (22.5)	1.27 (1.08–1.49)	0.19
LVEF <50%	307	49 (16.0)	173	30 (17.3)	1.44 (0.87–2.39)		127	23 (18.1)	0.94 (0.50–1.78)	
No COPD	2907	430 (14.8)	1619	279 (17.2)	1.18 (0.97–1.44)	0.36	1156	255 (22.1)	1.31 (1.12–1.52)	0.57
COPD	15	6 (40.0)	62	9 (14.5)	0.27 (0.05–1.52)		167	37 (22.2)	0.55 (0.09–3.56)	
No unstable angina	2471	351 (14.2)	1524	253 (16.6)	1.13 (0.92–1.40)	0.28	1224	275 (22.5)	1.23 (1.04–1.45)	0.16
Unstable angina	451	85 (18.8)	157	35 (22.3)	1.37 (0.90–2.10)		99	17 (17.2)	0.88 (0.47–1.64)	

Abbreviations as in Table S1 and Table S4.

*Multivariable Cox proportional-hazards regression was used with adjustment for all patient-level variables in Supplemental Table S1.

Supplemental Table S7. Baseline Demographic and Procedural Characteristics of the Propensity-score Matched Cohorts

Variable	Matched Cohort 1		Matched Cohort 2	
	Always Users n=1636	Inconsistent Users n=1636	Always Users n=1096	Never Users n=1096
Demographics				
Age, mean (SD), y	60.4 (8.8)	60.5 (9.3)	61.0 (8.8)	61.3 (9.1)
Male sex	81	82	81	81
BMI, mean (SD), kg/m ²	24.6 (2.8)	24.6 (2.9)	25.2 (2.8)	25.2 (2.7)
Medical history				
Smoker	53	54	51	51
Diabetes mellitus	31	30	29	30
Hypertension	59	58	68	67
Dyslipidemia	66	60	59	51
Peripheral vascular disease	3	4	5	6
Previous CVA	9	9	7	6
COPD	1	1	1	2
Chronic renal failure	1	1	1	1
Prior myocardial infarction	41	41	43	42
Prior PCI	9	10	8	8
Prior cardiac surgery	1	1	1	1
Congestive heart failure	5	5	4	3
Recent atrial fibrillation	3	3	3	3
LVEF, mean (SD), %	60 (9)	60 (9)	59 (8)	60 (9)
No. of diseased vessels				
2	11	11	12	12
3	87	86	85	84
Left main CAD	32	32	33	34
Status				
Elective	99	99	98	98
Urgent	1	1	2	2
EuroSCORE, mean (SD)	2.8 (2.0)	2.8 (2.1)	2.9 (2.0)	2.9 (2.1)
Procedural characteristics				
Grafts per patient, mean (SD), n	3.4 (0.9)	3.3 (0.9)	3.3 (0.9)	3.1 (0.9)

Off-pump procedure	57	61	75	81
LIMA-to-LAD graft	95	95	94	94
Complete revascularization	92	92	89	89

Abbreviations as in Table S1.

Values expressed as percentage unless otherwise indicated.

Supplemental Table S8. Sensitivity Analysis using β -Blocker Use as A Time-Dependent Covariate

	Unadjusted HR* (95% CI)	P Value	Adjusted HR* (95% CI)	P Value
All Patients				
All-cause death	2.04 (1.32–3.14)	0.001	2.08 (1.30–3.33)	0.002
Cardiac death	2.48 (1.35–4.57)	0.004	2.37 (1.23–4.55)	0.01
Myocardial infarction	1.06 (0.44–2.56)	0.90	0.95 (0.37–2.49)	0.92
Stroke	1.50 (1.19–1.89)	0.006	1.43 (1.11–1.84)	0.005
Repeat revascularization	0.85 (0.55–1.30)	0.45	0.75 (0.47–1.18)	0.21
MACCE	1.37 (1.14–1.65)	<0.001	1.29 (1.05–1.57)	0.01
Patients without Prior MI				
All-cause death	2.07 (1.16–3.70)	0.01	2.20 (1.18–4.10)	0.01
Cardiac death	1.58 (0.67–3.74)	0.30	1.63 (0.65–4.08)	0.29
Myocardial infarction	1.40 (0.42–4.62)	0.58	1.08 (0.30–3.98)	0.90
Stroke	1.37 (1.01–1.87)	0.05	1.32 (0.94–1.86)	0.11
Repeat revascularization	0.86 (0.50–1.49)	0.59	0.82 (0.46–1.47)	0.51
MACCE	1.31 (1.02–1.67)	0.03	1.25 (0.96–1.64)	0.10
Patients with Prior MI				
All-cause death	1.99 (1.03–3.83)	0.04	1.82 (0.88–3.73)	0.10
Cardiac death	3.90 (1.60–9.51)	0.003	3.05 (1.16–7.97)	0.02
Myocardial infarction	0.77 (0.20–2.97)	0.70	0.74 (0.17–3.25)	0.69
Stroke	1.67 (1.18–2.37)	0.004	1.57 (1.07–2.28)	0.02
Repeat revascularization	0.83 (0.41–1.65)	0.59	0.65 (0.31–1.39)	0.27
MACCE	1.46 (1.10–1.94)	0.008	1.30 (0.96–1.77)	0.09

Abbreviations as in Table S4.

The clinical outcomes were ascertained after hospital discharge until the most recent date for which follow-up data were available.

*The HRs were reported for patients not using β -blockers with users as reference. Results were adjusted for all patient-level variables in Supplemental Table S1.

Supplemental Table S9. Sensitivity Analysis in Patients without Contraindications to β -Blocker Therapy

	Always Users	Inconsistent Users			Never Users		
	No. of Patients/ n (%)	No. of Patients/ n (%)	Adjusted HR* (95% CI)	P Value	No. of Patients/ n (%)	Adjusted HR* (95% CI)	P Value
All Patients	2887	1606			1145		
All-cause death	112 (3.9)	105 (6.5)	1.94 (1.48–2.54)	<0.001	78 (6.8)	1.39 (1.00–1.97)	0.05
Cardiac death	58 (2.0)	60 (3.7)	2.20 (1.52–3.19)	<0.001	40 (3.5)	1.32 (0.81–2.16)	0.26
Myocardial infarction	37 (1.3)	15 (0.9)	0.82 (0.44–1.53)	0.52	19 (1.7)	0.98 (0.47–2.04)	0.95
Stroke	233 (8.1)	137 (8.5)	1.21 (0.97–1.50)	0.09	137 (12.0)	1.24 (0.95–1.61)	0.12
Repeat revascularization	99 (3.4)	40 (2.5)	0.66 (0.45–0.97)	0.03	53 (4.6)	0.82 (0.52–1.30)	0.40
MACCE	431 (14.9)	277 (17.2)	1.19 (0.98–1.44)	0.09	255 (22.3)	1.29 (1.11–1.51)	0.001
Patients without Prior MI	1630	950			672		
All-cause death	62 (3.8)	56 (5.9)	1.70 (1.17–2.48)	0.006	43 (6.4)	1.29 (0.79–2.11)	0.30
Cardiac death	33 (2.0)	28 (2.9)	1.75 (1.03–2.97)	0.04	17 (2.5)	0.95 (0.45–2.03)	0.90
Myocardial infarction	15 (0.9)	9 (0.9)	1.08 (0.44–2.66)	0.86	12 (1.8)	1.28 (0.41–3.95)	0.67
Stroke	131 (8.0)	82 (8.6)	1.21 (0.91–1.61)	0.19	76 (11.3)	1.16 (0.81–1.67)	0.41
Repeat revascularization	53 (3.3)	25 (2.6)	0.69 (0.42–1.14)	0.15	40 (6.0)	1.08 (0.60–1.95)	0.80
MACCE	238 (14.6)	160 (16.8)	1.20 (0.92–1.56)	0.18	150 (22.3)	1.24 (1.00–1.52)	0.04
Patients with Prior MI	1257	656			473		
All-cause death	50 (4.0)	49 (7.5)	2.14 (1.42–3.21)	<0.001	35 (7.4)	1.45 (0.86–2.43)	0.17
Cardiac death	25 (2.0)	32 (4.9)	1.86 (0.94–3.70)	0.08	23 (4.9)	2.93 (1.70–5.06)	<0.001

Myocardial infarction	22 (1.8)	6 (0.9)	0.72 (0.29–1.82)	0.49	7 (1.5)	0.85 (0.29–2.45)	0.76
Stroke	102 (8.1)	55 (8.4)	1.20 (0.85–1.67)	0.30	61 (12.9)	1.36 (0.92–2.02)	0.13
Repeat revascularization	46 (3.7)	15 (2.3)	0.64 (0.35–1.17)	0.15	13 (2.7)	0.50 (0.23–1.08)	0.08
MACCE	193 (15.4)	117 (17.8)	1.14 (0.85–1.53)	0.39	105 (22.2)	1.35 (1.07–1.71)	0.01

Abbreviations as in Table S4.

*Multivariable Cox proportional-hazards regression was used with adjustment for all patient-level variables in Supplemental Table S1.

Supplemental Figures

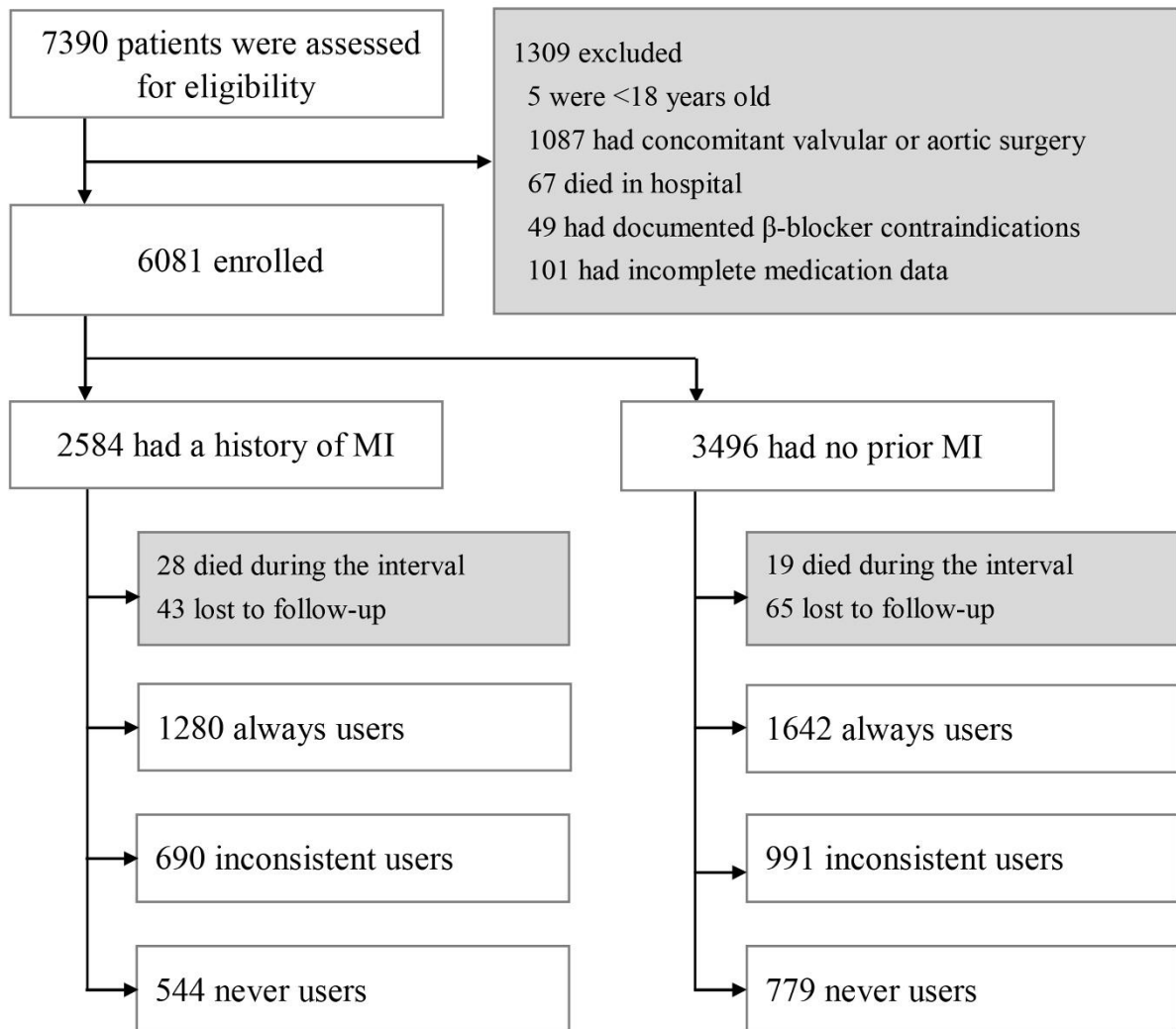


Figure S1

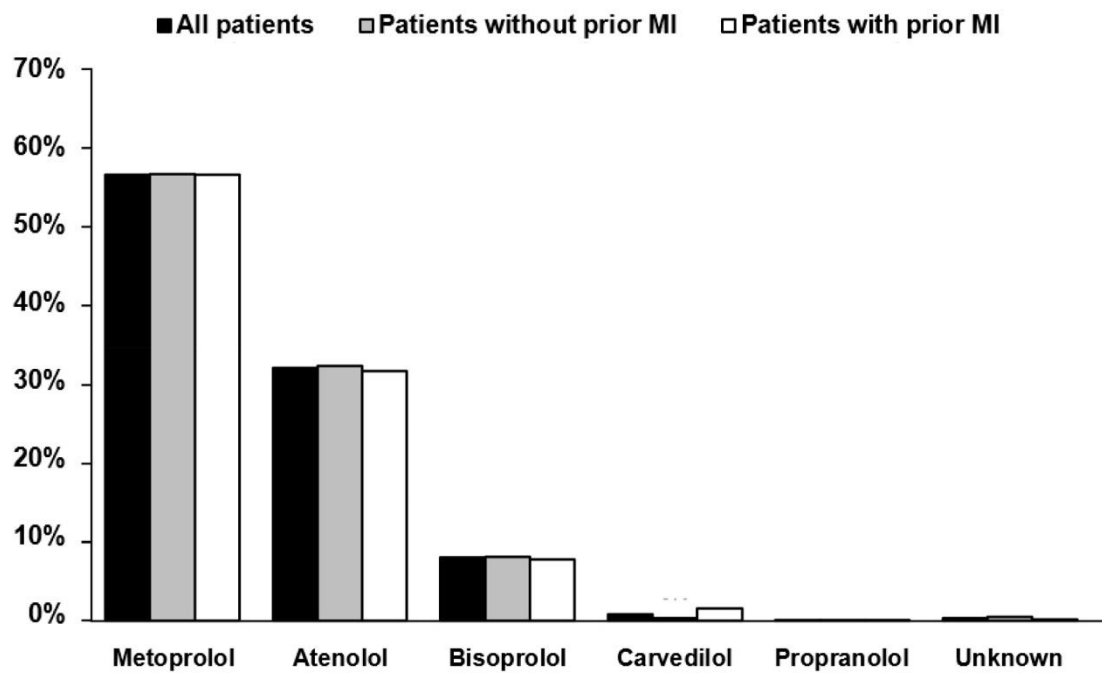


Figure S2

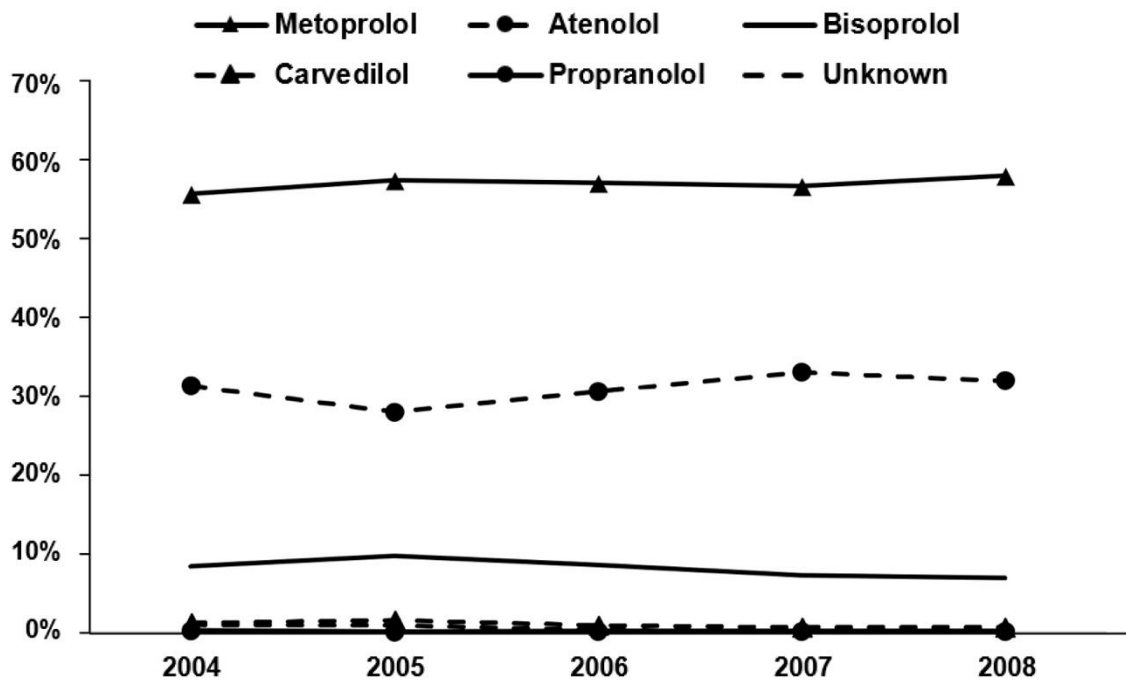


Figure S3

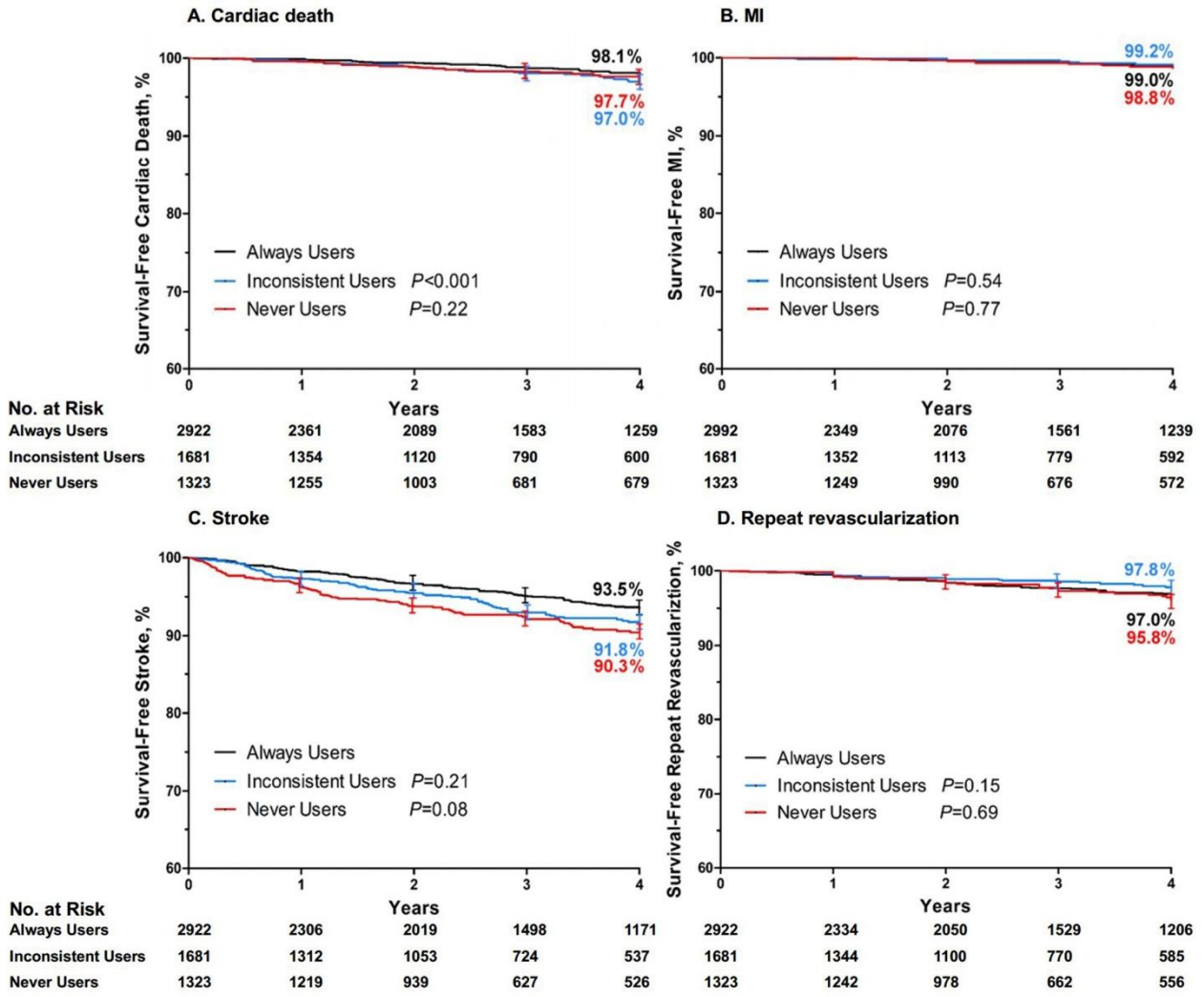


Figure S4

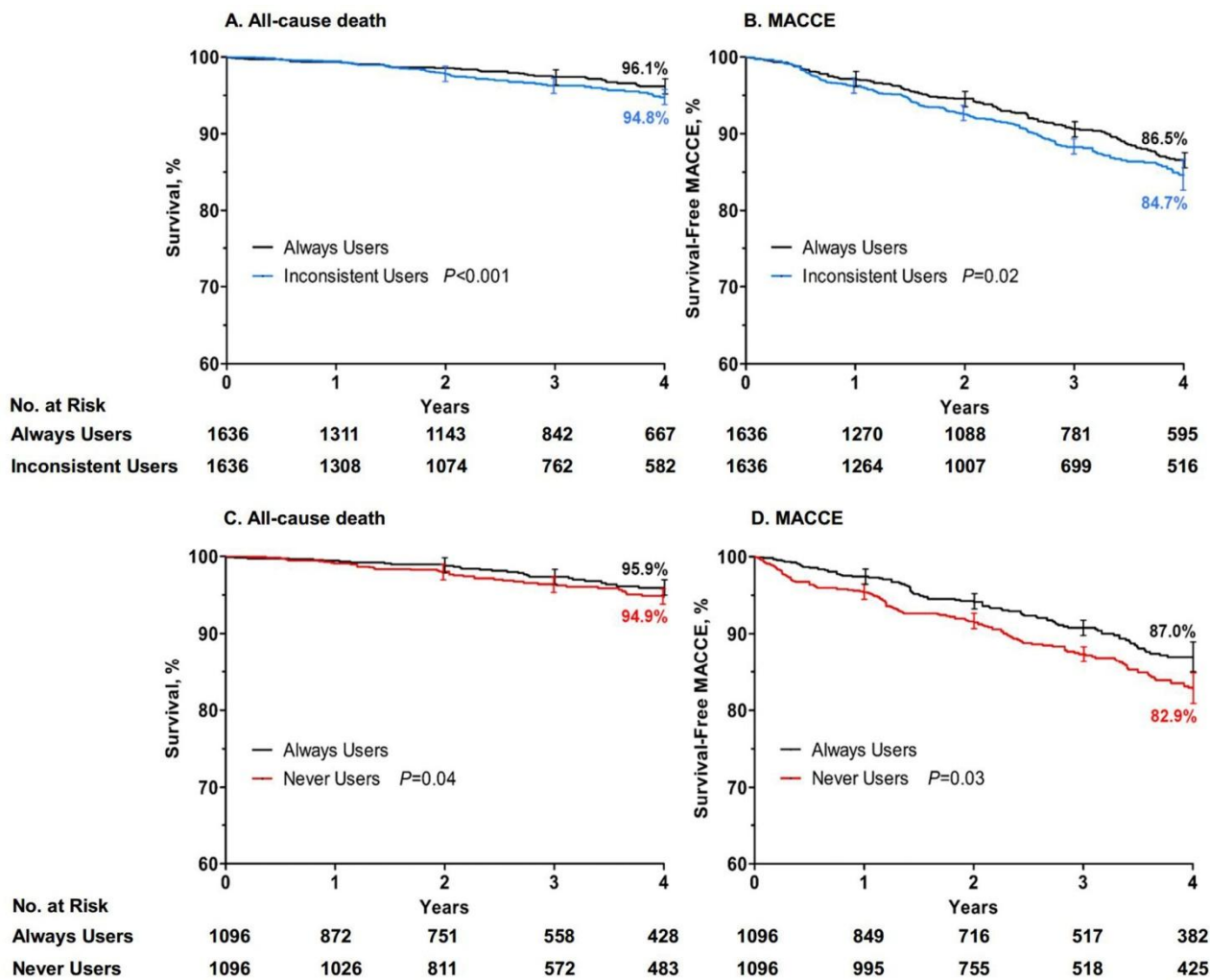


Figure S5