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Association of β-Blockers With Functional Outcomes, Death, and Rehospitalization in Older Nursing Home Residents After Acute Myocardial Infarction

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IMPORTANCE Although β-blockers are a mainstay of treatment after acute myocardial infarction (AMI), these medications are commonly not prescribed for older nursing home residents after AMI, in part owing to concerns about potential functional harms and uncertainty of benefit.

OBJECTIVE To study the association of β-blockers after AMI with functional decline, mortality, and rehospitalization among long-stay nursing home residents 65 years or older.

DESIGN, SETTING, AND PARTICIPANTS This cohort study of nursing home residents with AMI from May 1, 2007, to March 31, 2010, used national data from the Minimum Data Set, version 2.0, and Medicare Parts A and D. Individuals with β-blocker use before AMI were excluded. Propensity score–based methods were used to compare outcomes in people who did vs did not initiate β-blocker therapy after AMI hospitalization.

MAIN OUTCOMES AND MEASURES Functional decline, death, and rehospitalization in the first 90 days after AMI. Functional status was measured using the Morris scale of independence in activities of daily living.

RESULTS The initial cohort of 15 720 patients (11 140 women [70.9%] and 4580 men [29.1%]; mean [SD] age, 83 [8] years) included 8953 new β-blocker users and 6767 nonusers. The propensity-matched cohort included 5496 new users of β-blockers and an equal number of nonusers for a total cohort of 10 992 participants (7788 women [70.9%]; 3204 men [29.1%]; mean [SD] age, 84 [8] years). Users of β-blockers were more likely than nonusers to experience functional decline (odds ratio [OR], 1.14; 95% CI, 1.02-1.28), with a number needed to harm of 52 (95% CI, 32-141). Conversely, β-blocker users were less likely than nonusers to die (hazard ratio [HR], 0.74; 95% CI, 0.67-0.83) and had similar rates of rehospitalization (HR, 1.06; 95% CI, 0.98-1.14). Nursing home residents with moderate or severe cognitive impairment or severe functional dependency were particularly likely to experience functional decline from β-blockers (OR, 1.34; 95% CI, 1.11-1.61 and OR, 1.32; 95% CI, 1.10-1.59, respectively). In contrast, little evidence of functional decline due to β-blockers was found in participants with intact cognition or mild dementia (OR, 1.03; 95% CI, 0.89-1.20; $P = .03$ for effect modification) or in those in the best (OR, 0.99; 95% CI, 0.77-1.26) and intermediate (OR, 1.05; 95% CI, 0.86-1.27) tertiles of functional independence ($P = .06$ for effect modification). Mortality benefits of β-blockers were similar across all subgroups.

CONCLUSIONS AND RELEVANCE Use of β-blockers after AMI is associated with functional decline in older nursing home residents with substantial cognitive or functional impairment, but not in those with relatively preserved mental and functional abilities. Use of β-blockers yielded a considerable mortality benefit in all groups.

Invited Commentary

Supplemental content

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After acute myocardial infarction (AMI), β-blockers are a mainstay of guideline-recommended care for adults.[1,2] Randomized trials in middle-aged and young-old adults (ie, aged 65-75 years) show that treatment with β-blockers after AMI reduces mortality by 25% to 30%.[3-5] Multiple observational studies have found a similar level of mortality reduction in adults 85 years or older and in those with functional impairment or multiple chronic conditions.[6-9]

Despite the benefits of β-blockers across the age span, these medications are less often prescribed to older adults, especially those with functional impairment or multiple comorbidities.[6,7,10,11] Although studies have suggested that β-blockers are generally well tolerated in older adults,[12-14] few data on their adverse event profile in frail and highly vulnerable elders are available, including potential harms such as orthostasis, fatigue, and depression, which can negatively affect daily functioning and quality of life. This dilemma, where potential mortality benefits are weighed against an unclear level of harms, is common in the care of vulnerable older adults.[15-18] It is particularly important for the 1.4 million Americans who reside in nursing homes, who are at high risk for functional decline and often strongly value preserving whatever remaining functional independence they have.[19,20] In this study, we evaluated the effect of β-blockers on functional outcomes in older nursing home residents with AMI and compared these functional outcomes with the effect of β-blockers on death and rehospitalization in this population.

Key Points

Question What effect do β-blockers have on functional decline and death in older nursing home residents with acute myocardial infarction?

Findings In this cohort study, use of β-blockers was associated with a 26% lower rate of death but 14% higher odds of functional decline. Functional harms were particularly pronounced in nursing home residents with poor cognitive and functional status at baseline.

Meaning Decisions about treating older nursing home residents with β-blockers should consider the tradeoff between functional harms and mortality benefits.

Methods

Data Sources and Participants

We obtained data from Medicare Part A and Part D (prescription drug benefit) claims; the Online Survey Certification and Reporting System (OSCAR), which provides facility-level information on nursing home characteristics, staffing, and quality indicators; and the Minimum Data Set (MDS), version 2.0, which consists of assessments of nearly all nursing home residents in the United States. Minimum Data Set assessments occur a minimum of every 3 months, and more often for patients with a major recent change in clinical status and those receiving care under the Medicare Skilled Nursing Facility benefit. This study was approved by the institutional review boards of the University of California, San Francisco, and the Department of Veterans Affairs, who waived the need for informed consent.

Our study population consisted of US nursing home residents 65 years or older who were hospitalized for AMI from May 1, 2007, to March 31, 2010; had resided in a nursing home for at least 30 days before the AMI hospitalization; had not used a β-blocker for at least 4 months before hospitalization; and returned to a nursing home after hospital discharge[21] (eAppendix 1 in the Supplement provides additional details). We defined hospitalization with AMI based on a hospital admission or discharge claim with code 410.XX or 411.1 from the *International Classification of Diseases, Ninth Revision*, as a primary or secondary diagnosis. We excluded patients who died, were rehospitalized, or otherwise left the nursing home within 14 days of hospital discharge because reliable ascertainment of β-blocker use is difficult in such short-stay situations. We also excluded patients with a very poor prognosis at baseline (Changes in Health, End-stage Disease, and Signs and Symptoms [CHESS] score of 5 [range, 0-5, with higher scores indicating worse prognosis]),[22] patients on hospice, patients who were not continuously enrolled in Medicare Part D during the study period or had no Part D claims after hospitalization, and patients who were enrolled in a Medicare Advantage plan at any point during this period. Finally, we excluded patients with extremely poor functional status before hospitalization (Morris scale of independence in activities of daily living [ADL] score ≥24 [range, 0-28, with higher scores indicating greater dependency]) because they had little room for further functional decline.[23]

Measures

Our exposure of interest was use of a β-blocker in the immediate posthospital period. We defined this as a Part D claim for an oral β-blocker within 30 days of resuming Part D coverage after hospital discharge. Part D covers at least 81% of nursing home residents and in most cases is the sole source of prescription drug coverage for these patients.[24] For the subset of patients who return to the nursing home under the Medicare Skilled Nursing Facility benefit, resumption of Part D claims is temporarily delayed. Therefore, we conducted a companion validation study to evaluate the performance of our β-blocker exposure measure in this subset. This study confirmed the validity of our measure (eAppendix 1 in the Supplement).

Our primary outcome was functional decline. We defined this as a loss of 3 points on the validated Morris scale of independence in ADLs between the prehospital baseline assessment and the first available assessment after hospitalization, to 3 months after discharge.[23] A 3-point drop corresponds to a major loss of independence in 1 ADL or incremental losses in 2 or more ADLs. In a sensitivity analysis, we evaluated the outcome as a 4-point (more substantial) decline in function. We chose a 90-day outcome period because it is long enough to be clinically meaningful but short enough that many of these highly vulnerable patients have not yet died, a competing outcome that complicates interpretation of longer-term functional outcomes.

Other key outcome measures included death and rehospitalization within 90 days of the index hospital discharge. We used data from Medicare Part A and Medicare enrollment files to identify hospital admissions and date of death. We also explored the following 2 composite outcomes: time to hospitalization or death, and time to hospitalization, death, or functional decline.

Information on chronic conditions and characteristics of the index hospitalization were obtained from Medicare Part A data. Overall, this data source is more accurate for identifying chronic conditions than MDS 2.0.[25-28] The MDS 2.0 provided data on other patient characteristics, including functional and cognitive status, geriatric syndromes, and symptoms, including validated scales such as the Cognitive Performance Score and CHESS scores.[22,29] We used the OSCAR data set to evaluate a variety of nursing home facility characteristics such as staffing, resident mix, and quality indicators.

Statistical Analysis

We used propensity score–based methods to evaluate the association between β-blocker exposure and our outcomes of interest. Following an intention-to-treat framework, we defined participants as β-blocker users or nonusers throughout the study period based on their exposure in the immediate post-AMI period.

We estimated the propensity score via a logistic regression model that used 93 variables to predict β-blocker use. Variables included sociodemographic characteristics, chronic medical conditions, baseline medication use, hospitalization history, baseline functional and cognitive status, geriatric syndromes, symptoms, characteristics of the AMI hospitalization, and nursing home characteristics (eAppendix 2 in the Supplement). To evaluate whether vital signs, laboratory test results, and measures of cardiac function could result in unmeasured confounding, we conducted a companion validation study using national data from the Department of Veterans Affairs, which, unlike Medicare claims data, contains information on these variables. We found no evidence that the absence of these factors would substantially alter our results (eAppendix 3 in the Supplement).

To match β-blocker users with nonusers who had similar propensity scores, we first discarded participants in the top and bottom 1% of the propensity score distribution so as to exclude areas of nonoverlap. We then applied a 1:1 greedy 5-to-1 digit-matching algorithm without replacement.[30] We evaluated the quality of resulting matches by comparing standardized differences between groups for each covariate in our model and by using 2-tailed *t* tests to assess differences in the distribution of propensity scores.[31,32]

Our propensity matching yielded an excellent covariate balance, so we did not further adjust for baseline covariates in our models. Because we excluded people who died or were rehospitalized during the first 14 days after hospital discharge, we did not consider outcomes that occurred during this period, thus effectively beginning our outcome analyses at day 14 after hospitalization.

We used Cox proportional hazards regression models to determine the effect of β-blocker use on time to death. We used the method of Fine and Gray (similar to Cox regression) to evaluate the effect of β-blocker use on time to rehospitalization while accounting for the competing outcome of death.[33] Finally, we used multinomial logit models to evaluate the effect of β-blocker use on functional decline.[28] At the end of the 90-day follow-up, participants were classified as alive without functional decline, having had functional decline documented in the first MDS assessment of that period, or having died without evidence of functional decline on the first MDS assessment.

We used multiplicative and additive interaction terms to evaluate whether the effect of β-blockers on outcomes varied across participant characteristics. These characteristics included levels of baseline functional status, cognitive function, age, and presence or absence of an intensive care unit or cardiac care unit stay during the AMI hospitalization. The distribution of propensity scores was very similar for β-blocker users and nonusers within each subgroup, suggesting that stratifying patients into subgroups did not threaten covariate balance (eAppendix 4 in the Supplement).

The decision to exclude patients who died or were rehospitalized within 14 days after the AMI discharge has the potential to create selection bias. To evaluate this, we repeated our main analyses using inverse probability of selection weighting.[34,35] This approach weighted participants according to their similarity to individuals who were excluded owing to death (n = 1859) or rehospitalization (n = 2444) in the first 14 days, thus estimating treatment effects as if these people had been included in the analysis. In another sensitivity analysis, we controlled for post-AMI use of other cardiovascular medications with multinomial logistic regression in our propensity-matched cohort.

We also evaluated several alternate approaches to determine whether our results were stable across different analytic techniques. These approaches included stratifying by propensity score quintiles and deciles, controlling for propensity score as a covariate, using inverse probability of treatment weights, and performing time-dependent analyses. In each case, results were similar to our main approach (eAppendix 5 in the Supplement). We considered $P < .05$ to be statistically significant.

Results

Our initial cohort of 15 720 patients (11 140 women [70.9%] and 4580 men [29.1%]; mean [SD] age, 83 [8] years) included 8953 new β-blocker users and 6767 nonusers. Before matching, β-blocker users were more likely to have been in an intensive care unit or a cardiac care unit during the hospital stay and to return to the nursing home on the Medicare Skilled Nursing Facility benefit care pathway and less likely to have a prior diagnosis of angina pectoris or unstable angina (**Table 1**, **Table 2**, and eAppendix 6 in the Supplement).

Propensity score matching yielded a cohort of 5496 new β-blocker users and an equal number of nonusers (Tables 1 and 2). Mean (SD) age was 84 (8) years; 7788 were women (70.9%); and 3204 were men (29.1%). The distribution of propensity

Table 1. Characteristics of β-Blocker Users and Nonusers Before and After Propensity Score–Based Matching

Characteristic	Patient Cohort, No. (%)[a]			
	Before Matching		After Matching	
	β-Blocker Users (n = 8953)	β-Blocker Nonusers (n = 6767)	β-Blocker Users (n = 5496)	β-Blocker Nonusers (n = 5496)
Age, mean (SD), y	83 (8)	84 (8)	84 (8)	84 (8)
Female sex	6304 (70.4)	4836 (71.5)	3901 (71.0)	3887 (70.7)
Race				
White	7232 (80.8)	5597 (82.7)	4485 (81.6)	4497 (81.8)
African American	1158 (12.9)	756 (11.2)	644 (11.7)	646 (11.8)
Other	563 (6.3)	414 (6.1)	367 (6.7)	353 (6.4)
Chronic conditions				
Diabetes	2855 (31.9)	1942 (28.7)	1567 (28.5)	1582 (28.8)
Heart failure	4534 (50.6)	3051 (45.1)	2554 (46.5)	2562 (46.6)
COPD	2218 (24.8)	1942 (28.7)	1498 (27.3)	1504 (27.4)
Depression	1101 (12.3)	838 (12.4)	660 (12.0)	622 (11.3)
Elixhauser comorbidity score, median (IQR)	3 (2-4)	3 (2-4)	3 (2-4)	3 (2-4)
ADL status before hospitalization[b]				
Independent to limited assistance required	3054 (34.1)	2347 (34.7)	1834 (33.4)	1866 (34.0)
Extensive assistance required	3050 (34.1)	2188 (32.3)	1801 (32.8)	1778 (32.4)
Extensive dependency	2849 (31.8)	2232 (33.0)	1861 (33.9)	1852 (33.7)
Cognitive status before hospitalization[c]				
Intact or borderline intact	2790 (31.2)	1961 (29.0)	1580 (28.8)	1585 (28.8)
Mild to moderate dementia	4609 (51.5)	3505 (51.8)	3294 (59.9)	3305 (60.1)
Moderately severe to very severe dementia	1554 (17.4)	1301 (19.2)	622 (11.3)	606 (11.0)
CHESS score before hospitalization, mean (SD)[d]	0.6 (0.8)	0.6 (0.8)	0.6 (0.8)	0.6 (0.8)
Geriatric symptoms before hospitalization				
Dizziness, vertigo, or syncope	103 (1.2)	82 (1.2)	54 (1.0)	55 (1.0)
Falls	1843 (20.6)	1515 (22.4)	1193 (21.7)	1187 (21.6)
Dyspnea	621 (6.9)	645 (9.5)	461 (8.4)	455 (8.3)
No. of medications before hospitalization, median (IQR)	11 (8-15)	12 (9-15)	11 (8-15)	12 (8-15)
Medication use before hospitalization				
Statins	2584 (28.9)	1944 (28.7)	1559 (28.4)	1580 (28.7)
Antiplatelets	1453 (16.2)	1165 (17.2)	914 (16.6)	916 (16.7)
Warfarin	992 (11.1)	938 (13.9)	707 (12.9)	723 (13.2)
Psychotropics[e]	5400 (60.3)	4367 (64.5)	3547 (64.5)	3482 (63.4)
Length of hospital stay for AMI, median (IQR), d	6 (4-9)	6 (4-9)	6 (4-9)	6 (4-9)
No. of days in ICU or CCU				
None	3385 (37.8)	3277 (48.4)	2374 (43.2)	2361 (43.0)
1-2	2425 (27.1)	1589 (23.5)	1376 (25.0)	1396 (25.4)
≥3	3143 (35.1)	1901 (28.1)	1746 (31.8)	1739 (31.6)
Nursing home care pathway after hospitalization				
Skilled nursing facility benefit	6714 (75.0)	4569 (67.5)	3894 (70.9)	3867 (70.4)
Long-term care	2239 (25.0)	2198 (32.5)	1602 (29.1)	1629 (29.6)

Abbreviations: ADL, activities of daily living; AMI, acute myocardial infarction; CCU, cardiac care unit; CHESS, Changes in Health, End-stage Disease, and Signs and Symptoms; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; IQR, interquartile range.

[a] Percentages have been rounded and may not total 100.

[b] Measured by the Morris 28-point scale of independence in ADLs, and categorized as 0 to 14 (independent to limited assistance required), 15 to 19 (extensive assistance required), and 20 or higher (extensive dependency).

[c] Measured by the Cognitive Performance Scale and trichotomized as 0 to 1 (intact to borderline intact), 2 to 3 (mild to moderate dementia), and 4 to 6 (moderately severe to very severe dementia).

[d] Scores range from 0 to 5, with higher scores indicating greater health instability.

[e] Include antidepressants, antipsychotics, antianxiety medications, and sedatives or hypnotics.

scores was nearly identical between the matched groups (mean [SD], 0.57 [0.11] in β-blocker users vs 0.57 [0.11] in nonusers; $P = .63$), and all but 2 variables had standardized mean differences of 0.03 or less (eAppendix 6 in the Supplement). This result is consistent with excellent covariate balance between groups.[31] Users and nonusers of β-blockers had equal time

Table 2. Nursing Home Facility Characteristics of β-Blocker Users and Nonusers Before and After Propensity Score–Based Matching

Characteristic	Patient Cohort, No. (%)[a]			
	Before Matching		After Matching	
	β-Blocker Users (n = 8953)	β-Blocker Nonusers (n = 6767)	β-Blocker Users (n = 5496)	β-Blocker Nonusers (n = 5496)
Ownership				
For profit	6488 (72.5)	4909 (72.5)	4019 (73.1)	3991 (72.6)
Not for profit	1983 (22.1)	1451 (21.4)	1151 (20.9)	1195 (21.7)
Government	482 (5.4)	407 (6.0)	326 (5.9)	310 (5.6)
Size, No. of beds				
<100	1375 (15.4)	871 (12.9)	1535 (27.9)	1521 (27.7)
100-200	5258 (58.7)	3951 (58.4)	3206 (58.3)	3220 (58.6)
>200	2320 (25.9)	1945 (28.7)	755 (13.7)	755 (13.7)
Quality indicators				
Residents restrained, median (IQR), %	2.8 (0-6.5)	3.1 (0.4-6.9)	2.9 (0.4-6.6)	3.0 (0.3-6.7)
No. of quality-of-life deficiencies, mean (SD)	0.73 (1.1)	0.74 (1.1)	0.73 (1.0)	0.75 (1.1)
Residents with pressure sores, mean (SD), %	7.2 (4.5)	7.0 (4.3)	7.1 (4.6)	7.0 (4.3)
Direct care per resident per day, mean (SD), h	3.4 (0.8)	3.4 (0.8)	3.4 (0.7)	3.4 (0.8)

Abbreviation: IQR, interquartile range.

[a] Percentages have been rounded and may not total 100.

between nursing home readmission and their first ADL assessment (median, 22 days; interquartile range, 11-29 days; $P = .97$). New β-blockers users were more likely than nonusers to be prescribed other cardiovascular medications in the post-AMI period, including statins (2705 [49.2]% vs 1779 [32.4%]; $P < .001$) and angiotensin-converting enzyme inhibitors (2439 [44.4%] vs 1683 [30.6]%; $P < .001$), but not angiotensin receptor blockers (409 [7.4%] vs 448 [8.2%]; $P = .17$).

Within 3 months after hospital discharge, 1328 of 10 992 participants (12.1%) experienced functional decline; 2782 (25.3%) were rehospitalized; and 1541 (14.0%) died. Some patients experienced more than 1 outcome, such as rehospitalization and then death.

Users of β-blockers had a higher rate of functional decline than nonusers. In the first 90 days after AMI, the odds of functional decline were 1.14 (95% CI, 1.02-1.28) times greater in patients receiving β-blockers than in those not using β-blockers (**Table 3**). The number needed to treat to cause 1 patient to have functional decline was 52 (95% CI, 32-141). Results were similar using the more stringent threshold of a 4-point decline on the Morris ADL scale. Using this definition, 1165 subjects (10.6%) had functional decline, and β-blocker users were more likely to have a decline (odds ratio [OR], 1.16; 95% CI, 1.02-1.31).

Users of β-blockers were less likely than nonusers to die within 90 days of hospital discharge (hazard ratio [HR], 0.74; 95% CI, 0.67-0.83) (**Figure 1**A and Table 3). The number needed to treat to prevent 1 death was 26 (95% CI, 19-39). Use of β-blockers had no effect on time to rehospitalization (HR, 1.06; 95% CI, 0.98-1.14) (Figure 1B and Table 3).

Use of β-blockers had no significant effect on a composite outcome of time to death, hospitalization, or functional decline (HR, 0.98; 95% CI, 0.94-1.03). Use of β-blockers showed a borderline small protective effect for a composite outcome that only included time to death or hospitalization (HR, 0.94; 95% CI, 0.88-1.00).

The effect of β-blocker use on death was similar across a variety of patient characteristics (**Figure 2**). However, the effect of β-blocker use on functional decline varied according to patients' baseline cognitive and functional status (Figure 2 and eAppendix 7 in the Supplement). Among nursing home residents with moderate or severe cognitive deficits, β-blocker users were substantially more likely than nonusers to experience functional decline (OR, 1.34; 95% CI, 1.11-1.61), with a number needed to harm of 36 (95% CI, 24-76). In contrast, use of β-blockers did not increase the risk of functional decline in people with intact cognition or mild dementia (OR, 1.03; 95% CI 0.89-1.20; $P = .03$ for effect modification of treatment by cognition). Among residents with severe functional dependence at baseline, β-blocker users had greater risk of functional decline than did nonusers (OR, 1.32; 95% CI 1.10-1.59), with a number needed to harm of 25 (95% CI, 16-55). In contrast, β-blocker use did not increase the risk of functional decline in people in the best (OR, 0.99; 95% CI, 0.77-1.26) and intermediate (OR, 1.05; 95% CI, 0.86-1.27) tertiles of baseline ADL functioning ($P = .06$ for effect modification of treatment by baseline functional status).

The main results were similar after applying inverse probability of selection weights, although the point estimate for the effect of β-blockers on functional decline was slightly attenuated, with 95% CIs crossing 1 (OR, 1.09; 95% CI, 0.96-1.24). Similar patterns held for results of subgroup analyses using selection weights (eAppendix 8 in the Supplement). Finally, results were similar after controlling for use of other cardiovascular medications in the post-AMI setting (eAppendix 5 in the Supplement).

Table 3. Effect of β-Blockers on Main Outcomes

Outcome	β-Blocker Users vs Nonusers, OR/HR (95% CI)[a]	NNH or NNT, Point Estimate (95% CI)[b]
Functional decline	1.14 (1.02-1.28)	NNH 52 (32-141)
Death, HR (95% CI)	0.74 (0.67-0.83)	NNT 26 (19-39)
Rehospitalization, HR (95% CI)	1.06 (0.98-1.14)	NNH 82 (NNH 250 to ∞ to NNT 36)[c]

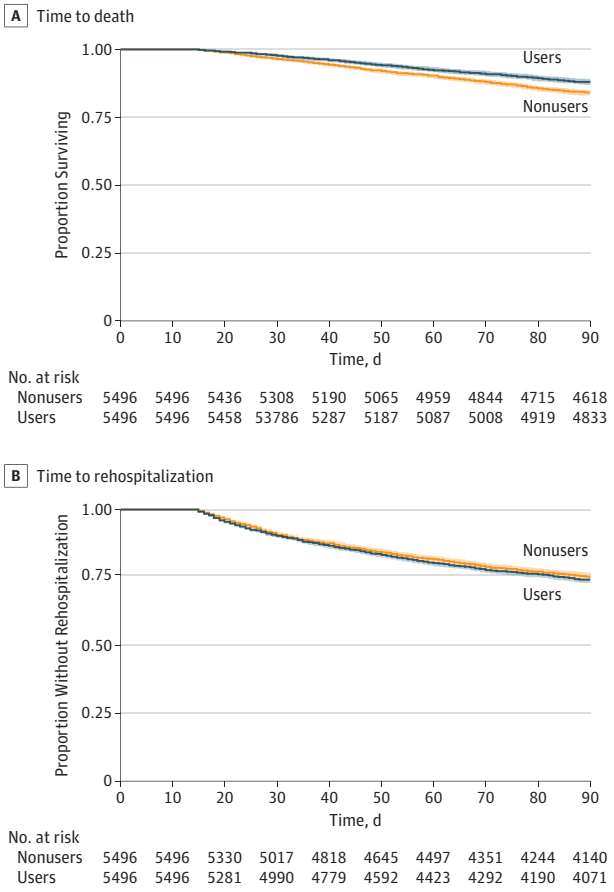
Abbreviations: HR, hazard ratio; NNH, number needed to harm; NNT, number needed to treat; OR, odds ratio.

[a] Data shown are ORs for functional decline and HRs for death and for rehospitalization.

[b] Calculated as 1/(control event rate − intervention event rate).

[c] The nonsignificant NNH/NNT is expressed in the format recommended by Altman.[36]

Figure 1. Association Between β-Blocker Use and Death or Rehospitalization



Patients are divided between users and nonusers of β-blockers. No events in the first 14 days after hospital discharge are recorded because patients who left the nursing home for any reason in the first 14 days after hospital discharge were excluded from analysis. Shaded areas indicate the 95% CIs around each survival curve.

Discussion

In this national study of older nursing home residents, using β-blockers after AMI resulted in a 26% relative reduction in 90-day mortality, with a number needed to treat of 26 to prevent 1 death. Similar levels of risk reduction were found across a wide variety of patient subgroups. However, β-blockers conferred a 14% relative increase in the odds of functional decline, with a number need to harm of 52 to cause 1 case of functional decline. This risk was particularly high for people with moderate or severe cognitive impairment or a high degree of functional dependence at baseline. In these groups, β-blockers increased the odds of functional decline by 32% to 34%, with a number needed to harm of 25 to 36. In contrast, nursing home residents with relatively preserved cognitive and functional abilities did not appear to experience adverse functional consequences from receiving β-blockers.

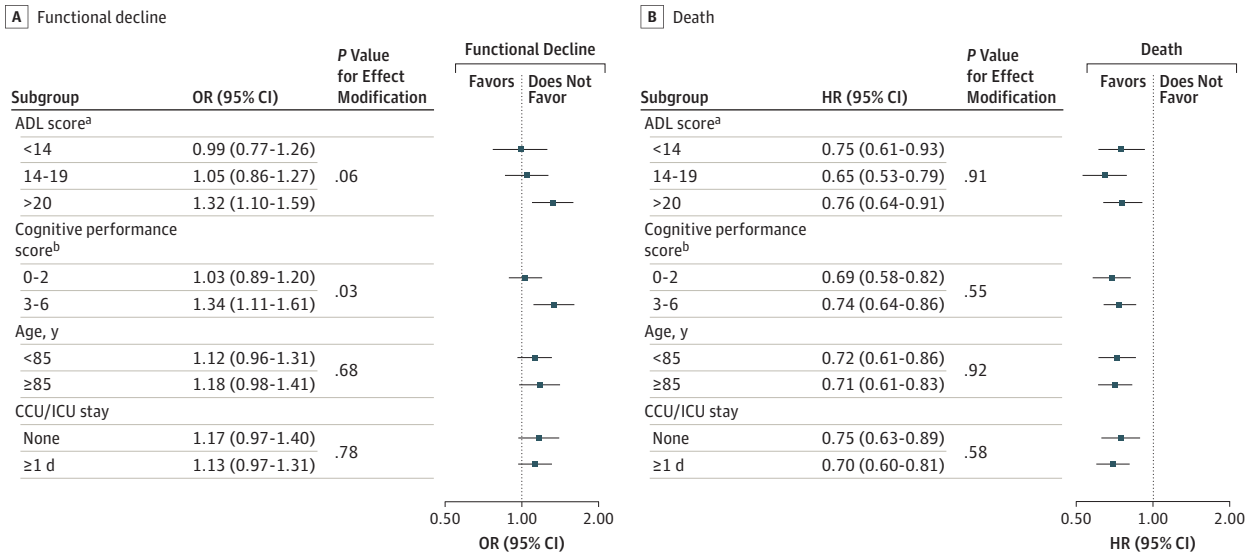
Our findings of mortality benefit are consistent with the results of other observational studies of β-blocker use among the old-old (aged ≥85 years), frail, and functionally impaired.[6-9,37,38] Regarding harms, little is known about the effect of β-blockers on functional status. However, these agents increase the risk for fatigue (particularly first-generation agents such as propranolol hydrochloride)[12] and have been associated with increased rates of dizziness[39,40] and a decreased subjective sense of well-being,[41,42] although no consistent effect has been found on rates of depression[12] or falls.[13,43]

Our results confirm the suspicion of many physicians that poor cognitive and functional status increases the risk for medication-induced harms in older adults. However, they call into question the more general practice whereby older adults are less likely to receive guideline-recommended medications after AMI regardless of their mental or physical abilities.[7,10,11,44] For nursing home residents with intact cognition or mild dementia and in those with nonsevere levels of functional dependency, we found substantial mortality benefit and no functional harms. Therefore, treatment is appropriate for most such patients. In contrast, for nursing home residents with extensive functional dependency or moderate to severe dementia (roughly corresponding to a Folstein Mini-Mental State Examination score of ≤14 of 30 points),[29] resolving the tradeoff between reduced mortality and increased risk for functional decline will depend on patient preferences, as expressed directly or through surrogate decision makers.[45,46] For cognitively or functionally impaired nursing home residents who are more concerned about functional decline than death, avoiding treatment may be preferable. This is a large population; more than half of nursing home residents have high levels of functional dependence, and two-thirds have moderate or severe cognitive impairment.[47]

Limitations

Because this study is observational, we cannot rule out the possibility of confounding. However, several factors support the robustness of our findings. We obtained an excellent balance of baseline covariates across treatment groups and consistent results using several alternate analytic approaches. Moreover, younger and healthier patients are more likely to receive secondary prevention medications after AMI.[7,10,11,44,48] This likelihood would bias results toward better outcomes in

Figure 2. Subgroup Analyses of the Effect of β-Blockers on Functional Decline and Death



P values show the significance of effect modification on the multiplicative scale (determined using the Wald test). Values for additive effect modification are expressed as relative excess risk due to interaction (RERI). For the outcome of functional decline, RERI for moderate dependence in activities of daily living (ADL) is 0.11 (95% CI, −0.36 to 0.58; *P* = .65) and for high dependence in ADL, 0.66 (95% CI, 0.20 to 1.13; *P* < .01), indicating positive additive interaction for high ADL dependence. The RERI for worse cognitive performance score (CPS) is 0.08 (95% CI, −0.12 to 0.29; *P* = .42); for increased age, −0.14 (95% CI, −0.38 to 0.11; *P* = .27); and for intensive care unit or cardiac care unit (ICU/CCU) stay, −0.03 (95% CI, −0.29 to 0.24; *P* = .85). For the outcome of death, RERI for moderate dependence in ADL is −0.35 (95% CI, −0.70 to 0.01; *P* = .05), indicating potential negative additive interaction. The RERI for higher ADL dependence is −0.19 (95% CI, −0.54 to 0.17; *P* = .31); for worse CPS, −0.15 (95% CI, −0.42 to 0.12; *P* = .29); for increased age, 0.00 (95% CI, −0.21 to 0.22; *P* = .97); and for ICU/CCU stay, −0.05 (95% CI, −0.26 to 0.14; *P* = .60). HR indicates hazard ratio; OR, odds ratio.

[a] An ADL score less than 14 corresponds to independence or requiring limited assistance with ADLs; 14 to 19, requiring extensive assistance; and 20 or higher, requiring extensive dependence on others to perform ADLs.

[b] A CPS score of 0 to 2 corresponds to normal to mildly impaired cognition, including mild dementia; 3 to 6, moderate or severe cognitive impairment (roughly equivalent to a Folstein Mini-Mental State Examination score of ≤14 of 30).

β-blocker users. Instead, functional outcomes were in the opposite direction of this expected bias. Cointerventions constitute another important consideration. People who used β-blockers after AMI were also more likely to receive statins and angiotensin-converting enzyme inhibitors in the post-AMI period. Controlling for these differences slightly attenuated the observed associations between β-blocker use and our outcomes of interest, although the overall pattern remained.

To enable robust assessment of β-blocker exposure, we excluded patients who died or were rehospitalized within the first 14 days of hospital discharge. This exclusion prevented us from evaluating the effect of β-blockers on outcomes during this period. Thus, our results should be interpreted as providing evidence about the effect of β-blocker use on outcomes starting 14 days after discharge, among people who had survived and remained in the nursing home until then. In addition, these exclusions could induce selection bias.[34,35] However, although our sensitivity analyses were consistent with the possibility of mild selection bias, we found little evidence of bias sufficiently large to invalidate our overall findings.

Conclusions

Use of β-blockers after AMI resulted in substantial reductions in mortality among older nursing home residents. At the same time, use of these agents resulted in worse functional outcomes among nursing home residents with substantial cognitive or functional deficits. In this highly vulnerable group, understanding the importance that individual patients place on avoiding death and on avoiding functional decline will be critical to guiding decision making about use of these medications.

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