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ORIGINAL INVESTIGATIONS

Adherence Tradeoff to Multiple Preventive Therapies and All-Cause Mortality After Acute Myocardial Infarction

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ABSTRACT

BACKGROUND Angiotensin-converting enzyme (ACE) inhibitors/angiotensin II receptor blockers (ARB), beta-blockers and statins are recommended after acute myocardial infarction (AMI). Patients may adhere to some, but not all, therapies.

OBJECTIVES The authors investigated the effect of tradeoffs in adherence to ACE inhibitors/ARBs, beta-blockers, and statins on survival among older people after AMI.

METHODS The authors identified 90,869 Medicare beneficiaries ≥65 years of age who had prescriptions for ACE inhibitors/ARBs, beta-blockers, and statins, and survived ≥180 days after AMI hospitalization in 2008 to 2010. Adherence was measured by proportion of days covered (PDC) during 180 days following hospital discharge. Mortality follow-up extended up to 18 months after this period. The authors used Cox proportional hazards models to estimate hazard ratios of mortality for groups adherent to 2, 1, or none of the therapies versus group adherent to all 3 therapies.

RESULTS Only 49% of the patients adhered (PDC ≥80%) to all 3 therapies. Compared with being adherent to all 3 therapies, multivariable-adjusted hazard ratios (95% confidence intervals [CIs]) for mortality were 1.12 (95% CI: 1.04 to 1.21) for being adherent to ACE inhibitors/ARBs and beta-blockers only, 0.98 (95% CI: 0.91 to 1.07) for ACEI/ARBs and statins only, 1.17 (95% CI: 1.10 to 1.25) beta-blockers and statins only, 1.19 (95% CI: 1.07 to 1.32) for ACE inhibitors/ARBs only, 1.32 (95% CI: 1.21 to 1.44) for beta-blockers only, 1.26 (95% CI: 1.15 to 1.38) statins only, and 1.65 (95% CI: 1.54 to 1.76) for being nonadherent (PDC <80%) to all 3 therapies.

CONCLUSIONS Patients adherent to ACE inhibitors/ARBs and statins only had similar mortality rates as those adherent to all 3 therapies, suggesting limited additional benefit for beta-blockers in patients who were adherent to statins and ACE inhibitors/ARBs. Nonadherence to ACE inhibitors/ARBs and/or statins was associated with higher mortality. (J Am Coll Cardiol 2017;70:1543-54) © 2017 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

ACE = angiotensin-converting enzyme

AMI = acute myocardial infarction

ARB = angiotensin II receptor blocker

CI = confidence interval

CVD = cardiovascular disease

HR = hazard ratio

PDC = proportion of days covered

Clinical guidelines recommend prescribing angiotensin-converting enzyme (ACE) inhibitors/angiotensin II receptor blockers (ARB), beta-blockers, and statins after an acute myocardial infarction (AMI). The effectiveness of these guideline-recommended preventive therapies is dependent on patient adherence (1-4). However, a recent U.S. study reported that almost 40% of the patients who initiated use of ACE inhibitors/ARBs, beta-blockers or statins following hospitalization for AMI became nonadherent during the first treatment year (5). Many seem to do so already during the first 6 months (6). Studies from other countries also suggest sub-optimal adherence to preventive therapies for the secondary prevention of cardiovascular disease (CVD) (7-9).

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Adhering to multiple therapies can present considerable challenges for older adults with multiple comorbidities and medications. The proportion of adults 65 years of age and older who take 5 or more prescription medications tripled from 13% to 39% between 1988 and 2010 (10). Patients with multiple comorbidities and polypharmacy have an increased risk of drug-drug interactions and adverse drug events (11). Furthermore, therapeutic and medication regimen complexity may decrease medication adherence (12,13). Patients may have tradeoffs in adherence; in other words, they may choose to adhere to some post-AMI preventive therapies, but not to others. Studies have shown notable variation in adherence across post-AMI preventive therapies (1,5,9,14,15). Clinicians who manage patients with complex treatment regimens are required to balance benefits and risks of preventive therapies, because evidence from randomized clinical trials mostly relates to the efficacy of a single preventive therapy on survival following AMI rather than combinations of therapies (16,17). Indeed, post-AMI beta-blocker trials were largely performed before statin use became widespread, and additive efficacy of beta-blockers in statin-treated patients remains undetermined.

If a patient is not able to adhere to all post-AMI preventive therapies long term, which therapies should clinicians emphasize for patient adherence? Little is known about the clinical impact of the tradeoffs in adherence made among the preventive therapies after AMI. Thus, the objective of this study was to investigate the effects of tradeoffs in adherence to ACE inhibitors/ARBs, beta-blockers, and statins on all-cause mortality after AMI in a large cohort of Medicare beneficiaries.

METHODS

DATA SOURCES AND STUDY COHORT. Data were sourced from the Center for Medicare & Medicaid Services Medicare Chronic Condition Data Warehouse 2007 to 2011 files that include enrollment summaries and inpatient, outpatient, skilled-nursing facility, physician office visits, and prescription claims. We first identified all Medicare beneficiaries meeting the following eligibility criteria: 1) age 65 years or older; 2) continuous enrollment for ≥365 days before and ≥180 days after the index AMI hospitalization in the Medicare fee-for-service and Part D prescription benefits; 3) index AMI hospitalization between January 1, 2008, and December 31, 2010; 4) discharge to home, and 5) survival for >180 days after the index hospitalization (**Figure 1**). Patients hospitalized for AMI were identified using an International Classification of Diseases, Ninth Revision, code of 410.x1 recorded either in the primary or secondary discharge diagnosis field in the inpatient files (5). The index AMI hospitalization was defined as each patient's first hospitalization for AMI between 2008 and 2010. The final study population comprised patients who had all 3 preventive therapies (ACE inhibitors/ARBs, beta-blockers, and statins) within 30 days of the index hospital discharge (**Figure 1**). Having a preventive therapy was defined as either having filled a prescription during the 30-day period, or having enough medication supply from a prescription filled before the AMI hospitalization to cover the 30-day period after discharge.

ASSESSMENT OF ADHERENCE AND ADHERENCE TRADEOFF. A timeline for measurement of patient

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