

EDITORIAL COMMENT

Reducing Post-Myocardial Infarction Mortality in the Elderly

The Power and Promise of Secondary Prevention*

William E. Boden, MD, FACC,†

David J. Maron, MD, FACC‡

Buffalo, New York; and Nashville, Tennessee

“Education is the best provision for old age.”

—Aristotle (1)

Major advances in the treatment of acute and chronic coronary heart disease (CHD) have occurred during the last half-century. An analysis of the Framingham Heart Study showed a 59% decrease in death rates from CHD between 1950 and 1999 (2) and, in just the last 2 decades alone, age-adjusted death rates for men and women in the U.S. have declined 43% (3). This profound decrease in CHD mortality has been fueled by substantial decreases in the prevalence of major cardiovascular risk factors (notably, cigarette smoking, elevated blood cholesterol, hypertension)

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and the dramatic evolution of evidence-based therapies (including antiplatelet agents, beta-blockers, angiotensin-converting enzyme inhibitors [ACEI], statins, and myocardial revascularization). Ford et al. (3) estimated that >90% of the clinical event rate reduction in CHD mortality during the last 2 decades of the 20th century was attributable to reductions in major risk factors and to the more widespread utilization of evidence-based medical therapies (3). Although there has likewise been a dramatic evolution in

myocardial revascularization (notably percutaneous coronary intervention [PCI]), only about 5% of the decline in CHD mortality between 1980 and 2000 in patients with chronic angina could be attributed to revascularization procedures (3).

Against this backdrop of clear clinical benefits from evidence-based medical practice, significant challenges remain in translating important results of randomized clinical trials, observational studies, registries, and epidemiological surveys into actual clinical practice. Indeed, a compelling rationale for formulating clinical practice guidelines, an important activity that represents one of the most meaningful missions of professional societies such as the American College of Cardiology (ACC) and the American Heart Association (AHA), is to provide physicians with evidence-based treatment recommendations and best practices to enhance clinical outcomes and reduce care variations—especially in high-risk patients who might be expected to derive the most clinical benefit.

The elderly are a high-risk group subject to a “treatment-risk paradox”: they tend to receive paradoxically less aggressive evidence-based secondary prevention than younger, lower risk patients (4). Current ACC/AHA clinical practice guidelines for the treatment of acute coronary syndromes (ACS) do not alter therapeutic recommendations based on age, apart from encouraging appropriate risk stratification, attention to comorbidities, and appropriate dosing of medications in elderly patients (5,6). However, on the basis of registry data obtained from the large CRUSADE national quality improvement initiative, Alexander et al. (7) demonstrated that the use of many recommended therapies in the elderly was significantly lower than in younger patients. Among 56,963 non-ST-segment elevation ACS patients in that registry whose in-hospital care was assessed with ACC/AHA clinical practice guidelines, 58% were ≥ 65 years, 35% were ≥ 75 years, and 11% were ≥ 85 years of age. After adjustment for age-related differences in treatments and outcomes and after controlling for contraindications and comorbidities, elderly patients with ACS were significantly less likely to receive acute antiplatelet and antithrombin therapy within the first 24 h, less likely to undergo early catheterization or revascularization, and less likely to receive clopidogrel and statins at hospital discharge. Importantly, although in-hospital mortality and complication rates increased with advancing age, patients ≥ 65 years of age who received more ACC/AHA guideline-recommended therapies had lower in-hospital mortality even after adjustment than those who did not (7). Similar data from GRACE (Global Registry of Acute Coronary Events), another large international registry of patients with ACS with or without ST-segment elevation, reported significantly decreased use of recommended therapies in the elderly (8). Thus, concordant findings from 2 ACS registries emphasize that even short-term outcomes in the elderly may be favorably im-

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From the †Division of Cardiovascular Medicine, University at Buffalo Schools of Medicine and Public Health; Kaleida Health and Buffalo General Hospital, Buffalo, New York; and the ‡Division of Cardiovascular Medicine, Department of Medicine, and Department of Emergency Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee. Within the past 12 months, Dr. Boden has received research grant support from Merck, Pfizer, Kos/Abbott Laboratories, and Sanofi-Aventis; been on the Speakers' Bureaus of Pfizer, Kos/Abbott Laboratories, Sanofi-Aventis, CV Therapeutics, Novartis, and PDL BioPharma; and served as a consultant for Kos/Abbott Laboratories and PDL Biopharma.

pacted by more widespread use of proven secondary prevention therapies. Little evidence, however, is available regarding the potential long-term benefits associated with the use of evidence-based medical therapies in the elderly.

In this issue of the *Journal*, Setoguchi et al. (9) studied temporal trends in mortality after hospitalization for acute myocardial infarction (MI) in 21,484 community-dwelling elderly patients (average age 80 years) who survived at least 30 days after discharge, by using data derived from pharmacy assistance programs and Medicare in New Jersey and Pennsylvania between 1995 and 2004. They found that after adjusting for patient demographics, comorbidities, duration of the MI hospitalization, patterns of previous health services use, and clustering of patients within hospitals, mortality after MI decreased significantly over time, by approximately 3% per year. After further adjustment for the use of statins, beta-blockers, ACEI, angiotensin receptor blockers, and antiplatelet drugs over time in this elderly cohort, the 10-year time trend in post-MI mortality improvement was completely abolished, indicating that the more favorable outcome in long-term mortality post-MI was likely due to the increased use of proven secondary prevention medications after discharge. In addition, although there was evidence that MI-related PCI procedures also may have contributed to improved survival, after adjusting for MI-related PCI procedural use during the index MI hospitalization, the temporal change associated with improved prognosis was largely attenuated. This suggests that improvement in short-term outcomes may have been attributable to PCI, whereas evidence-based secondary prevention therapies provided significant long-term prognostic benefit.

What do these data add to what we know about the importance of optimal medical therapy in reducing clinical events in patients with CHD? Several observational studies have shown improved survival after hospitalization for MI in the last 30 years (10–16), and clearly these improvements have been multifactorial, owing to more sensitive methods of detecting MI, coronary care units with arrhythmia monitoring, the advent of mechanical and pharmacologic reperfusion, and the expanding use of multiple medications that have been shown in placebo-controlled trials to reduce long-term mortality. More recently, data from randomized “strategy trials” comparing multifaceted, aggressive (optimal) medical therapy with PCI in both ACS (17,18) and chronic stable angina patients (19) have underscored the power and promise of secondary prevention as a proven approach to reduce major cardiovascular events. The provocative finding by Setoguchi et al. (9) extends the observation of Ford et al. (3) that the largest contributor to the decrease in CHD mortality is the use of evidence-based secondary prevention, and underscores the value of optimal medical therapy as was used in the ICTUS (Invasive Versus Conservative Treatment in Unstable Coronary Syndromes) (17), OAT (Occluded Artery Trial) (18), and COURAGE

(Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) (19) trials.

Additionally, as was observed in both the OAT and COURAGE trials, there were no differences in the overall trial primary end points for the prespecified subset of patients ≥ 65 years compared with patients < 65 years of age. In COURAGE, 40% of patients were ≥ 65 years of age, and in this age group the rate of death or MI during a 2.5- to 7-year follow-up was no greater in those randomized to an initial strategy of optimal medical therapy alone compared with optimal medical therapy plus PCI. The data from Setoguchi et al. (9) support the value of medical therapy in a large cohort of community-dwelling elderly patients whose mean age was 80 years and of whom 73% were women.

Nevertheless, there are certain limitations of the present study. The study population was derived from medical claims data of Medicare beneficiaries in 2 states and thus may not be generalizable to MI patients comprising a broader geographic and demographic distribution. A single International Classification of Diseases, revision 9, code was used to identify patients who were hospitalized for MI, which may include an unknown percentage of patients with small, incidental MI. Inclusion in the trial was restricted to patients who had been active participants in their insurance programs for at least 1 year before the index MI and who survived the first 30 days after the index MI discharge, meaning that most patients were likely censored for at least 5 weeks after their acute MI—a high-risk period associated with increased mortality, especially in the elderly (20,21). The use of antiplatelet and antithrombin therapy was not ascertained in the present analysis, nor was the possibly important contribution of lifestyle interventions (diet, exercise, weight control, and smoking cessation). Furthermore, the persistence of medication use after discharge was not measured.

In summary, the findings from the present study, although largely circumstantial, are nevertheless compelling and consistent with a large and expanding body of scientific evidence that has validated the importance of established secondary prevention therapies (aspirin, clopidogrel, statins, beta-blockers, ACEI/angiotensin receptor blockers—alone or in combination) in reducing long-term death and recurrent MI in CHD patients. In light of the fact that CHD is fundamentally a systemic disease with focal manifestations (acute plaque rupture triggering clinical events), it is both logical and intuitive that the use of antiatherothrombotic strategies would hold the greatest promise for achieving long-term clinical event reduction. It is particularly gratifying to see new evidence that the mortality benefit of secondary prevention extends to elderly patients. This should motivate clinicians to avoid the “treatment-risk paradox” and to apply evidence-based preventive interventions as readily and intensively in high-risk elderly CHD patients as in younger CHD patients at lower risk.

Reprint requests and correspondence: Dr. William E. Boden, Buffalo General Hospital, 100 High Street, Buffalo, New York 14203. E-mail: wboden@kaleidahealth.org.

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