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Improvements in Long-Term Mortality After Myocardial Infarction and Increased Use of Cardiovascular Drugs After Discharge

A 10-Year Trend Analysis

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Objectives We sought to assess the relationship between increasing use of cardiovascular medications and trends in long-term prognosis after myocardial infarction (MI) in the elderly.

Background During the past decade, statins, beta-blockers (BBs), angiotensin-converting enzyme inhibitors (ACEIs), and angiotensin-II receptor blockers (ARBs) have been increasingly used after MI. However, little is known about the relationship between increasing use of these medications and improvements in prognosis after MI.

Methods Using data from pharmacy assistance programs and Medicare in 2 states (1995 to 2004), we identified patients with MI who survived ≥30 days after discharge. We assessed age, gender, race, comorbidities, and coronary interventions during the MI hospitalization and recorded filled prescriptions for statins, BBs, ACEIs/ARBs, or antiplatelet agents within 30 days after discharge. All patients were tracked until they died or until the end of the eligibility/study period. We built multivariate Cox proportional hazards regression models to assess trends in long-term mortality and the contribution to increasing medication use after MI.

Results Of 21,484 patients identified, 12,142 died during 74,982 person-years of follow-up. After adjusting for demographics and comorbidities, we found that mortality after MI decreased significantly from 1995 to 2004 (hazard ratio for annual trend 0.97; 95% confidence interval 0.97 to 0.98), a 3% reduction in mortality each year. Adjusting for the use of statins, BBs, ACEIs/ARBs, and antiplatelet drugs after discharge completely eliminated the association between time trend and mortality (hazard ratio 1.00; 95% confidence interval 0.99 to 1.01).

Conclusions The observed improvement in long-term mortality in elderly patients with MI may be mainly due to increased use of cardiovascular medications after discharge. (J Am Coll Cardiol 2008;51:1247–54) © 2008 by the American College of Cardiology Foundation

Coronary artery disease is a major cause of morbidity and the leading cause of death in the elderly. At least 410,000 men and 372,000 women age >65 years are annually diagnosed with myocardial infarction (MI) in the U.S. (1). However, the incidence and mortality of coronary heart disease have been decreasing during the past 3 decades, presumably as the result of better control of coronary risk factors and better clinical management, including revascularization procedures and cardiovascular drugs (2–6). Studies suggest that the outcomes of MI had been improving from the 1980s to the 1990s (7–10), but little is known about more contemporary trends in North America.

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A wealth of evidence exists to support the efficacy of statins, beta-blockers (BBs), angiotensin-converting enzyme inhibitors (ACEIs), angiotensin-II receptor blockers (ARBs), and antiplatelet agents in patients with MI, and some studies have shown that these medications are also cost effective (11–18) Guidelines for the management of patients after acute MI emphasize use of these drugs for secondary prevention (19,20). We have previously found that the use of these medications for

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Abbreviations and Acronyms

ACEI = angiotensin-converting enzyme inhibitor
ARB = angiotensin-II receptor blocker
BB = beta-blocker
MI = myocardial infarction
NSTEMI = non–ST-segment elevation myocardial infarction
PCI = percutaneous coronary intervention

secondary prevention after discharge from MI has been increasing during the past decade in elderly populations (21). It is unknown, however, how that use has impacted outcomes in populations of community-dwelling elderly and to what extent the increasing use of these medications has contributed to improvements in long-term mortality observed in older patients after MI. In the current study, we assessed whether the mortality of community-dwelling elderly after MI improved over time and the extent to which the increasing use of preventive medications after discharge contributed to these changes in mortality.

Methods

Data sources and study population. We linked medical claims data from several sources. Drug utilization data from the New Jersey Pharmaceutical Assistance for the Aged and Disabled program (1994 to 2004) and the Pennsylvania Pharmaceutical Assistance Contract for the Elderly program (1994 to 2004) were merged with the complete Medicare claims for these beneficiaries. All traceable personal identifiers were removed from the analytic dataset to protect patients' privacy. These drug-assistance programs provide comprehensive prescription drug coverage for eligible elderly patients in New Jersey and Pennsylvania. Patients are eligible if their income is greater than the Medicaid annual income threshold but less than approximately $35,000, thus including primarily lower middle-class elderly. Neither of these programs had any restrictions or prior authorization programs in place for any of the study drugs.

We identified all patients who were admitted to a hospital for MI between January 1, 1995, and December 31, 2004. To ensure enrollment status, all patients were required to have at least 1 claim for any service and at least 1 filled prescription during the 365 days before the index MI hospitalization. An MI admission was defined as a hospitalization of at least 3 days and not more than 180 days with an International Classification of Diseases, version 9, diagnosis code of 410 in the primary or secondary position at discharge. This algorithm to identify MI hospitalizations has been validated and been shown to have a positive predictive value of 94% (22). We further required all study patients to survive and remain eligible for pharmacy benefits for at least 30 days from the discharge date of the index MI hospitalization. We excluded patients who were admitted to a nursing home in the year preceding the MI or the 30 days after discharge. Survival time for each patient was considered from the index date (the 31st day after discharge from the index MI) to the date of death, the date of lost eligibility, or the end of the follow-up period (August 31, 2005).

Covariates. We obtained information on each patient's age on the index MI admission, gender, and race (white vs. nonwhite [including black, Hispanic, Asian, and Native American]) from enrollment files. We used recorded diagnoses in inpatient and outpatient claims to assess the presence of comorbid conditions including other indications and contraindications for statin, BB, and ACEI/ARB during the 12-month period preceding the discharge date. The comorbid conditions included hypertension, coronary artery disease, previous MI (22), heart failure (23), cerebrovascular disease (24), peripheral artery disease (24), atrial fibrillation, arthritis (25), diabetes, chronic kidney disease (26), maintenance dialysis, chronic pulmonary disease, alcohol abuse, dementia, depression, other mental disease, any malignancy, obesity, and the Charlson comorbidity index. We also defined the characteristics of the index MI including length of stay for the index MI admission and administration of coronary interventions such as percutaneous coronary interventions (PCIs) (i.e., percutaneous transluminal coronary angioplasty or coronary stent placement), revascularization surgery, or infusion of thrombolytic agents. We created indicators for previous health care utilization (number of days for admissions, physician visits, and prescriptions for different medications filled). Finally, we assessed whether the patients had at least 1 filled prescription for any statin, BB, ACEI/ARB, and nonaspirin antiplatelet agent (clopidogrel or ticlopidine) within 30 days after discharge from the index MI hospitalization.

Statistical analysis. We constructed Kaplan-Meier cumulative mortality curves starting at the 31st day after discharge to describe unadjusted mortality among the patients discharged after MI (not shown). Adjusted time trends as well as the effect of each calendar year on mortality were analyzed in multivariate Cox proportional hazards regression models, including age, gender, race, comorbidities, and health service utilization measures (27). We accounted for clustering of patients within hospitals by using the robust sandwich estimator of Wei et al. (28). The sandwich estimator is a general method for estimating the covariance matrix of parameter estimates, which provides consistent estimates even when a model is not correctly specified. The proportionality assumption was tested by including interaction terms between calendar year and study time. To assess whether the change in cardiovascular drug use and/or thrombolytic therapies/revascularization procedures mediated the effect of calendar year on mortality, we sequentially introduced indicator terms for these therapeutic interventions into the multivariate Cox models described above (29). Hazard ratios are presented together with the corresponding 95% confidence intervals. We used SAS for Windows software (release 9.2) for all statistical analyses (SAS Institute, Cary, North Carolina).

Results

Study patients and characteristics. We identified 28,754 patients admitted for MI between January 1, 1995, and December 31, 2004, who had been active participants in their insurance programs for >1 year before the index MI admission and for ≥30 days after the index MI discharge. Of these, 21,484 (74.7%) survived at least 30 days after discharge, constituting the final study cohort. Characteristics of these patients overall and by calendar year are shown in Table 1. In the entire study population, the mean age was 80 years, and 73% were women. Several comorbid conditions were highly prevalent: 62% of all patients had previously been diagnosed with coronary artery disease, 66% had heart failure, 32% had cerebrovascular disease, 46% had diabetes, 39% had chronic pulmonary disease, and 17% were diagnosed with chronic kidney disease. When stratified by calendar year, we observed increases in age and the prevalence of diagnosis for hypertension, peripheral vascular diseases, cerebrovascular diseases, diabetes, chronic kidney disease, dementia, and depression over the study period. The use of PCI (percutaneous transluminal coronary angioplasty or stent) also increased over time (all p values <0.05), whereas the use of thrombolytic therapy as well as the length of stay for the index MI admission decreased. Use of statins, BBs, ACEIs/ARBs, and antiplatelet agents after the index MI admission also increased over time (all p values <0.01).

Mortality. Among the 21,484 study patients, there were 12,142 deaths during 74,982 person-years of follow-up. The 1-, 3-, and 5-year mortalities were 20%, 41%, and 57%, respectively.

Multivariate analysis. We estimated unadjusted and adjusted effects of calendar year by using Cox proportional hazards regression models (Table 2). In unadjusted analyses, we did not observe a temporal trend in mortality after MI. However, after simultaneously adjusting for changes in patient demographics, comorbidities, and health service use measures over time, we found that mortality after MI improved by 3% per year from 1995 to 2004 (Table 2). The fully-adjusted effect of calendar year was also estimated using indicator variables for each interval of the calendar year, which was consistent with the decreasing trend of mortality after MI observed in the previous model (Table 2, Fig. 1). We found no violation of the proportionality assumption ($p = 0.7$).

To assess whether the secular trends toward greater use of invasive cardiac procedures and/or the study medications explained the improvement in mortality after MI over time, we sequentially added these factors to the fully adjusted Cox proportional hazards regression model (Table 3). After adding the indicator terms for the use of the study medications (statins, BBs, ACEIs/ARBs, and antiplatelet agents) to the previously described fully adjusted Cox model, the temporal trend of improving mortality after MI disappeared (Table 3). However, when the indicator for PCIs was added to the fully adjusted model without including terms for the use of cardiovascular medications after MI, the associations of calendar year with mortality were attenuated but remained statistically significant. When we then added indicator terms for both PCIs and medication use, we found the effect of calendar year was very similar to those in the model with the term for medication use only without the term for PCI (Table 3), which suggests that the improving trend in mortality may be primarily attributable to increased use of recommended drugs, whereas the effect of PCI was much less pronounced than that attributable to medication use. These observations were displayed in Figure 1, by comparing the hazard ratios and 95% confidence intervals for each calendar year before and after adjusting for the use of coronary interventions or the use of the recommended cardiovascular drugs after discharge from MI.

Discussion

In this large sample of 21,484 community-dwelling elderly, we studied temporal trends in mortality after hospitalization for MI. After adjusting for patients' demographics, comorbidities, duration of the MI hospitalization, patterns of previous health services use, and clustering of patients within hospitals, post-MI mortality improved over time by approximately 3% per year. Further analyses revealed that this trend toward better prognosis after discharge from MI disappeared completely after adjustment for use of statins, BBs, ACEIs/ARBs, and antiplatelet agents, all generally recommended for use after MI. This relationship was not merely an ecological observation; it emerged by analysis of the medication use and mortality experience of each individual subject. Thus, our study suggests that the observed improvements in mortality over time may predominantly be attributable to and mediated through the increasing use of statins, BBs, ACEIs/ARBs, and antiplatelet agents over the decade of observation.

We also found that the association between calendar year and mortality was attenuated after adjusting for the use of coronary intervention during the index hospitalization, but was less pronounced than the reduction attributable to drug use. The findings suggest that coronary intervention may also have contributed to improved mortality, but to a lesser degree. Because use of coronary intervention was highly associated with use of recommended cardiovascular drugs (21), the attenuation of the calendar effect after adjustment for coronary intervention could also be explained by the apparent correlation between the use of procedures and drugs. Patients who underwent coronary interventions had improved long-term mortality, but the observed improvement of long-term mortality in the entire study patients was not fully explained by the change in the use of PCI. In-hospital mortality as well as 30-day mortality after MI admission also improved over time in a separate analysis (not shown). After adjusting for coronary intervention during the MI hospitalization, these temporal trends toward

Table 1 Characteristics of 21,484 Patients With MI Who Survived for >30 Days After Discharge, by Calendar Year

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	p Value for Trend	All Years
% nursing home patients prior to admission	6.1	7.4	9.1	10.3	12.1	13.2	13.7	14.3	13.9	16.3		
% nursing home patients within 30 days after discharge	11.4	13.7	17.6	22.5	22.4	26.0	27.9	27.6	30.2	29.5		
Total population (n)	2,697	3,123	2,518	2,278	2,158	1,953	1,773	1,809	1,715	1,460	—	21,484
Follow-up (yrs)	4.6 (3.6)	4.6 (3.3)	4.4 (3.0)	4.1 (2.6)	3.7 (2.3)	3.3 (1.9)	2.9 (1.5)	2.3 (1.1)	1.7 (0.7)	1.0 (0.4)	<.0001	3.5 (2.7)
Age (yrs)	78.7 (6.7)	79.2 (6.8)	79.3 (6.9)	79.9 (6.8)	79.8 (6.7)	80.5 (6.7)	80.2 (7.0)	80.2 (7.2)	80.3 (7.2)	80.5 (7.2)	<.0001	79.9 (6.9)
Male	28.0	28.4	27.2	27.5	27.1	25.6	26.3	27.6	27.9	28.0	0.4770	27.4
Race (black)	5.6	5.5	5.4	5.4	6.0	7.3	7.1	6.0	5.5	7.1	0.0122	6.0
Health service use												
Previous hospitalization	40.5	34.5	34.6	34.9	35.0	34.6	34.0	35.7	34.3	33.8	0.0010	35.4
No. of physician visits	10.1 (6.6)	9.6 (6.9)	9.7 (6.9)	10.2 (7.0)	9.9 (7.2)	10.2 (7.8)	9.8 (6.9)	10.5 (7.8)	10.5 (7.9)	10.5 (8.5)	<.0001	10.1 (7.3)
No. of medications	9.4 (5.5)	9.3 (5.4)	9.9 (5.8)	10.0 (5.6)	10.4 (5.9)	10.7 (6.1)	11.1 (6.3)	11.1 (6.0)	11.2 (5.9)	11.6 (6.2)	<.0001	10.3 (5.9)
Charlson comorbidity scores	2.6 (2.2)	2.4 (2.0)	2.5 (2.1)	2.6 (2.1)	2.7 (2.1)	2.7 (2.2)	2.7 (2.1)	2.9 (2.2)	2.8 (2.1)	2.7 (2.1)	<.0001	
Procedures during index MI admission												
Angiography including PCI	34.6	39.1	40.5	43.1	43.8	44.4	49.6	52.1	53.4	53.0	<.0001	44.1
Angiography only	21.3	23.2	24.8	23.2	24.0	23.6	24.4	25.8	24.6	22.5	0.0332	23.6
PTCA	13.2	15.8	15.6	19.6	19.5	20.5	24.7	25.8	28.3	30.3	<.0001	20.2
Stent	1.9	6.2	9.6	15.5	17.1	18.8	22.8	24.3	26.8	29.0	<.0001	15.4
Revascularization surgery	7.2	8.4	8.8	7.8	7.9	7.6	7.1	7.8	7.1	6.4	0.0468	7.7
Thrombolytic therapy	2.0	2.2	1.9	1.6	1.5	1.6	1.2	1.0	1.1	1.2	<.0001	1.6
Length of stay for the index MI	11.1 (7.4)	10.8 (7.4)	10.6 (7.9)	9.7 (6.2)	9.6 (6.6)	9.6 (7.2)	9.3 (7.1)	9.2 (6.6)	9.2 (6.8)	9.0 (7.2)	<.0001	10.0 (7.1)
Previous diagnosis												
Coronary artery disease	65.7	63.0	61.7	62.6	64.5	62.5	59.8	61.5	60.5	57.1	<.0001	62.2
Prior MI	9.4	6.4	5.9	5.6	6.8	7.4	7.8	6.3	8.1	9.4	0.1990	7.2
Atrial fibrillation	29.6	30.4	32.0	31.9	33.3	33.8	34.6	34.1	35.3	33.4	<.0001	32.5
Aortic aneurysms	3.7	4.1	3.1	3.8	3.4	5.3	3.8	4.4	5.5	5.1	0.0003	4.1
Peripheral vascular diseases	23.7	22.6	25.1	25.6	26.2	27.3	27.9	27.1	28.6	27.4	<.0001	25.8
Hypertension	66.4	68.2	70.1	71.7	72.3	74.9	78.6	80.2	83.8	82.1	<.0001	73.6
Cerebrovascular disease	29.4	29.0	29.2	29.5	31.8	34.0	35.0	33.9	35.2	34.7	<.0001	31.7
Heart failure	65.3	64.5	65.4	66.3	66.6	66.4	64.6	66.7	66.2	63.4	0.8278	65.5
Diabetes	46.2	42.9	45.1	45.3	46.6	45.1	47.1	47.9	50.1	49.3	<.0001	46.2
Chronic pulmonary diseases	36.7	36.0	37.5	39.2	41.9	39.0	38.9	43.0	41.9	41.0	<.0001	39.1
Chronic kidney diseases	14.5	13.5	15.3	15.9	16.0	18.1	17.5	19.6	22.6	22.9	<.0001	17.0
Dialysis	1.8	1.4	2.0	2.0	1.9	2.7	2.5	2.4	2.2	2.1	0.0066	2.0
Rheumatoid arthritis	3.2	3.4	3.8	5.1	4.6	3.8	4.1	4.4	4.4	3.6	0.0723	4.0
Osteoarthritis	34.0	33.4	35.2	36.3	36.1	39.3	39.6	39.2	40.8	38.2	<.0001	36.7
Cancer (except for nonmelanoma skin cancer)	20.2	19.1	19.5	19.5	19.6	20.7	21.6	23.3	21.5	19.5	0.0141	20.3
Dementia	7.5	7.5	7.3	7.8	9.4	10.3	11.4	10.9	12.5	12.9	<.0001	9.3
Depression	12.5	12.2	12.7	14.1	15.1	17.1	17.4	16.5	19.3	20.4	<.0001	15.2

Continued on next page

Table 1 Continued

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	p Value for Trend	All Years
Use of cardiovascular drugs after MI hospitalization												
Post-MI statin	7.6	9.9	16.3	22.2	27.7	31.9	39.3	45.4	48.2	50.7	<.0001	26.7
Post-MI BB	41.5	45.7	50.5	56.8	59.7	62.7	66.9	67.8	71.3	71.6	<.0001	57.3
Post-MI ACE/ARB	39.2	41.0	42.0	45.3	44.4	43.1	45.4	47.2	49.7	50.0	<.0001	44.1
Post-MI antiplatelet	2.6	7.9	12.3	19.6	26.8	26.6	37.6	44.7	49.2	50.9	<.0001	24.4

Values represent % for categorical variables and mean (SD) for continuous variables. Covariates were assessed during the 12-month period prior to and during the index MI admission. Prior MI does not include the index MI event.
ACE/ARB = angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; BB = beta blocker; MI = myocardial infarction; PCI = percutaneous coronary intervention; PTCA = percutaneous transluminal coronary angioplasty.

improved mortality were no longer present, suggesting that improvement in short-term mortality may be due to increased use of PCIs. These findings suggest that increased use of PCI may have predominantly improved acute and short-term mortality, whereas increased use of preventive medications may be responsible for improvements in longer-term outcomes in the population we studied.

Unadjusted analyses indicated that there was no change over time in temporal trends in mortality after MI. It was only after simultaneous control for differences in age, gender, race, and comorbidities that significant improvements in long-term mortality were observed. This is compatible with our findings of increases over time in age and major comorbidities in our population of MI patients (Table 1). A possible explanation of this may lie in the trends toward inclusion in the sample of older patients with more comorbidities in more recent years. Indeed, advances in acute and subacute treatment of MI during the past decade may have enabled older and sicker patients to survive their acute event, be discharged alive, and thus be selected into our study cohort.

The existing literature on trends in mortality after MI hospitalization in North America is rather limited, and most of its observations are now outdated. Using data for MI patients discharged from greater Worcester hospitals, Furman et al. (30) observed that multivariate adjusted 2-year mortality after discharge from hospitals declined over time for both Q-wave and non–Q-wave MI between 1975 and 1997. Using more recent data from the same data source and adjusting for demographics, cardiovascular comorbidity, and MI characteristics, Botkin et al. (31) found a modest improvement in the 1-year post-discharge mortality over the period between 1975 and 2001. Pashos et al. (7) reported from Medicare data that 30-day (26% to 23%) and 1-year (40% to 36%) mortality of elderly patients with MI improved throughout the U.S. from 1987 to 1990 (7). They also found that the proportion of patients undergoing revascularization procedures (both surgery and PCI) increased from 13% to 21% and concluded that this may explain the observed improvement in the mortality. Tu et al. (9) reported a similar observation in Ontario between 1992 and 1996. They found that both the overall 30-day risk-adjusted mortality and the 1-year risk-adjusted mortality declined modestly (16% to 14% for 30-day and 24% to 22% for 1-year mortality) along with a significant increase in the use of coronary intervention including surgery and PCI. Pilote et al. (10) demonstrated a mortality decrease in MI patients in Quebec between 1988 and 1995, which was paralleled by an increase in the use of cardiac procedures, aspirin, BBs, ACEIs, and lipid-lowering agents. Most recently, Ford et al. (32) attempted to explain the decrease in U.S. overall deaths from coronary disease between 1980 and 2000 using a previously validated modeling approach. They found that approximately 47% of the decrease in coronary deaths over that period was attributable to treatments, including revascularization

Table 2 Associations Between Calendar Year and Mortality After the Index Date in 21,484 Survivors of MI

Variables Adjusted for	Calendar Year	Hazard Ratio	95% Confidence Interval	p Value
a. None (unadjusted)	Trend	1.00	0.98–1.01	0.7805
b. Age	Trend	0.99	0.97–1.00	0.0464
c. Demographics (age, gender, and race)	Trend	0.99	0.97–1.00	0.0584
d. Demographics and comorbidities*	Trend	0.98	0.97–0.99	<.0001
e. Demographics, comorbidity, length of stay, Charlson score, and health service use†	Trend	0.97	0.96–0.98	<.0001
f. Previous model, but dummy coded for year instead of a trend indicator	1995	1.00	(Reference)	—
	1996	0.92	0.85–0.99	0.0221
	1997	0.87	0.82–0.93	<.0001
	1998	0.89	0.82–0.95	0.0008
	1999	0.88	0.83–0.94	<.0001
	2000	0.84	0.78–0.90	<.0001
	2001	0.82	0.76–0.88	<.0001
	2002	0.81	0.75–0.88	<.0001
	2003	0.79	0.72–0.87	<.0001
	2004	0.76	0.67–0.86	<.0001

*Comorbidities include previous MI, non-MI coronary artery diseases, heart failure, cerebrovascular diseases, peripheral vascular diseases, atrial fibrillation, aortic aneurysms, diabetes, hypertension, chronic pulmonary diseases, peptic ulcer diseases, liver diseases, chronic kidney diseases, dialysis, malignancy, rheumatoid arthritis, osteoarthritis, human immunodeficiency virus infection, dementia, depression, other mental disorders, obesity, and alcohol abuse. †Health service use measures include number of visits, number of generic medications prescribed, and any hospitalization.
Abbreviations as in Table 1.

and secondary prevention after MI. However, the modeling approach used in their article relied on data from many different sources and assumptions in estimating effectiveness of the medications and procedures. On the other hand, we used real-world observations from a well-defined population that allowed us to directly estimate effectiveness of the treatment and link individual prognosis and use of drugs and procedures.

Our study covers more contemporary years with a decade of observations and showed that the mortality trend after MI has further improved. Beyond previous studies, we assessed the contribution of the use of recommended medications after discharge for MI in the outpatient setting rather than during the MI hospitalization. Because providers of care after discharge are often different from physicians caring for patients during hospitalization, drug use after discharge may be a better marker of long-term use of these drugs. To our knowledge, this is the first study to suggest that improvements in prognosis after MI may be attributable to increased use of medication for secondary prevention using actual observations from the real-world population.

Study limitations. The following limitations should be noted. First, we used the International Classification of Diseases, version 9, code of 410 to identify patients who were hospitalized for MI. Although this definition was shown to have very high accuracy, the use of this code has gradually evolved to include patients diagnosed for MI based on troponin values using increasingly sensitive assays, especially after publication of the American Heart Association/American College of Cardiology guidelines with a revised definition of MI in 2000 (33). As a result, patients diagnosed in recent years may include MI patients who had

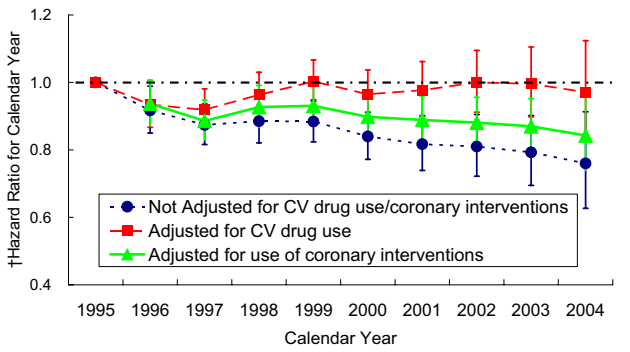

Figure 1 Hazard Ratio for Calendar Year Before and After Adjusting for CV Drug or Coronary Intervention

After adjusting for changes in demographics and comorbidities over time **(red squares)**, we found that long-term mortality after myocardial infarction (MI) decreased significantly from 1995 to 2004, with a 3% reduction in the risk of death each year. Next, we adjusted for the use of statins, beta-blockers, angiotensin-converting enzyme inhibitors/angiotensin-II receptor blockers, and nonaspirin antiplatelet drugs after discharge, which eliminated the association between time trend and mortality **(blue circles)**. This means that the change in mortality may be primarily attributable to increased use of recommended drugs. In contrast, adjusting for the use of coronary interventions, but not for the study drugs **(green triangles)**, diminished the time trend slightly but did not eliminate the effect completely †Hazard ratios for calendar years were estimated from the multivariate Cox proportional hazards regression model that includes indicators for each calendar year, age, gender, race, comorbidities (previous MI, non-MI coronary artery diseases, heart failure, cerebrovascular diseases, peripheral vascular diseases, atrial fibrillation, aortic aneurysms, diabetes, hypertension, chronic pulmonary diseases, peptic ulcer diseases, liver diseases, chronic kidney diseases, dialysis, malignancy, rheumatoid arthritis, osteoarthritis, human immunodeficiency virus infection, dementia, depression, other mental disorders, obesity, and alcohol abuse) and health service use measures (number of visits, number of generic medications prescribed, and any hospitalization). The p value for the trend was estimated from the same model replacing the indicators for each calendar year by 1 continuous variable for calendar year. CV = cardiovascular.

Table 3 Associations between Calendar Year and Mortality in 21,484 Survivors of MI: Impact of Increasing Utilization of Coronary Interventions* and of Recommended Cardiovascular Medications after Discharge

Variables Adjusted for	Calendar Year	Hazard Ratio	95% Confidence Interval	p Value
Model e. in Table 2 + statin, ACE/ARB, BB, and antiplatelet after discharge from MI	Trend	1.00	0.99–1.01	0.522
Model e. in Table 2 + PCI during MI admission but without cardiovascular drug use	Trend	0.99	0.98–1.00	0.007
Model e. in Table 2 + statin ACE/ARB, BB, and antiplatelet after discharge from MI, and PCI, revascularization surgery, and use of thrombolytic agents during MI admission	Trend	1.01	1.00–1.02	0.271
Previous model, but dummy coded for year instead of a trend indicator	1995	1.00	(Reference)	—
	1996	0.96	0.89–1.03	0.233
	1997	0.93	0.87–0.99	0.031
	1998	1.01	0.95–1.08	0.794
	1999	1.04	0.98–1.10	0.195
	2000	1.02	0.95–1.09	0.613
	2001	1.04	0.96–1.13	0.322
	2002	1.06	0.97–1.16	0.179
	2003	1.07	0.97–1.18	0.195
	2004	1.04	0.91–1.20	0.554

*Coronary interventions include PCIs, revascularization surgery, or infusion of thrombolytic agents during the index MI hospitalization.
Abbreviations as in Table 1.

previously been classified as non-MI or unstable angina including non–ST-segment elevation MI (NSTEMI). However, although short-term prognosis (in-hospital or 30-day mortality) has been shown to be better in NSTEMI, long-term mortality has been shown to be similar or worse with NSTEMI (30,34,35). Because we assessed long-term rather than short-term prognosis, the observed mortality trend is unlikely to be explained by the change in the diagnostic method, coding, or relative contribution of STEMI versus NSTEMI. Furthermore, if the change in inclusion of STEMI versus NSTEMI is the reason for improving mortality over time, the trend in mortality would not be mediated by cardiovascular drug use, but rather should remain significant after the inclusion of these terms. Nonetheless, our results could be explained in part by the change in the method of diagnosing MI.

Another limitation is that our data did not contain any information on other recommended strategies for secondary prevention; aspirin is available over the counter, which leads to underascertainment of its use from claims data. However, studies have showed that rates of aspirin use after MI have remained relatively constant over the past decade (36,37). Information on counseling for and successful implementation of smoking cessation, weight control, diet modification, exercise, and other life-style modifications also was not available in our study. We cannot rule out that increased use of the study drugs is associated with more health-conscious behaviors, thus contributing to the beneficial effect that we might attribute to medication use alone. However, life-style interventions have been recommended for the secondary prevention of MI for several decades; thus, these behaviors are unlikely to have increased to a similar extent compared with the use of the study drugs or coronary interventions.

Many factors are associated with prognosis after MI, and some were not measured in the present study, but these would need to meet certain conditions to allow an alternative explanation for our findings. These unmeasured factors would have to be associated with the calendar year and with cardiovascular medication use after discharge. Although our study has a number of limitations, these factors cannot be easily measured in the large population-based samples represented in this study. Our study generated a hypothesis that increasing drug use may explain improved long-term mortality of MI patients in the past decade. Further investigation will be necessary to elucidate the relative and individual contributions of these unmeasured factors.

Conclusions

This large study of community-dwelling elderly with MI indicates that long-term mortality from MI after discharge has improved significantly during the last decade and that the observed decrease in mortality may be attributable in large part to improved practice related to use of cardiovascular medications after MI. To a lesser degree, it may be attributable to increased use of PCIs during MI hospitalizations. Our results suggest that the efficacy of these medications after MI for secondary prevention has been effectively translated into nontrial elderly populations. These data should encourage clinicians to continue use of these proven therapies in the management of elderly patients after MI.

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