Long-Term Trends in the Incidence of Heart Failure After Myocardial Infarction

Raghava S. Velagaleti, MD; Michael J. Pencina, PhD; Joanne M. Murabito, MD; Thomas J. Wang, MD; Nisha I. Parikh, MD; Ralph B. D’Agostino, PhD; Daniel Levy, MD; William B. Kannel, MD; Ramachandran S. Vasan, MD

Background—Although mortality after myocardial infarction (MI) has declined in the United States in recent decades, there have been few community-based investigations of the long-term trends in the incidence of heart failure after MI, and their results appear to be conflicting.

Methods and Results—We evaluated 676 Framingham Heart Study participants between 45 and 85 years of age (mean age 67 years, 34% women) who developed a first MI between 1970 and 1999. We assessed the incidence rates of heart failure and of death without heart failure in each of 3 decades (1970 to 1979, 1980 to 1989, and 1990 to 1999). We estimated the multivariable-adjusted risk of events in the latter 2 decades, with the period 1970 to 1979 serving as the referent. The 30-day incidence of heart failure after MI rose from 10% in 1970 to 1979 to 23.1% in 1990 to 1999 (P for trend 0.003), whereas 30-day mortality after MI declined from 12.2% (1970 to 1979) to 4.1% (1990 to 1999). The 5-year incidence of heart failure after MI rose from 27.6% in 1970 to 1979 to 31.9% in 1990 to 1999 (P for trend 0.02), whereas 5-year mortality after MI declined from 41.1% (1970 to 1979) to 17.3% (1990 to 1999). In multivariable analyses, compared with the period 1970 to 1979, we observed higher 30-day (risk ratio 2.05, 95% confidence interval 1.25 to 3.36) and 5-year (risk ratio 1.74, 95% confidence interval 1.07 to 2.84) risks of heart failure in the decade 1990 to 1999. These trends were accompanied by lower 30-day (risk ratio 0.21, 95% confidence interval 0.09 to 0.47) and 5-year (risk ratio 0.31, 95% confidence interval 0.18 to 0.54) mortality rates in 1990 to 1999.

Conclusions—In the present community-based sample, we observed an increase in the incidence of heart failure in recent decades that paralleled the decrease in mortality after MI. (Circulation. 2008;118:2057-2062.)

Key Words: heart failure ■ myocardial infarction ■ prognosis ■ risk factors ■ epidemiology
MI (due to reperfusion therapy) could lead to an increased pool of “high-risk” patients who are more susceptible to HF. Yet, major therapeutic advances (such as use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers after MI) may have reduced the occurrence of left ventricular dysfunction and stemmed the susceptibility to HF. A potential limitation of the aforementioned investigations is a lack of analyses that explored concurrently the incidence of HF and of mortality after MI without HF as competing events. Such an analytical strategy could elucidate the relative contributions of the divergent trends noted above to the incidence of HF after MI.

We hypothesized that the incidence of HF after MI may have increased in recent times owing to a lower mortality associated with the condition. We tested this hypothesis by evaluating trends in the incidence of HF and death after a first MI in Framingham Heart Study participants over the time period 1970 to 1999.

Methods
Study Sample and Design
The design and characteristics of the original and the offspring cohorts of the Framingham Heart Study have been detailed elsewhere. Briefly, 5209 participants (original cohort) were enrolled in 1948 and have been evaluated approximately every 2 years. The members of the Framingham offspring cohort, comprising 5124 individuals (children of the original cohort and their spouses), were enrolled in 1971 and have been evaluated approximately every 4 years. Participants from both cohorts who attended routine examinations between the years 1970 and 1999 constituted the sampling frame for the present study. All participants provided written informed consent, and the study was approved by the Institutional Review Board of Boston Medical Center.

Participants 45 to 85 years of age who experienced a first MI between the years 1970 and 1999 were eligible for the present investigation (n=715). After the exclusion of participants who had a history of HF before the index MI (n=39), 676 individuals remained eligible for the present investigation. We grouped participants with a first MI according to the decade of onset of the event (ie, 1970 to 1979, 1980 to 1989, or 1990 to 1999). We chose the 3 decades of interest to capture the prethrombolysis, thrombolysis, and percutaneous coronary intervention eras in the management of MI. We could not extend observations to the most recent decade (2000 onward) because participants with an MI in the present decade would not have a follow-up comparable to that for the previous decades. Also, we wanted to minimize ascertainment bias in the diagnosis of MI and HF as a result of the increased use of highly sensitive biomarkers of acute myocardial necrosis (eg, cardiac troponins) or neurohormonal activation (eg, B-type natriuretic peptide), respectively, in the post-2000 time period.

Only the MI event should have occurred in the decade of interest for the participant to be grouped under that decade. Thus, a participant who developed a first MI in 1978 and then developed HF in 1981 would be classified in the decade 1970 to 1979.

Ascertainment of End Points
All Framingham participants are under surveillance for risk of cardiovascular events (including HF) and death, which are identified from data collected at each Framingham examination and from hospitalization records and physician office visits. An end-point review committee, consisting of 3 physicians, reviews all records and adjudicates the occurrence of events. Criteria for these events have been published previously. Briefly, MI was considered to have occurred when participants demonstrated 2 of 3 criteria: new diagnostic Q waves on ECGs, prolonged ischemic chest discomfort, and elevation of circulating cardiac enzymes that suggested myocardial necrosis.

The Framingham criteria for HF were used to adjudicate episodes of HF after MI. Briefly, a diagnosis of HF requires the presence of 2 major or 1 major and 2 minor criteria. The major criteria include a history of paroxysmal nocturnal dyspnea or orthopnea, presence of jugular venous distention, hepatogenous reflux, pulmonary rales, presence of third heart sound, increasing radiographic cardiomegaly, radiographic evidence of acute pulmonary edema, presence of a third heart sound, and evidence of weight loss >4.5 kg during the first 5 days of treatment for suspected HF. The minor criteria include history of a nocturnal cough, dyspnea on ordinary exertion, presence of bilateral ankle edema, hepatomegaly, heart rate >120 bpm, and radiographic evidence of bilateral pleural effusions or pulmonary vascular congestion. Major or minor criteria were attributed to HF only when no alternative explanation could be found for the symptoms or signs (eg, other medical conditions such as cirrhosis, renal failure, or chronic pulmonary disease).

Statistical Analyses
First, participants with a first MI were classified into 3 groups based on the decade of incidence (ie, 1970 to 1979, 1980 to 1989, and 1990 to 1999). Next, we evaluated the incidence of HF or death (free of HF) on follow-up during the 30-day and 5-year time periods after MI. Mortality free of HF was evaluated as opposed to total mortality because mortality in individuals with both MI and HF may be attributable to HF, and we intended to assess mortality as a competing event to the incidence of HF (ie, people who die free of HF “escape” HF). Third, we performed multivariable analyses comparing the incidences of HF and death (separate analyses for each outcome) over the 30-day and 5-year follow-up periods (separate analyses for each follow-up period) after MI occurrence in each of the 3 decades, with the decade 1970 to 1979 serving as the referent group. Fourth, we repeated analyses evaluating the 5-year incidence of HF and death among participants with an MI who survived beyond 30 days (ie, these analyses paralleled earlier analyses but excluded people who died or developed HF within 30 days). Fifth, we performed additional analyses that evaluated incidence of HF or death at time points between 30 days and 5 years (ie, at 6 months, 1 year, and 2 years after MI). Poisson regression was used for modeling events during the 30-day period after MI, whereas Cox proportional hazards regression was used for incidence of events over the 5-year period after MI. All regression models adjusted for the following covariates (obtained from the Framingham Heart Study examination that preceded the incident MI event): age, sex, body mass index, smoking status, systolic blood pressure, hypertension treatment, diabetes mellitus, and total cholesterol. Given the changes in ascertainment of MI across the decades, we conducted additional analysis adjusting for the proportion of MIs diagnosed without diagnostic ECG changes (ie, on the basis of cardiac biomarkers and clinical history without diagnostic Q waves) in each decade. All statistical analyses were performed with SAS software version 8.0 (SAS Institute, Cary, NC), and P<0.05 was used to denote statistical significance.

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results
The study sample consisted of 676 participants with a first occurrence of MI over the 3 decades of observation. The baseline characteristics of study participants are shown in Table 1 according to the decade of MI incidence (data for covariates being obtained from the examination that preceded the onset of MI). Participants with a first MI in the most recent decade were older and were more likely to be women, to have diabetes, and to be taking antihypertensive agents, but they had lower serum cholesterol concentrations and smoking
The incidence of HF during the 30 days after MI was higher in each decade separately for the initial 30 days after MI and for the 5-year period after the MI.

The Figure displays the age- and sex-adjusted survival free of HF after MI during the 30-day post-MI period, and the 5-year post-MI period. We did not observe any temporal trends in the incidence of the composite outcome of death or HF after MI during the 30 days after MI. The observed trends in post-MI HF incidence across decades remained robust.

The Appendix Table (online-only Data Supplement) presents data on incidence of HF and death at 6 months, 1 year, and 2 years after MI. These data suggest that the higher incidence of HF observed at 30 days in recent decades was maintained in analyses of HF and death after MI at these time points as well.

### Discussion

#### Principal Findings

Our principal findings are 2-fold. First, participants with a first MI had a decreasing trend for mortality free of HF between 1970 and 1999 and a concomitant increasing trend for the incidence of HF. These trends were evident for both the 30-day post-MI period and the 5-year post-MI period. Additional analyses suggested that these trends were not influenced by the increasing trend for ascertainment of MI based on biomarkers (and the resultant potential change in case mix of MI). Also, we consistently used the same set of criteria for the ascertainment of HF across the decades; however, trends in the ascertainment of HF based on a greater performance of imaging tests or a greater diagnostic suspicion in more recent decades may have contributed to the present finding of a greater incidence of HF in the 1990s. Second, in the participants who survived beyond the 30-day post-MI period without HF, we did not observe any temporal trends in the incidence of HF after MI. These data suggest that the rising trend in incidence of HF after MI was driven largely by the trend for increased incidence noted for the 30-day post-MI period in recent decades. It is conceivable that our observations are consistent with the well-acknowledged lower mortality and better myocardial salvage of individuals with an MI in the 1990s. Survivors of MI have residual myocardial damage and a higher risk of developing HF. Improved survival in recent decades may have contributed to an increase in the pool of people at risk for developing HF, thereby explaining the increasing trend in the incidence of HF after MI from 1970 to 1999; such individuals may have experienced higher mortality rates in the earlier decades.
Of note, a previous Framingham report that evaluated trends in the incidence of HF (of any cause) in the time period 1950 to 1999 demonstrated that incidence is stable in men but may be decreasing in women. In the present report, we demonstrate an increasing trend in post-MI HF over the time period from 1970 to 1999. It may be important to analyze trends in incidence of HF due to specific causes, because temporal patterns may vary on the basis of the cause of HF. For instance, it is conceivable that HF caused by hypertension may have declined in more recent decades owing to better control of high blood pressure, thereby explaining the decline in overall incidence of HF in women (in whom the contribution of high blood pressure is greater relative to that of MI).

### Trends in HF After MI Incidence: Comparison With Previous Literature

The results of the present investigation vary from those of some other reports in the published literature. Differences in

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<th>Table 2. Age- and Sex-Adjusted Event Rates After MI and Adjusted Relative Risk of Events Across Decades</th>
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Multivariable models adjust for the following covariates: age, sex, body mass index, systolic blood pressure, hypertension treatment, total cholesterol, diabetes mellitus, and smoking.

*All event rates are age and sex adjusted per 100 people.
the case mix in the study samples (inclusion of first versus recurrent MI; incident versus prevalent HF), varying durations of follow-up (in-hospital versus short- and long-term follow-up after MI), and distinctions in the time periods of observation (inclusion of the early and late 1990s versus analysis of data from the early 1990s) may have contributed to the apparently dissimilar findings across these studies, as detailed below.

An investigation of the Olmsted County, Minnesota, population by Hellerman et al7 that used a study sample and design similar to the present study (prospective cohort with incident MIs, no prevalent HF, and mean follow-up of 7.6 years) reported a 28% decline in the incidence of post-MI HF between 1979 and 1994. A major difference between that report and the present report is the time period under study (1979 to 1994 versus 1970 to 1999). As noted by Goldberg et al,9 the use of primary percutaneous intervention as a treatment for MI became more common in the late 1990s. It is possible that the increased survival of “sicker” patients with MI because of the efficacy of primary percutaneous intervention led to an accrual of more susceptible people in the latter half of the 1990s, which could explain why we observed an increasing trend in post-MI HF by studying people up to 1999.

Several reports from the Worcester Heart Attack Study (WHAS), a longitudinal, community-based surveillance study, also have evaluated temporal trends in the incidence of HF after MI. These reports were based on abstraction of hospitalization records of patients with MI in the Worcester Standard Metropolitan Area in different time periods, focused on incidence of HF during the initial hospital stay, evaluated all patients hospitalized with MIs (both first and recurrent), and included patients with or without prevalent HF. In contrast, the present investigation evaluated both short- and long-term incidence (both during and beyond the initial hospital stay) of HF after a first MI. An initial analysis of 20 years of data (up to the year 1995) by Spencer et al9 from WHAS showed an inconsistent trend for HF incidence. The 25-year analysis (up to year 2001) reported by Goldberg et al9 showed unadjusted HF incidence rates that were similar across the time periods evaluated; however, after statistical adjustment for age, sex, prevalent coronary artery disease, and MI order and type, the investigators observed an increasing trend in HF incidence in recent decades. As noted above, it is possible that the latter findings are consistent with the present observations because of the similarity in the time periods studied.

Strengths and Limitations

The present study extends prior observations in several respects. We evaluated both in-hospital HF and events after the index MI over a period of 5 years. Furthermore, we concomitantly evaluated trends in both incidence of HF and death (free of HF) to assess how changing case-fatality rates may influence the incidence of post-MI HF.

Nevertheless, several limitations of the present investigation must be noted. We did not model temporal trends in the use of specific treatments (such as use of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, aldosterone antagonists, or β-blockers) or revascularization procedures for participants with an MI. It is more likely that higher proportions of participants in the latter decades received these therapies than participants in the decade of 1970 to 19799; however, treatments that improve post-MI survival have also been shown to decrease the incidence of HF. Another limitation of the present study is the lack of information on the type of HF (systolic versus diastolic) or the occurrence of left ventricular systolic dysfunction after MI. Lastly, the present study sample is predominantly white and of European ancestry, and caution must be exercised in generalizing these results to other ethnicities.

Conclusions

Our longitudinal observations on a large, community-based sample demonstrate reciprocal trends of a decrease in mortality after MI accompanied by an increase in incidence of HF in more recent years (1990s) relative to the 1970s. Greater salvage of high-risk MI patients in recent time periods may contribute to these trends.

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Disclosures

None.

References


5. Lewis EF, Moyer LA, Rouleau JL, Sacks FM, Arnold JM, Warnica JW, Flaker GC, Braunwald E, Pfeffer MA. Predictors of late development of
Mortality due to myocardial infarction (MI) has decreased in recent decades; however, few community-based epidemiological investigations have addressed the long-term trends in the incidence of heart failure after MI. We evaluated trends in the incidence of heart failure after MI in the time period 1970 to 1999 in the Framingham Heart Study cohort. We related the decade of MI incidence to the occurrence of heart failure in the early (within 30 days of MI) and late (after 30 days and up to 5 years) post-MI periods and to the incidence of death free of heart failure. We observed a striking increase in the incidence of heart failure after MI in the decade 1990 to 1999 (compared with the decade 1970 to 1979), accompanied by a decrease in the incidence of death without heart failure after MI over the same time period. We conclude that the increase in heart failure incidence after MI in recent decades was explained primarily by increases in the early post-MI period, in part due to a major decrease in mortality during this period in recent decades. The present data are consistent with the notion that a greater salvage of high-risk patients in recent time periods may have contributed to the observed trends in post-MI heart failure.

CLINICAL PERSPECTIVE

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