Temporal Trends in Event Rates After Q-Wave Myocardial Infarction
The Framingham Heart Study

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Background—Short-term (<30 day) mortality after Q-wave myocardial infarction (MI) has declined over the decades, but it is unclear if rates of long-term sequelae after Q-wave MI have improved.

Methods and Results—In 546 Framingham Heart Study subjects (388 men with a mean age of 60 years; 158 women with a mean age of 69 years) with an initial recognized Q-wave MI from 1950 through 1989, we investigated time trends in risk for coronary heart disease (CHD) death (n = 199), all-cause mortality (n = 287), reinfarction (n = 108), and congestive heart failure (CHF; n = 121). With 1950 through 1969 as the reference period, hazards ratios (HRs) for these outcomes were determined for the 1970s and 1980s. Trend analyses across the 3 time periods were performed for each outcome. Compared with the 1950 through 1969 reference period, the HRs for CHD death were lower in subsequent decades (1970 through 1979: HR, 0.69; 95% CI, 0.49 to 0.98; 1980 through 1989: HR, 0.48; 95% CI, 0.33 to 0.72). All-cause mortality also declined (1970 through 1979: HR, 0.70; 95% CI, 0.52 to 0.94; 1980 through 1989: HR, 0.59; 95% CI, 0.43 to 0.81). There were no significant temporal changes in the risks for recurrent MI or CHF.

Conclusions—Substantial reductions in risk of CHD death and all-cause mortality occurred over these 4 decades, coincident with improvements in post-MI therapies. The absence of a decline in CHF incidence may be due to improved post-MI survival of individuals with depressed left ventricular systolic function who are at high risk for CHF.

Key Words: myocardial infarction • morbidity • mortality • heart failure • epidemiology

Age-adjusted mortality from coronary heart disease (CHD) in the United States has declined since the mid-1960s.1 This decline has been attributed to both primary and secondary prevention efforts.1–3 Nevertheless, heart disease remains the leading cause of death in the United States.1

Although it is clear that short-term mortality from myocardial infarction (MI) has declined,4–13 studies examining long-term mortality after MI have yielded conflicting results. A 1991 meta-analysis reported no change in 5-year mortality after MI from the 1960s through the 1980s.5 The Worcester Heart Attack Study also found no difference in long-term survival in patients discharged from the hospital after an acute MI in 1984 versus 1975.6 On the other hand, in the Minnesota Heart Survey, 4-year post-MI survival rates improved by 35% for men and 27% for women from 1970 to 1980.7 In a subsequent Minnesota Heart Survey report, 3-year post-MI survival improved further from 1985 to 1990.8 In addition, the Atherosclerosis Risk in Communities (ARIC) study reported that from 1987 through 1994, rates of recurrent MI also declined.4

Another consequence of MI is congestive heart failure, which was recently described as 1 of the “new epidemics” for the turn of the 21st century.14 The growing burden of heart failure has been attributed to the aging of the population and the improved survival of patients with MI.14 There is a paucity of information on temporal trends in risk for heart failure after MI.

The objective of this investigation was to examine time trends in CHD death, all-cause mortality, recurrent MI, and heart failure after initial Q-wave MI. The diagnostic criteria for Q-wave MI have been stable since 1950 and are unaffected by improvements in the biochemical markers that have led to an increase in detection of non-Q-wave MI.12 The Framingham Heart Study, with its long-term, population-based design, provides a unique opportunity to determine whether the prognosis after Q-wave MI has changed over 4 decades of observation.

Methods

Subjects
The Framingham Heart Study began in 1948 as a prospective investigation of 5209 men and women who were 28 to 62 years of age. The study population was followed for a mean of 37.7 ± 11.5 years. The 1990-1992 examination wave included 4442 individuals (85% of those alive in 1992). Mortality data were obtained from the National Death Index and the Social Security Administration. Mortality data and medical records for living participants were obtained from the Framingham Heart Study and the Community Health Study. All-cause and CHD death were ascertained for the 1950 through 1989 period. CHD death was defined as death from ischemic heart disease, sudden death, or congestive heart failure.

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TABLE 1. Clinical Characteristics* by Time Period of Initial Q-Wave MI

|---------------------|-----------|-----------|-----------|--------
| Subjects, n         | 214       | 154       | 178       |        |
| Male, %             | 79        | 68        | 65        |        |
| Age, y              | 60±0.7    | 64±0.8    | 65±0.8    |        |
| Body mass index, kg/m² | 26±0.3   | 27±0.3    | 27±0.3    |        |
| Cholesterol, mg/dL  | 262±3     | 242±4     | 233±4     |        |
| Diabetes, %         | 6         | 12        | 13        |        |
| Hypertension, %     | 75        | 68        | 56        |        |
| Smokers, %          | 47        | 52        | 45        |        |
| Left ventricular hypertrophy, % | 5   | 3         | <1        |        |

*Least-squares means±SE or adjusted proportions.

Sex distribution was unadjusted; age comparisons were sex adjusted; all other covariates were sex and age adjusted.

TABLE 2. Risk of CHD Death After an Initial Q-Wave MI

|--------------------|-----------|-----------|-----------|--------
| ≤10 y of follow-up |           |           |           |        |
| Events/subjects, n | 90/214    | 62/154    | 47/178    |        |
| HR                 | 1         | 0.69      | 0.48      | 0.70   |
| 95% CI             | Reference | 0.49–0.98 | 0.33–0.72 | 0.57–0.84 |
| First 29 d of follow-up |         |           |           |        |
| Events/subjects, n | 35/214    | 29/154    | 24/178    |        |
| HR                 | 1         | 0.74      | 0.49      | 0.70   |
| 95% CI             | Reference | 0.44–1.25 | 0.28–0.87 | 0.53–0.93 |
| 30 d to 10 y of follow-up |       |           |           |        |
| Events/subjects, n | 55/178    | 33/123    | 23/153    |        |
| HR                 | 1         | 0.61      | 0.47      | 0.67   |
| 95% CI             | Reference | 0.38–0.97 | 0.27–0.80 | 0.51–0.88 |

Diagnosis of Cardiovascular Events

A panel of physicians reviewed each cardiovascular event and accompanying ECGs according to standard criteria.16 For the present study, the initial MI had to be an acute recognized Q-wave MI. A recognized MI required that the clinical circumstances led a physician to make the diagnosis. A recognized Q-wave MI was designated when serial ECG changes consisting of the development of pathological Q-waves of ≥0.04-second duration or loss of R waves occurred compared with previous ECGs. A posterior Q-wave MI by ECG was coded when the R wave was ≥0.04 seconds and was greater than the S wave in V₁ or V₂ in the absence of a right bundle-branch block and represented a serial change from prior tracings. A recognized non–Q-wave MI was determined by a history of ischemic chest pain and elevation of cardiac enzymes in the absence of development of Q waves on serial ECGs. An unrecognized Q-wave MI was based on the presence of ≥2 major criteria (eg, rales, paroxysmal nocturnal dyspnea, or neck vein distension) or 1 major plus 2 minor criteria (eg, bilateral ankle edema, nocturnal cough, or dyspnea on ordinary exertion) for congestive heart failure. Criteria for heart failure did not change over the 40-year period studied.21

Statistical Analysis

Analyses compared 10-year event rates after an initial Q-wave MI for 3 time periods: 1950 through 1969, 1970 through 1979, and 1980 through 1989. The 10-year follow-up periods began at the onset of the Q-wave MI. Cox proportional-hazards regression models22 were used to investigate the risk for CHD death, all-cause mortality, recurrent MI, and congestive heart failure according to the decade of the initial MI. On the basis of published literature, the following potential confounders were included in the models: sex; age at first MI; body mass index; presence of diabetes, hypertension, or left ventricular hypertrophy; and current smoking. A substantially greater proportion of subjects had missing cholesterol values than the other covariates. To determine whether cholesterol could be omitted from our analyses, we compared Cox models with and without cholesterol included. Cholesterol level was not associated with any of the 4 outcomes, and hazards ratios (HRs) and overall time trends...
were almost identical in models with and without cholesterol. Therefore, cholesterol was omitted from all models presented.

With 1950 through 1969 as the reference period, adjusted HRs and 95% CIs were determined for the 1970s and 1980s. In addition, trend analyses across the 3 time periods were performed for each outcome (dummy variable, 0, 1, or 2). Secondary analyses were performed for each outcome to assess trends in early (<30 days) and late (≥30 days) follow-up after MI. Because of small numbers of early recurrent MIs, only analyses of overall (0 to 10 year) recurrence are presented. An additional secondary analysis was performed to further examine time trends in the type of recurrent MI (Q-wave versus non-Q-wave MI). Throughout the analysis, \( P < 0.05 \) was the criterion for statistical significance. Statistical analyses were performed with SAS. Cumulative incidence curves for each outcome by time period of initial MI were generated by use of the mean values for all covariables from the Cox models.

### Results

From 1950 through 1989, there were 589 incident MI cases; 43 (7%) were excluded because of incomplete covariable information (42 had not attended an examination within 4 years; 1 had sporadic missing data). Of the 546 eligible MI cases, 71% were in men. Table 1 shows the age- and sex-adjusted demographic and clinical characteristics of subjects by decade of MI occurrence. The mean age at initial MI (adjusted for sex) was 60 years in the 1950 through 1969 time period, 64 years in the 1970s, and 65 years in the 1980s. Across the time periods, there was an increasing proportion of women and diabetics. There was a decrease in the proportion of subjects with hypertension and left ventricular hypertrophy, and the mean cholesterol level was lower in the later decades. Body mass index was similar across all 3 time periods.

Among the 546 cases of initial MI, there were 199 CHD deaths. Compared with 1950 through 1969, the HR for CHD death after a Q-wave MI was 0.69 (95% CI, 0.49 to 0.98) in the 1970s and 0.48 (95% CI, 0.33 to 0.72) in the 1980s (Table 2). The overall trend for CHD death was a 30% decline per decade. The trends in early (<30 days) and late (30 days to 10 years) risks for CHD death were similar. Figure 1 displays the cumulative incidence of CHD death as a function of the time period of initial Q-wave MI.

During follow-up, there were 287 deaths. Compared with 1950 through 1969, the HR for all-cause mortality after a Q-wave MI was 0.70 (95% CI, 0.52 to 0.94) in the 1970s and 0.59 (95% CI, 0.43 to 0.81) in the 1980s (Table 3). The overall trend for all-cause mortality was a 23% decline per decade. Separate analyses of early and late follow-up for all-cause mortality revealed a steeper temporal decline in early deaths. Figure 2 displays the cumulative incidence of all-cause mortality as a function of the time period of initial Q-wave MI.

During follow-up, there were 108 recurrent MIs. The HR for recurrent MI was 0.57 (95% CI, 0.34 to 0.93) in the

### Table 3. Risk of All-Cause Mortality After an Initial Q-Wave MI

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found no difference in the long-term survival rates of patients discharged from the hospital after an acute MI in 1975, 1978, 1981, or 1984 despite a 32% overall decline in the in-hospital case-fatality rate over the 10-year period. Weinblatt et al10 similarly found that declines in CHD mortality between 1968 and 1976 were due to declines in in-hospital mortality. Those authors found no difference between the long-term prognoses (4.5 years) of men who had survived an acute MI in the mid-1960s and survivors in the 1970s.10

In contrast, Minnesota Heart Survey investigators reported a 35% improvement in the 4-year survival rate for men and 27% improvement for women after an MI in 1980 compared with 1970. In the subgroup of patients discharged alive after an MI in 1980 compared with 1970, significant improvement in 4-year survival persisted for men but not for women.7 In a subsequent study comparing 1990 and 1985 cohorts, investigators from the Minnesota Heart Survey found a 24% decline in the relative risk of dying within 3 years of hospitalization for MI, with a similar decline noted in the subgroup of subjects who survived the first 28 days.8 Most recently, Goldberg and colleagues11 reported a significant improvement in 1- and 2-year survival rates after hospital discharge after acute MI in patients <85 years of age from the mid- to late 1970s to the mid-1990s.

The ARIC study examined time trends for recurrent MI and CHD death after MI. In addition to finding a decline in age-adjusted CHD mortality from 1987 to 1994 (28% in men, 31% in women), those authors also found a concomitant 19% decline in recurrent MI for men and a 15% decline (nonsignificant) for women.4 It is interesting that despite improvements in biochemical tests for the diagnosis of MI12 and therefore improved detection of recurrent MI, the ARIC study observed declines in recurrent MI. In contrast, our study did not find an overall decline in recurrent MI. Unlike the ARIC report, we considered only index Q-wave infarctions.

This Framingham Heart Study investigation of time trends in prognosis after Q-wave MI is generally in agreement with the most recent studies4,7,8,11 and helps to clarify that short- and long-term CHD death rates and all-cause mortality have improved during the 4 decades of observation. Most of the studies of time trends in prognosis after MI examined survival after MI.4–13 The Worcester Heart Attack Trial also reported on trends for recurrent MI4 and the ARIC study reported on both recurrent MI and CHD death.4 The Framingham Heart Study is 1 of the first large prospective population-based studies to look at time trends in CHD death, recurrent MI, and incident congestive heart failure, in addition to all-cause mortality after MI. Our study also differs from prior reports examining time trends in prognosis after MI because we examined the sequelae of initial Q-wave MIs exclusively, an end point that is unaffected by improvement in biochem-

1970s and 0.81 (95% CI, 0.50 to 1.3) in the 1980s compared with the 1950 through 1969 reference period (Table 4). There was no significant trend for risk of recurrent MI after initial Q-wave MI across the decades. A secondary analysis to separately examine trends in recurrent Q-wave MIs (n = 66) and non–Q-wave MIs (n = 42) revealed no change in either event over the decades. Figure 3 displays the cumulative incidence of recurrent MI as a function of the time period of initial Q-wave MI.

There were 121 incident cases of congestive heart failure. The risks for congestive heart failure after a Q-wave MI did not change significantly over the decades (Table 5). Analyses of early follow-up revealed no decline in heart failure. In contrast, for late follow-up, there was a decline (1970s: HR, 0.70; 95% CI, 0.38 to 1.29; 1980s: HR, 0.51; 95% CI, 0.26 to 1.00). The trend across the 3 time periods was a 29% decline per decade in late-incident heart failure. Figure 4 displays the cumulative incidence of congestive heart failure as a function of the time period of initial Q-wave MI.

### Discussion

Over the past 40 years, survival after an initial Q-wave MI improved considerably in this large population-based sample. From the 1950 through 1969 reference period through the 1980s, there was a 41% decline in all-cause mortality and a 52% decline in the risk of death from CHD after an initial Q-wave MI. In contrast, there were no significant changes in the risks of recurrent MI and congestive heart failure.

Although case-fatality rates after acute MI have declined,4–13 it is not clear whether long-term outcomes after MI have shown similar temporal improvements. Despite a decrease in in-hospital case-fatality rates from the reference period of 1966 through 1967 through 1971, Goldberg et al9 found no significant improvement in long-term prognosis (3 years) among hospitalization survivors of MI in a database of 24 Baltimore hospitals. The Worcester Heart Attack Study,

**Figure 3.** Cumulative incidence of recurrent MI as function of time period of initial Q-wave MI.
ical markers of MI. With longer follow-up and examination of all the major sequelae of a Q-wave MI (CHD death, all-cause mortality, recurrent MI, and congestive heart failure), this investigation contributes to a better understanding of how the natural history of initial Q-wave MI has changed over the decades.

The favorable time trends in the sequelae of MI are paralleled by improvements in the short-term care and long-term treatment of MI. There was no known treatment in 1950 that was capable of prolonging life after an MI. In the 1960s, the advent of the coronary care unit was associated with decreases in in-hospital mortality. Goldberg et al compared the prognosis of 504 patients hospitalized with acute MI in 1966 through 1967 with 803 patients hospitalized in 1971 and found that in-hospital case-fatality rates were lower in the latter period (27.5% versus 20%). They suggested that the introduction of coronary care units reduced in-hospital deaths. In the 1970s, coronary revascularization increased. In the Minnesota Heart Survey, coronary angioplasty increased from 0% to 7% of CHD patients, and CABG rates increased from 0.4% to 12% of CHD patients from 1970 to 1985. The late 1970s marked the advent of β-blockers, which increased in use after an MI from 39% in 1979 to 87% in 1987. The early 1980s introduced the thrombolytic era. In addition, the 1980s coincided with the increasing use of aspirin, β-blockers, ACE inhibitors, lipid-lowering agents, and revascularization procedures. The Minnesota Heart Survey documented an increase in the use of thrombolytic agents for acute MI from 0% in 1979 to 8% in 1985. McGovern et al attributed 20% of the observed improvement in 28-day survival among patients hospitalized for an acute MI in 1990 compared with 1985 to the use of thrombolytics. Aspirin use after an MI doubled between 1979 and 1987 from 40% to 80%. The proportion of patients prescribed ACE inhibitors after an MI increased from 14% in 1989 through 1991 to 23% in 1994. In a study of 345 hyperlipidemic patients with symptomatic cardiovascular disease, prescriptions for lipid-lowering drugs increased from 13% in 1982 to 59% in 1989. Using a CHD policy model (a computer-simulation model), Hunink et al attributed 71% of the 34% national decline in CHD mortality from 1980 to 1990 to improvements in the treatment of subjects with established CHD.

Although we found no overall decline in risk for congestive heart failure from 1950 to 1989, secondary analyses examining early (<30 days) versus late (≥30 days) follow-up suggest an explanation (Table 5). Higher risk for heart failure during the first 30 days after an MI in recent decades masked the declining long-term risk. For example, a slightly higher early risk among MI cases in the 1980s (HR, 1.35; 95% CI, 0.65 to 2.83) offset the lower late risk (HR, 0.51; 95% CI, 0.26 to 1.00). A plausible explanation for these findings is that improvements in MI care in the 1980s may have salvaged more MI patients with extensive left ventricular dysfunction, leading to an expanding pool of MI survivors at high risk for heart failure in the short term.

This study has several limitations that must be considered when the results are interpreted. First, although we controlled in our models for the most accepted clinical predictors of the 4 cardiac outcomes, there were no measures of left ventricular function available to compare across the decades. It is likely that on average survivors of an initial MI in the 1950s, when there was no therapy available, had smaller infarcts than those in the 1980s. Thus, the inherent risk for subsequent cardiac events may be lower for MI survivors in the 1950s by virtue of their differing disease severity. Second, our statistical power to look at important subgroups of recurrent MI,
including early and late follow-up and Q-wave versus non-Q-wave MI, was limited. Third, we lacked information on interventions that may have contributed to improved outcome, eg, post-MI drug therapy and revascularization.

**Conclusions**

Effective short- and long-term therapeutic modalities likely account for the declines in both early and late CHD death and all-cause mortality after an initial Q-wave MI observed in Framingham Heart Study participants over the course of the 4 decades of observation. Despite these declines, the risk for recurrent MI has not changed. Paradoxically, improved survival after an MI may explain the absence of a significant decline in congestive heart failure rates. Late follow-up (≥30 days), however, revealed evidence of an overall decline in risk for heart failure of a degree consistent with declines in CHD death and all-cause mortality. Declines in the sequelae of MI are likely to continue if both short-term treatment and long-term prevention efforts remain a public health priority.

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**References**

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