Incidence of Heart Failure after Myocardial Infarction: Is It Changing over Time?

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Improved survival after myocardial infarction (MI) could result in MI survivors’ contributing to the US heart failure epidemic. Conversely, since the severity of MI is declining over time, a decline in post-MI heart failure might also be anticipated. This study tested the hypothesis that the incidence of post-MI heart failure was declining over time in a geographically defined MI incidence cohort. Between 1979 and 1994, 1,537 patients with incident MI and no prior history of heart failure were hospitalized in Olmsted County, Minnesota. Framingham Heart Study criteria were used to ascertain the incidence of inpatient and outpatient heart failure over a mean follow-up period of 7.6 years (standard deviation 5.5). Overall, 36% of patients experienced heart failure. After adjustment for factors related to post-MI heart failure (age, hypertension, smoking, and biomarkers), the incidence of heart failure declined by 2% per year (relative risk = 0.98, 95% confidence interval: 0.96, 0.99; p = 0.01). The relative risk of developing heart failure among persons with MIs occurring in 1994 versus 1979 was 0.72 (95% confidence interval: 0.55, 0.93), indicating a 28% reduction in the incidence of heart failure. Administration of reperfusion therapy within 24 hours after MI was associated with lower risk of post-MI heart failure and accounted for most of the temporal decline in heart failure. This suggests that improved survival after MI is unlikely to be a major contributor to the heart failure epidemic.

Heart failure, congestive; myocardial infarction

Abbreviations: CI, confidence interval; MI, myocardial infarction; RR, relative risk.

Hospital discharge rates for heart failure in the United States increased by 155 percent over the past 20 years, and 4,790,000 Americans carry a diagnosis of heart failure (1). In this context, heart failure has been singled out as an emerging epidemic (2). However, the determinants of the heart failure epidemic have not been fully characterized. Indeed, while epidemiologic studies point towards hypertension as a leading factor in the genesis of heart failure (3, 4), other researchers underscore the high prevalence of coronary disease in heart failure trials (5) to emphasize its contribution to the burden of heart failure. These discrepancies indicate a need for studies defining the role of coronary disease in heart failure.

With regard to acute myocardial infarction (MI), clinical trials carried out in the 1990s (6, 7) convincingly demonstrated the efficacy of reperfusion therapy, resulting in its incorporation into clinical practice. This coincided with temporal improvement in MI case fatality rates in the population. While this improvement in post-MI survival clearly underscores the effectiveness of reperfusion therapy in the community (8, 9), it also leads to the hypothesis that survivors of acute MI have contributed to the heart failure epidemic (2). However, this hypothesis remains to be tested, particularly in view of data indicating that the severity of MI has declined over time, a trend that would more probably lead to a decline in post-MI heart failure (10, 11).

Despite the importance of delineating the contribution of MI to the heart failure burden, there is a paucity of data on temporal trends in post-MI heart failure in the population. In the Framingham Heart Study, no decline in post-MI heart failure...
failure was detected (12), but non-Q-wave MIs were excluded; thus, a portion of the spectrum of MI was missed. The Worcester Heart Attack Study (13) reported an encouraging, albeit modest, decline in the incidence of heart failure during initial hospital stays for acute MI but did not include data for the period beyond hospitalization. However, as the length of hospitalization for MI decreases over time, data on the period beyond hospital dismissal are required for ascertainment of post-MI heart failure. Thus, data on post-MI heart failure, which are critical to characterization of the contribution of acute MI to the heart failure epidemic, are currently incomplete.

Community surveillance studies, which measure population trends in disease incidence and outcome, are ideally suited to addressing this question. Among the few currently active community surveillance studies in the United States, the Olmsted County Study in Olmsted County, Minnesota, is uniquely positioned to provide such data, since it includes all age groups and captures longitudinal data beyond initial hospitalization, including outpatient events. Thus, this study was undertaken to address this gap in knowledge and to examine time trends in the incidence of post-MI heart failure and its determinants in a validated MI incidence cohort.

MATERIALS AND METHODS

Study setting

Epidemiologic research in Olmsted County is possible because the county is relatively isolated from other urban centers and nearly all medical care is delivered to local residents by a small number of providers. Except for the fact that a higher proportion of the working population is employed in the health care industry, the characteristics of the population of Olmsted County are similar to those of all US Whites (14).

The Mayo Clinic provides approximately half of the primary care and nearly all specialty care for the community. Olmsted Medical Center and its affiliated hospital provide the remainder of the primary care, as well as some specialty care. The epidemiologic potential in the community is enhanced by the fact that each provider uses a comprehensive medical record system, whereby all data collected on an individual are assembled in one place. Thus, the details of every inpatient and outpatient encounter, including visits to the emergency department, laboratory results, pathology reports, and correspondence concerning each patient, can be accessed. The records are easily retrievable because the Mayo Clinic has maintained since the early 1900s extensive indices based on clinical and histologic diagnoses and surgical procedures (15, 16). Since 1966, similar indices have been developed for non-Mayo health care providers under the aegis of the Rochester Epidemiology Project. The result is the linkage of medical records from all sources of medical care used by the Olmsted County population. This record linkage system provides investigators with a unique opportunity to ensure complete ascertainment of data on post-MI heart failure, including both inpatient and outpatient episodes.

Data collection

The MI incidence cohort. The procedures used to assemble the MI incidence cohort have been reported in detail elsewhere (17). Briefly, for case-finding, we used lists of patients discharged from hospitals in Olmsted County with diagnoses compatible with MI, using the following codes from the International Classification of Diseases, Ninth Revision: code 410, acute MI; code 411, other acute and subacute forms of ischemic heart disease; code 412, old MI; code 413, angina pectoris; and code 414, other forms of ischemic heart disease. All events coded 410 were reviewed, while 50 percent of events with code 411 and 10 percent of events with codes 412–414 were reviewed. The sampling fractions were comparable to those used in other studies (18, 19). Trained registered nurse abstractors reviewed criteria for residency in Olmsted County. The entire community medical record was used to search for prior history of MI in order to ascertain incident MI status. On average, more than four decades’ worth of information was available in the record prior to the incidence date (18). We included all patients with incident MI, irrespective of their clinical presentation in years prior to the MI, to obtain a comprehensive incidence cohort of all first cases of MI. Abstractors collected information on cardiac pain, creatine kinase ratio, and electrocardiographic results. Because of the change in the normal values and corresponding ranges over time, peak creatine kinase ratios were considered abnormal if they were twice the upper limit of normal values for the time period-specific reference range. Peak creatine kinase ratio was used as a marker for severity of MI and was expressed as multiples of twice the period-specific upper limit of the normal value. Copies of up to three electrocardiograms were assigned a Minnesota code by the Electrocardiogram Reading Center at the University of Minnesota (20). Standardized epidemiologic criteria were used to assign MI diagnoses on the basis of cardiac pain, creatine kinase values, and Minnesota coding of the electrocardiographic results (19). All initial MIs were included irrespective of the duration of patients’ survival.

Baseline characteristics and endpoint definitions. The characteristics of patients at the time of the index MI were determined through review of the community medical records. Patients were considered to have a history of smoking if they were either a former smoker or a current smoker. Clinicians’ diagnoses were used for history of hyperlipidemia, hypertension, and diabetes mellitus. A modification of the Charlson Comorbidity Index (21) was used as an indicator of noncardiovascular comorbidity. This modification excluded congestive heart failure, diabetes, peripheral vascular disease, and cerebrovascular disease from the summary score. Reperfusion therapy was defined as thrombolysis or coronary angioplasty within 24 hours after hospital admission.

We reviewed community medical records to ascertain incident heart failure following the index MI. Patients with a clinical history of heart failure prior to the index MI were excluded (13). Heart failure was diagnosed using the Framingham Heart Study criteria (summarized in table 1), which require the simultaneous presence of at least two
TABLE 1. Framingham Heart Study criteria for the diagnosis of heart failure

<table>
<thead>
<tr>
<th>Major criteria</th>
<th>Minor criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroxysmal nocturnal dyspnea or orthopnea</td>
<td>Ankle edema</td>
</tr>
<tr>
<td>Neck vein distension</td>
<td>Night cough</td>
</tr>
<tr>
<td>Rales</td>
<td>Dyspnea upon exertion</td>
</tr>
<tr>
<td>Cardiomegaly</td>
<td>Hepatomegaly</td>
</tr>
<tr>
<td>Acute pulmonary edema</td>
<td>Pleural effusion</td>
</tr>
<tr>
<td>S3 gallop</td>
<td>Vital capacity decreased by one third from maximum</td>
</tr>
<tr>
<td>Increased venous pressure ≥16 cm of water</td>
<td>Tachycardia rate of ≥120 beats/minute</td>
</tr>
<tr>
<td>Circulation time ≥25 seconds</td>
<td>Weight loss of ≥4.5 kg in 5 days in response to treatment</td>
</tr>
<tr>
<td>Hepatofugal reflux</td>
<td></td>
</tr>
</tbody>
</table>

* Reproduced from Ho et al. (3, 22). Heart failure is present with two major criteria or one major criterion and two minor criteria.

major criteria or one major criterion in conjunction with two minor criteria (3, 22). Nurse abstractors collected data on all inpatient and outpatient heart failure episodes until one episode of heart failure met the Framingham criteria.

Statistical analyses

The data are presented as frequencies or mean values with standard deviations. Associations between time and several baseline characteristics were tested with chi-square tests for categorical variables and t tests for continuous variables. With regard to quality control for heart failure ascertainment, interabstractor agreement was evaluated for a random sample of 30 cases randomly selected from the MI incidence cohort using kappa coefficients.

The incidence of heart failure after incident MI was estimated using three different analytical approaches. Firstly, distributions of heart failure within 1 year after the incident MI by tertile of the study period were examined and tested for a change over time in the proportion of cases experiencing heart failure using the Mantel-Haenszel chi-square test for trend. Secondly, time trends in post-MI heart failure were analyzed with Kaplan-Meier survival curves, while censoring at death in order to account for the effect of changes in post-MI case fatality rates in the analysis. Thirdly, cumulative incidence curves were generated with death as a competing risk event (23).

Weighted proportional hazards regression models were used to examine the association between post-MI heart failure and several baseline characteristics. The analyses were weighted by the inverse of the sampling fraction in the corresponding International Classification of Diseases, Ninth Revision, code stratum. Because the study hypothesis was that the incidence of post-MI heart failure had declined over time, the analyses focused on year as the exposure variable of interest. Thus, the associations between other baseline characteristics and post-MI heart failure were examined with hierarchical modeling aimed at assessing the potential confounding of the association between year and heart failure. In a secondary analysis, heart failure occurring during the index hospitalization for MI was excluded. Results of the final selected models were summarized by calculation of relative risks and 95 percent confidence intervals for each variable. A p value of 0.05 was selected for the threshold of statistical significance.

This study was approved by the Mayo Foundation Institutional Review Board.

RESULTS

Baseline characteristics of the MI incidence cohort

Between 1979 and 1994, the cohort of patients with incident hospitalized MI included 1,757 persons. Of these, 220 (13 percent) had a history of prior heart failure and were excluded from these analyses, leaving 1,537 patients for the study. The mean age was 66 years (standard deviation 14), and 39 percent were women (table 2). The proportion of persons with a history of hypertension or hyperlipidemia increased over the study time period. No other change in the baseline characteristics was noted. Overall, 17 percent of the patients had a history of diabetes mellitus, while 68 percent were current or former smokers. The peak creatine kinase ratio declined over time. Sixty-seven percent of the patients had no noncardiovascular comorbidity. The frequency of administration of reperfusion therapy within 24 hours of hospital admission increased from 6 percent to 41 percent over the study time period (p < 0.001).

Quality control for ascertainment of heart failure

Missing data were infrequent in this cohort, and Framingham criteria, which were used to ascertain heart failure, could be applied in 96 percent of the cases. The reliability of the Framingham criteria for ascertainment of heart failure was assessed by reabstraction of the records of 30 patients for measurement of intraobserver variability, which yielded excellent agreement (κ = 0.87, 95 percent confidence interval (CI): 0.78, 0.96).

Secular trends in heart failure after incident MI

After a mean follow-up period of 7.6 years (standard deviation 5.5), 656 initial episodes of heart failure meeting the Framingham criteria had occurred. Of these, 69 (11 percent)
of the episodes were diagnosed solely in the outpatient setting, and this proportion did not change over time. The remaining 587 patients had in-hospital heart failure, 354 during the initial hospitalization for the index MI; 372 episodes of heart failure occurred during the first 28 days of the initial hospitalization for the index MI, and 280 occurred during the first 2 days.

Figure 1 shows the Kaplan-Meier survival curves of time to heart failure by tertile of the study time period. The 28-day occurrence of heart failure after MI in the time periods 1979–1984, 1985–1989, and 1990–1994 was 27 percent (95 percent CI: 23, 31), 24 percent (95 percent CI: 20, 27), and 23 percent (95 percent CI: 20, 27), respectively (log-rank \( p \) value = 0.068). At 5 years, 36 percent of patients had experienced heart failure (95 percent CI: 34, 39). Five-year heart-failure-free survival after MIs occurring in the time periods 1979–1984, 1985–1989, and 1990–1994 was 60 percent (95 percent CI: 55, 64), 65 percent (95 percent CI: 61, 70), and 67 percent (95 percent CI: 63, 71), respectively (log-rank \( p \) value = 0.068).

Additionally, competing risk analyses were conducted to estimate the cumulative incidence of heart failure with the competing risk of death. These analyses indicated that 35 percent of patients were alive and had a heart failure event at 5 years, whereas 12 percent of patients died. Thus, the incidence of post-MI heart failure derived from the competing risk model was similar to that derived from the Kaplan-Meier method, and this remained the case over the study period. This indicates little effect of the analytical approach on the estimate of the incidence of post-MI heart failure and on the association between year and post-MI heart failure and attests to the robustness of these results.

### Other determinants of post-MI heart failure

Associations between selected baseline characteristics and post-MI heart failure are shown in table 3. Having experienced the index MI more recently (in a more recent year) was associated with a reduction in the risk of post-MI heart failure, and the univariate relative risk of developing heart failure for patients with MIs occurring in 1994 versus 1979 was 0.82 (95 percent CI: 0.63, 1.00). Additionally, age, hypertension, and diabetes mellitus were associated with...
increased risk of post-MI heart failure, as was peak creatine kinase ratio.

The final multivariable weighted proportional hazards regression model (table 3) included variables associated with post-MI heart failure, which confounded the association between year and post-MI heart failure. These variables included age, hypertension, smoking, peak creatine kinase ratio, and comorbidity. After adjustment for these factors, there was a 2 percent reduction in the risk of post-MI heart failure with each calendar year. This corresponds to a relative risk of heart failure after an MI that occurred in 1994 (as compared with 1979) of 0.72 (95 percent CI: 0.55, 0.93). The inclusion of Killip class in a model with postdischarge heart failure as the outcome measure indicated that Killip class 3 or 4 was positively associated with postdischarge heart failure (relative risk (RR) = 2.01, 95 percent CI: 1.63, 2.48; p < 0.001). The occurrence of an MI subsequent to the index MI was not independently associated with post-MI heart failure.

Role of reperfusion therapy

The univariate association between reperfusion therapy and post-MI heart failure indicated a substantial protective effect (RR = 0.48, 95 percent CI: 0.39, 0.59; p < 0.001), which was somewhat attenuated after adjustment for age, hypertension, smoking, peak creatine kinase ratio, and comorbidity (RR = 0.67, 95 percent CI: 0.53, 0.84; p < 0.001). The association between year and post-MI heart failure was markedly attenuated by the addition of reperfu-

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**TABLE 3. Predictors of post-myocardial-infarction heart failure in weighted proportional hazards regression analyses, Olmsted County, Minnesota, 1979–1994**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>RR*</th>
<th>95% CI*</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Univariate analyses</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year of MI†</td>
<td>0.99</td>
<td>0.97, 1.00</td>
<td>0.13</td>
</tr>
<tr>
<td>Age at index MI</td>
<td>1.05</td>
<td>1.05, 1.06</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>1.65</td>
<td>1.41, 1.93</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of smoking</td>
<td>0.60</td>
<td>0.51, 0.70</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of diabetes</td>
<td>1.97</td>
<td>1.65, 2.37</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peak CK† level</td>
<td>1.04</td>
<td>1.02, 1.05</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Charlson Comorbidity Index</td>
<td>1.16</td>
<td>1.10, 1.21</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Multivariate analyses</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year of MI</td>
<td>0.98</td>
<td>0.96, 0.99</td>
<td>0.01</td>
</tr>
<tr>
<td>Age at MI</td>
<td>1.05</td>
<td>1.04, 1.06</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>1.43</td>
<td>1.21, 1.68</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Charlson Comorbidity Index</td>
<td>1.06</td>
<td>1.00, 1.12</td>
<td>0.05</td>
</tr>
<tr>
<td>Second tertile of CK values†</td>
<td>1.21</td>
<td>0.99, 1.48</td>
<td>0.07</td>
</tr>
<tr>
<td>Third tertile of CK values†</td>
<td>1.50</td>
<td>1.23, 1.82</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* RR, relative risk; CI, confidence interval; MI, myocardial infarction; CK, creatine kinase.
† The reference level was the first tertile of the CK distribution. CK values that were invalid because of trauma or other circumstances were accounted for in the models.

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**DISCUSSION**

In this geographically defined MI incidence cohort, the occurrence of heart failure after MI declined over time, with a 28 percent reduction in the risk of post-MI heart failure between 1979 and 1994. This is consistent with data indicating that the severity of MI is declining over time (10, 11).

**Post-MI heart failure in the community: implications for the heart failure epidemic**

There is limited information available on post-MI heart failure. The Framingham investigators (12) did not detect a temporal decline in post-MI heart failure among 546 patients with Q-wave MI. The authors reported diverging trends in the incidence of early heart failure versus late heart failure in secondary analyses, pointing towards a possible masking of a decline in late heart failure by increasing trends in early heart failure. However, this study did not include non-Q-wave MIs, which constitute a large proportion of MIs in the community. In addition, the low numbers of MI cases and heart failure events probably limit power to assess secular trends, thereby explaining the lack of an association between time and post-MI heart failure. Finally, as is the case for all cohort studies, the Framingham data are subject to the "healthy volunteer" effect, which may limit external validity (24).

Community surveillance studies are crucial for assessment of population trends in cardiovascular disease incidence and outcome. There are few such studies currently active in the United States (8, 9, 19, 25). Among these, only the Worcester Heart Attack Study and the Olmsted County Study include persons above age 74 years, the fastest-growing segment of the population and the segment that is also at greatest risk of heart failure. In an incidence cohort including both Q-wave and non-Q-wave MIs, the Worcester investigators reported a modest decline in in-hospital heart failure (13). However, no long-term data on the period after hospital discharge were included, and outpatient episodes of heart failure were not captured.

The present study from Olmsted County extended these data by measuring, in a population-based incidence cohort, a decline in post-MI heart failure over a longer follow-up period. Moreover, it included out-of-hospital events, which contributed 11 percent of the episodes of heart failure. These results indicate that while heart failure remains frequent after MI, its incidence is declining over time. This is consistent with the measured decline in the severity of MI (10, 11).

In this context, MI incidence trends recently measured in Olmsted County and elsewhere indicate that overall MI incidence rates are stable (8, 17). Even with stable incidence rates, an increasing number of MI cases would be expected because of the growth of the aged population, in turn resulting in more cases of heart failure. However, integration of the trends in MI incidence with the post-MI heart failure trends reported herein suggests that it is unlikely that MI is a major contributor to the heart failure epidemic.
With regard to risk factors for heart failure after MI, age, smoking, and hypertension were independently associated with post-MI heart failure. The well-known association between age and heart failure underscores the importance of including all age groups to fully capture the burden of heart failure, as the present study does. The independent association between hypertension and post-MI heart failure highlights the crucial importance of sustained hypertension control in addition to aggressive in-hospital management of acute MI.

**Role of reperfusion therapy**

During the past decade, major changes in the treatment of acute MI emerged. The results of randomized clinical trials (6, 7) led to the widespread use of reperfusion therapy (26), which in turn coincided with improved post-MI survival in the community (9, 27, 28). This led to the hypothesis that MI survivors were then at greater risk for subsequent cardiovascular events and that this could, in turn, increase the burden of cardiovascular disease. Our data do not support this hypothesis with regard to heart failure, since they indicate that the temporal decline in post-MI heart failure occurred concomitantly with the increase in the use of reperfusion therapy for acute MI. Indeed, when added to the model, reperfusion therapy was associated with a lower risk of heart failure and accounted for most of the temporal decline in post-MI heart failure.

**Potential limitations**

These results provide important insights into trends in morbidity after MI and into the relative contribution of MI to the heart failure epidemic. However, some potential limitations should be kept in mind. While the population of Olmsted County is becoming more diverse, the generalizability of these data to racial and ethnic groups that are not adequately represented in the county studied may be limited. While there was a small number of cases in which the Framingham criteria were not met, the 4 percent of the subjects who could not be classified with the Framingham criteria did not differ in any noticeable manner from those meeting the Framingham criteria. These subjects were initially treated as having no heart failure in the analyses. However, when the analyses were repeated with these subjects coded as having heart failure, the associations did not change. In particular, the effect of year, the exposure variable of interest in these analyses, remained identical (RR = 0.98, 95 percent CI: 0.96, 0.99; p = 0.008). Measurements of left ventricular function were not consistently obtained throughout the time period. Thus, the association between left ventricular function and heart failure and the relative contribution of systolic versus diastolic heart failure could not be examined.

Caution should be exerted while drawing inferences from concomitant changes in outcome and medical care as described herein. As in any observational study, the potential for unmeasured confounding limits the strength of causal inference for the association between reperfusion therapy and declining incidence of heart failure after MI. Indeed, nonmeasured trends in other aspects of medical care, including the impact of other drugs administered before hospital admission or after discharge, could play a major role. Characteristics of the population may also have contributed to the decline in post-MI heart failure. Nonetheless, an important inference from our findings is that the improvement in post-MI survival that occurred concomitantly with the introduction of new treatments is not associated with increased heart failure.

**Conclusion**

In this geographically defined MI incidence cohort, the occurrence of heart failure after MI declined over a time period coinciding with the increased use of reperfusion therapy. These trends suggest that improved survival post-MI is unlikely to be a major contributor to the heart failure epidemic in the population.

**ACKNOWLEDGMENTS**

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