Heart Failure After Acute Myocardial Infarction
A Lost Battle in the War on Heart Failure?

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Improvements in the treatment of acute myocardial infarction (AMI), especially use of reperfusion therapy, have led to larger numbers of survivors. In patients who would have survived despite reperfusion therapy, use of this treatment should lead to greater myocardial salvage and a reduced extent of ventricular injury in many. However, others who might not have survived previously may now do so, but with substantial left ventricular damage.1-2 The net consequence of these 2 opposing effects on the early and later risk of developing heart failure after AMI is uncertain. There has been concern, however, that an increasing pool of survivors of AMI might fuel an “epidemic” of heart failure.

Although we have a substantial amount of data on the rates of heart failure overall, rates of heart failure after AMI have been less well studied. Furthermore, the clinical trials, registries and epidemiological studies that have reported the rate of heart failure after AMI have used different case ascertainment and diagnostic criteria. Examination of 4 of the major trials of fibrinolysis (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries [GUSTO I], Global Use of Strategies to Open Occluded Coronary Arteries [GUSTO IIb and GUSTO III], and the Assessment of the Safety and Efficacy of a New Thrombolytic trial [ASSENT II]) in AMI revealed that heart failure was present at admission in 12.5% of the 61,041 participants, with 29.4% having evidence of heart failure at any time during admission.3 The rate was similar in the 15,078 patients enrolled in the Intravenous nPA for the Treatment of Infarcting Myocardium Early II study (INTIME II), where 23.1% of patients, with 24.5% being discharged on a diuretic.7 These clinical trials and registries, despite methodological differences, tend to agree that heart failure is a common occurrence after AMI.

An epidemiological study reported by Velagaleti et al8 in the current issue of Circulation reports that the rate of heart failure after AMI in the Framingham and Framingham Offspring cohorts between 1970 to 1999, was 24%. This finding appears to be in agreement with the registries and clinical trials. These new data also concur with a study from Olmsted County, Minn,9 where the 30-day rate of heart failure after AMI was also 24%. Only the Worcester Heart Attack Study (WHAS) seems to differ, reporting a much higher (40%) rate of heart failure reported after AMI.10 However, in the WHAS, 36% of AMIs were recurrent rather than incident events, as examined in the Framingham and Olmsted analyses, which probably biased the results, given that recurrent AMI is associated with a higher risk of heart failure than a first AMI.5

More importantly, these studies also differ in their description of trends in rates of heart failure after AMI. In Framingham, the rates appeared to increase during the period of study,8 whereas in the other surveys they appeared to fall.10,11 In the current Framingham report, the period examined (1970 to 1999) spanned an era of dramatically changing treatment of AMI and would appear to confirm the concern that a consequence of increased survival after AMI is an increase in the rate of development of heart failure.1 In the 676 participants with a Q-wave AMI, the age- and sex-adjusted 30-day rate of heart failure, as defined by Framingham heart failure criteria, was 11.8 per 100 in 1970 to 1979 but rose to 19.2 per 100 in 1990 to 1999. The adjusted rate ratio for heart failure at 30 days was 2.05 (95% confidence interval [CI] 1.25 to 3.36) and at 5 years was 1.74 (95% CI 1.07 to 2.84) for the period 1990 to 1999 versus 1970 to 1979. Over this period, adjusted rates of death free from heart failure after an AMI fell from 15 per 100 to 3.4 per 100. Although the present study may seem relatively small in comparison to the aforementioned registries and clinical trials, it is strengthened by the consistent definitions of both AMI and heart failure usage over time. However, an analysis of heart failure rates in the WHAS during a similar time frame (1975 to 1995) showed the opposite trend.10 After adjustment, the odds of developing heart failure after an AMI in 1993 to 1995 versus 1975 to 1978 was 0.81 (95% CI 0.69 to 0.96). How can we explain this apparent discrepancy?

In the Framingham analysis, age, sex, body mass index, systolic blood pressure, hypertension treatment, total choles-
terol, diabetes mellitus, and smoking were all adjusted for in the multivariable models. In the WHAS analysis, age, sex, comorbid conditions, AMI order, AMI type (Q wave versus non-Q wave), and AMI location were adjusted for. Other differences may have contributed to the discrepancy in trends. In the WHAS, different criteria were used to define heart failure and non-Q-wave AMIs were included. Whereas recurrent AMIs were included, which would be expected to increase rates; no increase in the proportion of these was seen over the study period. In a more recent analysis of the WHAS, which included data until 2001, the previous trend was reversed, with increasing rates of heart failure after AMI. The adjusted odds of heart failure in 2001 versus 1975 to 1978 was 1.37 (95% CI 1.15 to 1.64) after adjusting for age, sex, history of cardiovascular disease, AMI order, and AMI type. However, a statistically significant increase in the proportion of recurrent AMIs was noted in this analysis (33.3% in 1970 to 75 versus 36.7% in 2001, P<0.01), which could have contributed to the reversal in trend.

Perhaps a better comparison is with residents of Olmsted County. In that study of 1537 patients with an incident AMI and no previous history of heart failure, the Kaplan–Meier estimates of the rate of heart failure at 30 days were 27% in 1979 to 1984 and 23% by 1990 to 1994. These rose to 40% and 33%, respectively, at 5 years. However, after adjustment for age, hypertension, smoking, peak creatine kinase ratio, and comorbidity, a 2% annual reduction in the risk of heart failure was seen. Thus, the relative risk of heart failure after AMI in 1994 versus 1979 was 0.72 (95% CI 0.55 to 0.93). Again, the differing methods of adjustment in the multivariable models may explain the discrepancy. However, the investigators in Olmsted County used the Framingham criteria to define heart failure, and they also only examined first AMIs. It may be that the inclusion of non–Q-wave AMIs reduced the rate of heart failure over time, and although the proportion of non–Q-wave AMI is not stated, the severity of AMI, measured by peak creatinine kinase ratio, did fall, possibly explaining some of the difference.

How do the results of this current analysis relate to the overall epidemic of heart failure? Despite the rising rates of heart failure until the early 1990s, recent studies have suggested that rates are beginning to fall. In the mid 1990s we reported that there appeared to be the beginnings of a fall in the rates of hospitalization for heart failure (fall from 1994 to 1996), which was subsequently confirmed by others in Sweden (fall from 1993 to 2000) (though more uncertainty surrounds possible falls in the community incidence of heart failure). This trend may represent a relatively recent success in the war on heart failure where AMI is only one of the many causes of heart failure. Therefore, it may be that only more recent data on the incidence of heart failure after AMI will confirm these overall trends, because the studies mentioned above, WHAS, Olmsted County, and the current report from Framingham all examined this relationship using data from the midst of the epidemic, possibly giving rise to the conflicting results.

What might we expect to see in such future data? The epidemiology and treatment of AMI has not stood still. We have witnessed a change in the presentation of acute coronary syndromes recently with ST-elevation myocardial infarction (STEMI) rates falling and rates of other forms of acute coronary syndrome, non-STEMI and unstable angina pectoris, increasing. The Global Registry of Acute Coronary Events (GRACE) registry suggests that rates of heart failure are similar in each type of myocardial infarction, at around 18%, although the rate in those with unstable angina pectoris was only 10%. Primary percutaneous coronary intervention (PCI) has become the treatment of choice for AMI although there must be the same uncertainty about its net effect on the risk of heart failure as with thrombolytic therapy. Indeed, the Which Early ST-elevation Myocardial Infarction Therapy (WEST) trial reported that the rate of heart failure at 30 days was higher in those assigned to primary PCI (18%) than in those who received contemporary pharmacotherapy (15%) or fibrinolysis combined with early PCI (14.4%). However, in a recent propensity-matched analysis of routine databases from Alberta, Canada, the use of primary PCI as opposed to no PCI was associated with lower rates of heart failure in hospital (17% versus 24%) and at discharge (4% versus 7%) after AMI in 13 472 individuals. Indeed, the GRACE registry has reported that in this changing area of acute coronary syndromes, with increasing rates of primary PCI for STEMI and PCI after non-STEMI, and increasing use of evidence-based pharmacotherapies, rates of heart failure fell by 9% in those with a STEMI and by 6.9% in those with a non-STEMI. Even though these results are encouraging, they do highlight 2 important facts. Firstly, heart failure after myocardial injury is still a common occurrence and we will continue to see this complication despite the changes in the epidemiology of acute coronary syndromes. Secondly, despite the report of Velagaleti et al, it may be premature to declare the battle against heart failure after myocardial infarction as lost. Continued vigilance on this front and further robust studies will be required to monitor the impact of beneficial therapies on rates of heart failure after AMI if we are to win the war on heart failure.

Disclosures
None.

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