A Communitywide Perspective of Sex Differences and Temporal Trends in the Incidence and Survival Rates After Acute Myocardial Infarction and Out-of-Hospital Deaths Caused by Coronary Heart Disease

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Background. The purpose of the study was to examine overall differences and temporal trends therein between men and women regarding the incidence rates, in-hospital and long-term survival after initial acute myocardial infarction (AMI), and out-of-hospital deaths caused by coronary disease.

Methods and Results. This nonconcurrent prospective study was carried out in 16 teaching and community hospitals in Worcester, Mass., in six time periods between 1975 and 1988. A total of 3,148 patients hospitalized with validated initial AMI comprised the study sample. The age-adjusted incidence rates of initial AMI increased between 1975 and 1981 in the two sexes, with a marked decrease thereafter; these rates declined by 26% in men and by 22% in women between 1975 and 1988. The overall unadjusted in-hospital case–fatality rates after initial AMI were significantly higher in women (21.7%) than in men (12.7%). Age- and multivariable-adjusted in-hospital case–fatality rates, however, were not significantly different for men compared with women (multivariate-adjusted OR, 0.90; 95% CI, 0.78, 1.16). No clear trends in in-hospital case–fatality rates were observed in men or women over the periods under study. There were no significant sex differences in the age-adjusted long-term survival rates of discharged hospital survivors of AMI. The multivariate-adjusted risk of total mortality among discharged hospital survivors, however, was significantly increased in men (multivariate-adjusted OR, 1.20; 95% CI, 1.03, 1.39); neither of the sexes experienced an improvement over time in long-term prognosis. The incidence rates of out-of-hospital deaths caused by coronary disease declined by 60% in men and 69% in women between 1975 and 1988.

Conclusions. The results of this multihospital, community-based study suggest declines in the incidence rates of AMI and out-of-hospital deaths caused by coronary disease in men and women over the period under study (1975–1988). No significant sex differences in in-hospital survival were observed, whereas a poorer long-term survival experience after hospital discharge was observed for men compared with women after controlling for potentially confounding prognostic factors. (Circulation 1993;87:1947–1953)

Key Words • sex • acute myocardial infarction • survival

A number of studies1–5 have assessed differences in the in-hospital and long-term survival after acute myocardial infarction (AMI) in men compared with women. Several studies1–3 have reported a poorer in-hospital survival for women than men, whereas others have not.4–5 An inconsistent pattern also emerges concerning sex differences in long-term survival after AMI: some studies suggest a poorer posthospital discharge prognosis for women,1,2,6 whereas others have observed no difference5,7,8 or a worse long-term prognosis for men.4,9–11 Differences in these results may be due in part to discrepancies in the clinical and demographic characteristics of the various populations under study, inclusion of patients hospitalized at tertiary care referral centers versus those hospitalized at community hospitals, the control or lack thereof for potentially confounding factors affecting short and/or long-term survival after AMI, or to differences in the therapeutic management of men compared with women.12 Few studies have examined recent changes over time in either the in-hospital or long-term survival after AMI in men compared with women. Limited population-based data exist comparing differences in the incidence rates of AMI or out-of-hospital deaths attributed to coronary heart disease between men and women as well as changes over time in these outcomes according to sex.

The purpose of the present multihospital, community-based study is to examine changes over time (1975–
in the incidence rates, in-hospital and long-term survival after AMI with further characterization of overall differences in these end points, and temporal trends therein between men and women. In addition, changes over time (1975–1988) in out-of-hospital deaths attributed to coronary heart disease in men compared with women are examined.

Methods

The population under study consists of patients hospitalized with a primary or secondary discharge diagnosis of AMI (International Classification of Disease [ICD] code 410) in 16 Worcester, Mass., Standard Metropolitan Statistical Area (SMSA) hospitals during calendar years 1975, 1978, 1981, 1984, 1986, and 1988. In addition, a random sample of related diagnostic rubrics (ICD codes 411–414) in which AMI might have been diagnosed was carried out during each of the periods under study.13,14 The medical records of all patients with a discharge diagnosis of AMI from these hospitals were individually reviewed and validated according to preestablished diagnostic criteria that have been described previously.13–15 These criteria consist of a suggestive clinical history, serum enzyme level elevations, and serial ECG findings showing characteristic changes in the ST segment and/or Q waves. At least two of these three criteria needed to be satisfied for inclusion in the study. All autopsy-proven cases of AMI were included irrespective of the other criteria. In addition, patients had to be a resident of the Worcester SMSA, since the study is population based. Patients who were admitted for surgery and who developed AMI during surgery were not included in this study. For the six periods under study, the various clinical complications of AMI were assessed on the basis of information available from the clinical charts.16 Out-of-hospital deaths attributed to coronary heart disease were defined as those deaths occurring among noninstitutionalized adults (age, ≥25 years) in whom coronary disease was listed as the underlying cause of death on the death certificate. Individuals in whom malignant neoplasm, trauma, or accidents were listed on the death certificates as contributing causes of death as well as residents of nursing homes or chronic care facilities were excluded from further consideration.

Data Collection

The medical records of male and female residents of the Worcester SMSA who were hospitalized with validated AMI during the time periods under study were abstracted for demographic and clinical data including age, medical history (angina, diabetes, hypertension), complications during hospitalization (e.g., congestive heart failure, cardiogenic shock), AMI extent (Q wave or non–Q wave), location (anterior or inferior/posterior), and peak serum creatine kinase findings. Data concerning the use of various therapeutic approaches and surgical interventions during the acute hospitalization for AMI were also collected. Since one of the major objectives of this study was to identify new cases of AMI in order to calculate incidence rates, when the review of the hospital chart indicated that the present hospitalization was not the first for coronary heart disease, records of previous hospitalizations for coronary disease were reviewed where available. The approaches used to ascertain survival status after hospital discharge included a review of medical records for additional hospitalizations at participating area hospitals and a statewide search of death certificates for residents of the Worcester SMSA. We have previously used this combination of surveillance approaches to successfully follow up study patients on a long-term basis.13,14 For patients discharged from the hospital, follow-up was continued through the end of calendar year 1989. The maximum follow-up period varied from 1 to 14 years, and mortality from all causes of death was examined.

Data Analysis

Differences in the distribution of selected characteristics between men and women hospitalized for initial AMI were examined with the use of χ² tests of statistical significance for discrete variables and t tests for continuous variables. All tests of significance were two tailed. The short-term prognosis in each period was examined by calculating in-hospital case fatality rates according to sex. Age adjustment was carried out by the direct method using the age structure of the entire population at risk. The simultaneous effect of several potentially confounding variables that might influence in-hospital survival was accounted for by means of a multiple logistic regression model. A life-table approach was used to examine differences in all-cause mortality between men and women to include patients followed up for various lengths of time after hospital discharge.17 The log rank test was used to compare differences between the long-term survival curves of men and women discharged from the hospital after AMI. A proportional hazards regression approach was used to examine differences between the sexes in long-term survival after hospital discharge for AMI while controlling for various potentially confounding prognostic factors.18 Annual attack rates of AMI were calculated in the usual manner. Age-adjusted rates were computed by means of the direct method of standardization using the Worcester SMSA population census estimates in 1980. Population estimates between national census estimates in 1970, 1980, and 1990 were obtained by linear extrapolation within 5-year age groupings. The present report is based on 1,916 men and 1,232 women hospitalized with an initial validated AMI over the periods under study. Patients with prior myocardial infarction were excluded from the present investigation.

Results

Incidence Rates of Acute Myocardial Infarction

Both men (Figure 1) and women (Figure 2) showed an increased risk for the development of initial AMI with increasing age overall as well as during each year under study. Although men experienced higher age-specific incidence rates for initial AMI during each study year, sex differences in the risk of initial AMI declined with advancing age.

Differences over time in the age-specific incidence rates of initial AMI were seen between the sexes. Between 1975 and 1988, the age-specific incidence rates of initial AMI declined by 25.9% in men aged 25–54 years, 14.5% in those 55–64 years, 24.8% in those 65–74 years, 33.4% in those 75–84 years of age, and 53.7% in those ≥85 years of age. The age-specific incidence rates
of AMI in women declined by 0.6% in those 25–54 years of age, 29.1% in those 55–64 years, 23.8% in those 75–84 years, and 54.8% in those ≥85 years of age. There was a 14.6% increase in the incidence rate of initial AMI in women aged 65–74 years between 1975 and 1988.

Age-adjusted incidence rates of initial AMI increased for both men and women between 1975 and 1981, with a marked decrease thereafter. Between 1975 and 1988, the age-adjusted incidence rates of initial AMI declined by 25.5% (323 of 100,000, 1975; 240 of 100,000, 1988) in men and by 22.2% (176 of 100,000, 1975; 137 of 100,000, 1988) in women.

Baseline Characteristics of Men and Women Hospitalized With Acute Myocardial Infarction

Women compared with men were significantly older and included a significantly greater proportion of patients with prior angina, diabetes, and hypertension (Table 1). Women were significantly more likely to experience non-Q wave AMI, infarcts anterior in location, and smaller infarcts reflected by lower peak serum creatine kinase levels. Women were significantly more likely to develop congestive heart failure and cardiogenic shock during the acute hospitalization. In terms of therapeutic approaches used during the acute hospital phase, women were significantly more likely to receive digoxin and diuretics, whereas men were more likely to receive antiplatelet agents, β-blockers, lidocaine, other antiarrhythmics, nitrates, and thrombolytic agents. Men were also significantly more likely to undergo coronary angioplasty during the acute hospital admission compared with women.

In-Hospital Case–Fatality Rates for Acute Myocardial Infarction

The in-hospital case–fatality rates after AMI exhibited a curvilinear decline over the periods examined. In-hospital case–fatality rates declined from 18.7% in 1975 to 16.1% in 1978 and 1981, 13.1% in 1984, and subsequently increased to 16.3% in 1986 and to 16.8% in 1988. With the exception of 1988, women experienced a consistently poorer in-hospital survival compared with men after adjusting for differences in age (Figure 3). The crude in-hospital case–fatality rates were significantly increased in women (21.7%) compared with men (12.7%), with these differences narrowing after adjustment for age (17.9% of women dying, 15.2% of men dying). There was an inconsistent pattern observed in
crude and age-adjusted in-hospital case-fatality rates among men and women over the periods under study. Since men and women differed regarding a variety of factors that could affect in-hospital survival after AMI (Table 1), two multiple logistic regression analyses were carried out to examine differences in in-hospital survival for men and women while controlling for these factors. In the first of these analyses, only age was controlled for. The factors controlled for in the second multivariable analysis included age, study period, medical history, AMI location (anterior versus inferior/posterior), AMI type (Q wave versus non-Q wave), peak serum creatine kinase levels, occurrence of congestive heart failure and cardiogenic shock during the acute hospitalization, and use of various therapies and surgical interventions. The results of each of these analyses revealed no statistically significant differences in the risk of dying during the acute hospital phase for men compared with women, although in both analyses, men were observed to be at lower risk of dying. The age-adjusted odds ratio for dying during hospitalization for men compared with women was 0.85 (95% CI, 0.69, 1.05), whereas the multivariate-adjusted odds ratio was 0.90 (95% CI, 0.70, 1.16).

Long-term Survival After Hospital Discharge for Acute Myocardial Infarction

Analysis of the long-term survival patterns of patients discharged from hospitals in the Worcester metropolitan area between 1975 and 1988 failed to provide evidence for secular improvements in postdischarge prognosis after AMI.

In examining the long-term prognosis after AMI in women compared with men, women experienced significantly poorer crude unadjusted overall long-term survival rates ($p<0.05$). After adjustment for age, however, there were no significant differences seen in long-term survival for men or women after discharge from the hospital for AMI (Figure 4). No significant improvement over time in the long-term prognosis of discharged hospital survivors was observed in men or women.

Similar to the examination of baseline characteristics in hospitalized men compared with women (Table 1), female discharged hospital survivors of AMI were significantly older, included a greater proportion of those with a medical history of angina pectoris, diabetes, and hypertension, those with a non-Q wave anterior myocardial infarction, infarcts characterized by lower peak creatine kinase levels, and those who developed congestive heart failure during the acute hospitalization ($p<0.025$). Women discharged from the hospital after AMI were also significantly more likely to have been treated with digoxin and diuretics during the acute hospitalization but were significantly less likely to have received antplatelet agents, β-blockers, lidocaine, other antiarrhythmics, and thrombolytic agents ($p<0.05$).

Two proportional hazards regression analyses were carried out to examine the independent influence of sex on long-term prognosis after hospital discharge for AMI. In the first of these analyses, only age was adjusted for; the second multivariable analysis simultaneously controlled for age and factors that were significantly different between male and female discharged hospital survivors. Controlling for age alone resulted in men having a nonstatistically significant poorer long-term survival experience than women (adjusted OR, 1.10; 95% CI, 0.95, 1.26); after controlling for age and several additional prognostic factors, men experienced a significantly poorer long-term survival than women (adjusted OR, 1.20; 95% CI, 1.03, 1.39).

Out-of-Hospital Deaths Attributed to Coronary Heart Disease

There was a consistent and marked decline in the out-of-hospital death rates caused by coronary disease in both men and women over the 13-year study period (Figure 5). Among men, the incidence rates of out-of-hospital coronary deaths among noninstitutionalized adults declined by 60%, whereas a 69% decline was seen among women.

Discussion

The results of the present multihospital, population-based study suggest a decline over the period studied (1975–1988) in the age-adjusted incidence rates of initial AMI in both men and women, no statistically significant sex differences in in-hospital survival after controlling for other important prognostic factors, and an inconsistent pattern over time in in-hospital survival after AMI in women and in men. In addition, a significantly poorer long-term outlook was observed for men discharged from the hospital after AMI after adjusting for confounding prognostic factors, no improvement...
was noted over time in long-term survival for either men or women, and a significant decline in out-of-hospital deaths caused by coronary heart disease was seen in both men and women.

An encouraging finding from the present study was that despite an increase in the crude as well as age-adjusted incidence rates of initial AMI between 1975 and 1981 in men and women, there was a dramatic decline in these attack rates between 1981 and 1988. Despite the appropriate caution that needs to be exercised in interpreting data from various population-based studies that have examined changes over time in the incidence rates of AMI given potential differences in the socio-demographic characteristics of the populations under study, population health care-seeking patterns, and the fact that the diagnostic criteria for AMI may have differed in these studies, the present findings of declining incidence rates are in accord with studies carried out at the Kaiser Permanente Medical Care Program, in Pee Dee and Columbia, S.C., Rochester, Minn., St. Paul–Minneapolis, Minn., and among employees of DuPont. On the other hand, data from the National Hospital Discharge Survey, which uses information from patients discharged from short-term-stay nonfederal hospitals, showed an increase in both the number of patients hospitalized with a first-listed diagnosis of AMI and in the annual discharge rate of patients with this diagnosis between 1968 and 1986. Part of the increase in the latter study may be attributed to a coding decision to reclassify circulatory diagnoses involving AMI, thereby creating a possible artifact in the interpretation of temporal trends in these data; the National Hospital Discharge Survey findings are also based on nonvalidated discharge summaries of patients hospitalized with AMI, and no distinction is made between initial and recurrent cases. Although we did not collect data concerning accompanying changes in the population levels of the major coronary risk factors, national as well as more select population surveys have shown encouraging declines over the past several decades in cigarette smoking and serum cholesterol levels and increases in the population awareness and control of elevated blood pressure. Despite the appropriate caveats that must be borne in mind in extrapolating from these studies to the results of the present investigation, the observed declines in the incidence rates of AMI are most likely the result of favorable population changes in these as well as other less-established coronary risk factors and to a lesser degree because of improved diagnosis and therapy of chronic ischemic heart disease.

Numerous studies have shown the attack rates of AMI to be greater among men than women, with differences in the age-specific incidence rates of AMI declining with advancing age. For example, findings from the Framingham Heart Study suggest that whereas the absolute incidence rates of initial AMI were consistently greater among men than women, the risk of a first AMI was approximately six times greater among men compared with women 30–39 years of age, approximately four times greater for those 40–49 years, and approximately 2.5 times greater for those 50–59 years of age. The results of the present study are in agreement with these findings showing a greater incidence of age-adjusted as well as age-specific rates of initial AMI in men compared with women, with the observed sex differences narrowing with increasing age.

Concomitantly with encouraging declines in the age-adjusted incidence rates of initial AMI, the age-specific incidence rates also decreased over time in the two sexes, with larger declines seen among the elderly compared with the young. Two exceptions to these favorable trends were nonetheless observed among women: among those <55 years of age, there was essentially no change over time in the incidence rates of AMI, whereas there was a 15% increase in these rates for older women aged 65–74 years. Reasons for either the lack of change or the actual increase in these incidence rates among these subgroups of women remain unknown.

Similar to previous concerns expressed regarding the interpretation of secular trends in the incidence rates of AMI from studies carried out in different population settings, appropriate reservation needs to be exercised in the interpretation of data examining short-term case-fatality rates after AMI. Factors such as differing socio-demographic and clinical characteristics and sizes of the samples being compared, diagnostic criteria for AMI, and therapeutic interventions used make interpretation of findings across studies difficult. Nonetheless, studies carried out in male employees of the DuPont Company suffering AMI and in patients hospitalized with AMI in metropolitan Baltimore, Md, Minneapolis–St. Paul, Minn., Rochester, Minn., and in the Pee Dee area of South Carolina show an improvement over time in in-hospital survival after AMI, with the sole exception to these trends being the study of nonvalidated cases of AMI admitted to greater Boston hospitals. Temporal declines in in-hospital case-fatality rates after AMI for men and women have also been seen in data compiled from the National Hospital Discharge Survey. Although the results of the present study are in agreement with most studies that have examined temporal trends in in-hospital survival after AMI, increases in in-hospital mortality were nonetheless observed during the most recent two periods under study among men and women, and no clear trends in short-term mortality were seen in the two sexes over the periods under study. These findings provide further reinforcement for the application of those intervention strategies shown to be efficacious in improving short-term prognosis after AMI and in reducing the extent of acute myocardial necrosis.
The suggestive trends for a higher crude age-adjusted risk as well as multivariate-adjusted risk for dying during the in-hospital phase of AMI for women are consistent with the majority of published reports. Although there were differences in various baseline characteristics that might affect in-hospital prognosis in men and women as well as in the therapeutic and surgical management of men compared with women in the present study, control of these factors by regression analyses confirmed the poorer although statistically nonsignificant in-hospital prognosis for women. Reasons for the increased risk of dying during the hospital phase of AMI among women remain unknown but may be in part related to their older age at the time of onset of AMI (although this factor was statistically controlled for), more extensive underlying coronary atherosclerosis and accompanying comorbid chronic disease conditions (e.g., hypertension, diabetes) at the time of presentation, more extensive preexisting myocardial damage (e.g., prior angina), and clinical complications incurred during the acute event or to other comorbid factors. Recent findings from the Israeli SPRINT study have shown that not only is chronic angina more common among women in patients presenting with their first AMI but that preexisting angina was associated with an increased risk of in-hospital and postdischarge mortality.35 It is of interest to note that women were significantly less likely to be treated with certain potentially beneficial therapies including antiplatelet agents, β-blockers, thrombolytic agents, and coronary angioplasty. Lesser use of thrombolytic therapy in women may be related to their older age at the time of presentation for AMI, to the greater prevalence of contraindications to the use of these agents during the period under study, or to clinical trial protocols in use during the time of this study that excluded the elderly from the receipt of thrombolytic agents. Recent studies have also shown differences in the use of diagnostic and therapeutic procedures in men and women with coronary heart disease,36,37 with questions raised concerning disparities in clinical decision making in the treatment of men compared with women.38 In two recent publications from the Worcester Heart Attack Study, we have shown that after controlling for a variety of patient-related factors that could affect physician prescribing patterns, women were significantly more likely to receive diuretics during hospitalization for AMI, whereas men were significantly more likely to be treated with antiplatelet agents, lidocaine, and other antiarrhythmic agents.39 In examining sex differences in the receipt of a number of diagnostic and revascularization procedures for AMI, after controlling for other potentially confounding covariates that might affect rates of utilization, men were significantly more likely to undergo radionuclide studies, Holter monitoring, exercise treadmill testing, cardiac catheterization, and coronary angioplasty than women. On the other hand, women were significantly more likely to undergo echocardiography during hospitalization for AMI.40

Studies carried out in hospital survivors of AMI in Baltimore, Md.,31 Rochester, Minn.,32 and among male enrollees of the Health Insurance Plan of New York41 failed to demonstrate an improvement over time in the long-term prognosis of discharged hospital survivors of AMI. In concert with these findings, we previously failed to observe improvements over time in the post-discharge survival experience of patients with AMI hospitalized in greater Worcester hospitals between 1975 and 1984.14 The sole population-based study demonstrating an improvement in long-term survival of discharged hospital patients after AMI, the Minnesota Heart Survey, noted a 35% improvement in the 4-year survival rates for men discharged from Minnesota hospitals after a definite AMI in 1980 compared with those discharged in 1970 and a 27% improvement in long-term survival among women.42 In updating findings from the Minnesota Heart Survey, 3-year survival rates among discharged male hospital survivors significantly improved from 1970 to 1985, whereas no such change was seen among women studied in the 1970, 1980, and 1985 cohorts; most of the improvement in long-term survival occurred between 1970 and 1980, with little change thereafter.43 In the present study, neither sex experienced an improvement in long-term prognosis after AMI between 1975 and 1988.

The suggestive finding of a poorer long-term survival after hospital discharge for AMI in men compared with women after multivariate adjustment for additional factors related to long-term prognosis is in agreement with several studies44-51 but is in contrast to those of others that have either failed to find differences in the long-term prognosis after AMI in men compared with women or have found a worse long-term prognosis for women compared with men.1-3,5-8 It should be noted that no significant sex differences in either crude or age-adjusted long-term survival rates were seen in the present study. Because of the method of data collection, we were unable to examine differences in the long-term management of male or female AMI survivors.

Finally, the decline in out-of-hospital deaths caused by coronary disease, although rates of out-of-hospital mortality were higher among men than women during each of the six time periods under study, was striking and consistent in the two sexes. Despite the use of different criteria to define out-of-hospital deaths attributed to coronary heart disease, a number of studies examining changes over time in out-of-hospital death rates caused by coronary disease or of sudden cardiac deaths have shown consistent declines in the incidence rates of these events.21,22,43 Using routinely collected death certificate data from the National Center for Health Statistics from 40 US states, the age-adjusted out-of-hospital deaths plus emergency room deaths attributed to ischemic heart disease declined by between 15% and 20% in white and black men and women between 1980 and 1985.44

The present community-wide study, carried out in a population whose socio-demographic and socio-economic characteristics, with the exception of race, reflect those of the continental United States, demonstrates declines in the occurrence rates of confirmed AMI in the two sexes. In-hospital case–fatality rates remain increased for women compared with men. The application of current as well as newer therapeutic interventional strategies should have a positive impact on in-hospital and long-term survival after AMI in the two sexes. Encouragement of positive lifestyle changes should also be maintained over time.

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