Coronary Heart Disease Death and Sudden Cardiac Death: A 20-Year Population-based Study

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Trends in out-of-hospital coronary heart disease (CHD) death, a surrogate for sudden cardiac death (SCD), are important for understanding the decline in CHD mortality. Little is known about out-of-hospital CHD death without prior CHD diagnosis, the definition of unexpected SCD. The authors analyzed secular trends in CHD death and unexpected SCD over a 20-year period (1979–1998) to examine the association between prior CHD and SCD and to test the hypothesis that in-hospital deaths declined more than SCDs. The yearly decline in CHD mortality rates was 5.3% for in-hospital deaths and 1.8% for out-of-hospital deaths ($p = 0.001$). Among all SCDs, the proportion of unexpected SCD was 49%. Mortality rates for both unexpected SCD and SCD with prior CHD declined over time, but unexpected SCD declined at a slower rate than SCD with prior CHD ($p = 0.001$). The relative odds of prior CHD were higher among persons with SCD than among controls, but there was a modest decline in the magnitude of the association. Thus, during the past 20 years, the decline was greater for in-hospital CHD deaths than for SCDs. Since approximately half of the SCDs were unexpected and rates of these deaths declined less over time than rates of SCD with prior CHD, primary prevention is becoming increasingly more important in sustaining the decline in CHD mortality.

coronary disease; death, sudden, cardiac; mortality

Abbreviations: CHD, coronary heart disease; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; SCD, sudden cardiac death.

Editor’s note: An invited commentary on this article appears on page 771.

While age-adjusted mortality due to coronary heart disease (CHD) has declined during the past three decades, determinants of the decline have not been fully elucidated, which hinders prevention. Recent US data indicate little change in the incidence of hospitalized myocardial infarction, in contrast to the larger declines in CHD mortality (1, 2), which suggests a greater contribution of secondary prevention to the mortality decline as opposed to primary prevention. Conversely, data from the MONICA Project underscored
that changes in CHD attack rates were the major determinant of the decline (3, 4). These diverging findings call for further analysis of the relative contribution of secondary prevention versus declining incidence to the CHD mortality decline with inclusion of all age groups, since neither of the above studies included persons above age 74 years, the fastest-growing segment of the population (1–4). The study of trends in the locations of CHD deaths can provide important insight into the determinants of the decline, since in-hospital CHD deaths relate mainly to secondary prevention, whereas out-of-hospital CHD death, often used as a surrogate for sudden cardiac death (SCD), is traditionally associated with primary prevention.

However, as data from the Framingham Study indicated, a sizable proportion of SCD occurs in individuals with overt CHD, which markedly increases the risk of SCD in comparison with persons without CHD (5, 6). Thus, linking all SCD to primary prevention is overly simplistic, because primary prevention relates chiefly to SCD not preceded by overt CHD, that is, unexpected SCD.

Thus, a more complete understanding of SCD trends requires knowledge of CHD diagnosis before death. This in turn allows for better delineation of the role of primary prevention, conceptualized as prevention related to unexpected SCD, versus the role of secondary prevention of chronic CHD, which is related to SCD among persons with overt CHD. Little is known about secular trends in the proportion of SCDs, which are truly unexpected during a time period when primary and secondary prevention efforts are being intensified; yet this information has important potential implications for understanding of the CHD mortality decline and for prevention.

The Rochester Epidemiology Project provides a unique infrastructure for addressing these issues through surveillance of the population of Olmsted County, Minnesota. In particular, the availability of extensive medical record data optimizes the ascertainment of prior overt CHD. Furthermore, recently published Olmsted County data validate the use of out-of-hospital CHD death as a surrogate measure for SCD (7).

Thus, the present study was undertaken to examine trends in the locations of CHD deaths in the geographically defined population of Olmsted County, Minnesota, between 1979 and 1998 and trends in out-of-hospital CHD death according to the presence or absence of prior overt CHD. The goals of these analyses were to test the hypothesis that in-hospital deaths declined more over time than SCD and to examine the effect of time on the association between prior CHD and SCD. Because previously reported CHD trends in Olmsted County differed by age and sex, age- and sex-specific analysis were planned a priori (8, 9).

MATERIALS AND METHODS

Study setting

Population-based research is possible in Olmsted County 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. All medical care providers, including the Mayo Medical Center and the Olmsted Medical Group and its affiliated hospital, Olmsted Community Hospital, employ a unit medical record system. Thus, detailed information on all inpatient, outpatient, and emergency department visits and all laboratory results, pathology reports, correspondence, and records of physician visits to nursing homes or private homes are kept in one place. Since the early 1960s, extensive indices based on clinical or histologic diagnosis, surgical procedures, and billing data have also been kept for all providers of health care under the auspices of the Rochester Epidemiology Project. This allows linkage of information from essentially all sources of health care available to and used by the residents of Olmsted County.

Enumeration of deaths

We searched death certificate data obtained from the Minnesota Department of Health to identify individuals aged 25 years or older who were listed as residents of Olmsted County at the time of death. Information on date of birth, date of death, age, sex, underlying cause of death, and site of death was collected. The International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), was used to classify the deaths during the entire study period. The underlying cause of death was assigned by a state nosologist.

Since 1968, all death certificates issued in Minnesota have described the site of death as coded by the Minnesota Department of Health. Out-of-hospital deaths were defined as those coded as occurring outside of acute-care or long-term-care hospitals, including deaths occurring in emergency departments, private homes, public places, nursing or boarding-care homes, and infirmaries, as well as deaths among persons declared dead on arrival at a hospital. In-hospital deaths were those coded as occurring in acute-care or long-term-care hospitals.

The underlying cause of death was classified using ICD-9-CM codes, based on the algorithm used by the National Center for Health Statistics (10). For this study, CHD deaths included code 410, acute myocardial infarction; code 411, other acute or subacute coronary artery heart disease; code 412, old myocardial infarction; code 413, angina; and code 414, other forms of chronic ischemic heart disease.

This choice of codes was based on a recently reported validation study indicating that in Olmsted County, a death certificate diagnosis of CHD (defined as an underlying cause of death with ICD-9-CM codes 410–414) among out-of-hospital decedents is a correct surrogate for true SCD, defined as out-of-hospital physician-validated CHD death occurring less than 24 hours between symptom onset and death (7).

Prior overt CHD diagnosis

To examine the association between prior overt CHD diagnosis and SCD, we determined the presence or absence
of an antemortem diagnosis of CHD from the medical record using the Rochester Epidemiology Project index of diagnoses. All codes pertaining to angina pectoris, coronary disease, coronary atherosclerosis, myocardial infarction, and all relevant synonyms were used. Prior overt CHD diagnoses were assigned to all cases of SCD, and four population-based controls per SCD case were identified through an enumeration of the Olmsted County population made available through the Rochester Epidemiology Project. Control subjects were matched to the cases on sex, length of follow-up, date of birth within 1 year of the index case, and registration in the same year as the case. This matching scheme provided control subjects who were similar to cases in terms of age, sex, and duration of medical record in the community. Controls had similar opportunities for medical diagnosis as the cases and were also assigned prior overt CHD diagnoses using criteria identical to those used in controls.

Statistical analyses

**In- and out-of-hospital CHD mortality rates.** Age-, sex-, and year-specific rates of myocardial infarction incidence were calculated. The counts of out-of-hospital and in-hospital CHD deaths were used as the numerators; the denominators were the Olmsted County population as determined by census data for the years 1970, 1980, and 1990, with linear interpolation for the intercensal years (11) and extrapolation after 1990. The rates were directly adjusted to the age distribution of the 2000 US population. Standard errors and 95 percent confidence intervals around the point estimates were calculated on the basis of the Poisson error distribution.

Poisson regression models were used to assess trends in heart disease mortality rates. Age- and sex-specific counts were used as the unit of observation. We examined mortality trends according to location of death by including location of death in the Poisson regression model. Other variables in the model included age of the decedent, sex, and calendar year of death. Midpoints of 10-year age groups were used as the values for age in the regression model. Age and calendar year were entered as continuous variables, with a linear and a quadratic component being tested for each. Comparison of time trends by location of death, across age groups, and between sexes was accomplished by including the two-way interaction terms year × location, year × age, and year × sex. Estimates of percentage declines, based on model estimates using all data from the study period, are reported.

**Prior overt CHD diagnosis and SCD.** The proportion of unexpected SCD among all decedents experiencing SCD was determined. The Mantel-Haenszel test for trend was used to examine how this proportion changed over time. Logistic regression was used to examine the association between the proportion of unexpected SCD and time while adjusting for age and sex. Testing for interaction between year and age or sex was conducted.

For the matched case-control study, conditional logistic regression was performed. The dependent variable was SCD, and antemortem heart disease diagnosis was the predictor variable of interest. To test whether the odds ratio for antemortem heart disease diagnosis changed over time, between sexes, or by age group, we included interaction terms for these variables and prior diagnosis of CHD. Calendar year was modeled using year quartiles, and age was dichotomized into less than 75 years and 75 years or greater.

Incidence rates of unexpected SCD and SCD with prior diagnosis of CHD were generated through the following approach. Using the controls, we calculated the percentage with prior diagnosis of CHD for each year within several age groups (ages 25–64, 65–74, 75–84, and ≥85 years), and we applied these percentages to the Olmsted County population to estimate the proportion of the population with a prior diagnosis of CHD. We calculated crude incidence rates of unexpected SCD and SCD with prior diagnosis of CHD using the estimated populations of persons without prior diagnosis of CHD and with prior diagnosis of CHD, respectively, in the denominator. Rates were directly adjusted to the age distribution of the 2000 US population.

**RESULTS**

**Time trends in SCD and in-hospital mortality**

During the study period, 2,924 CHD deaths occurred, and 1,795 (61 percent) occurred outside of a hospital, thus meeting validation criteria for this analysis of SCD (7).

Of the total number of CHD deaths, 1,353 (46 percent) occurred in women and 1,833 (63 percent) in persons aged 75 years or older. The time trends in in-hospital and out-of-hospital CHD mortality rates, adjusted to the age distribution of the 2000 US population, are shown by sex in figure 1. Both in-hospital and out-of-hospital CHD mortality rates declined during the study period. However, the Poisson regression models indicated that the time trends in age-adjusted CHD mortality differed according to the location of death (for the location × year interaction term, p = 0.0001). Compared with the reference year, 1979, the relative risk of in-hospital CHD death in 1998 was 0.36 (95 percent confidence interval (CI): 0.30, 0.43), and for out-of-hospital CHD death it was 0.71 (95 percent CI: 0.62, 0.82) (table 1). This equates to a yearly mortality decline of 5.3 percent for in-hospital deaths and 1.8 percent for out-of-hospital deaths. Because of the greater decline in in-hospital CHD mortality than in out-of-hospital CHD mortality, the relative risk of out-of-hospital mortality compared with in-hospital mortality increased from 1.13 (95 percent CI: 1.00, 1.29) in 1979 to 2.22 (95 percent CI: 1.93, 2.56) in 1998.

Both in-hospital and out-of-hospital CHD mortality rates were lower for women than for men (p = 0.0001). Sex did not modify the effect of location of death on the CHD mortality decline (for the time × sex × location interaction term, p = 0.33).

**Effect of age**

The Poisson regression models indicated that the decline in CHD mortality was less pronounced among older persons in both out-of-hospital and in-hospital settings. Table 1 illustrates the effect of age and location of death with some sample model-based calculations of relative risk of CHD death. Mortality rates for the respective age groups in either
location in 1979 are the reference categories and thus have a relative risk of 1. In 1998, the relative risk of in-hospital CHD death in a 60-year-old person was 0.23 (95 percent CI: 0.18, 0.30), corresponding to a 77 percent decrease in the risk of in-hospital CHD mortality during the study period. In an 80-year-old person, conversely, the relative risk of in-hospital CHD death was 0.37 (95 percent CI: 0.31, 0.46), indicating a 63 percent reduction in in-hospital mortality between 1979 and 1998. For out-of-hospital locations, a similar pattern of lesser decline among older persons was noted. Indeed, 60-year-olds experienced a 53 percent (relative risk = 0.47, 95 percent CI: 0.38, 0.60) decline in out-of-hospital CHD death over the study period versus a lesser 24 percent reduction in the risk of out-of-hospital CHD death over the study period among 80-year-olds (relative risk = 0.76, 95 percent CI: 0.65, 0.89). No interaction between sex and location of death or between sex and year was detected.

**Antemortem CHD and SCD**

Association between SCD and antemortem CHD. Table 2 shows the results of the matched case-control analysis and the odds ratios for antemortem diagnosis of CHD among sudden cardiac decedents versus controls by sex, age, and year group. There was a strong positive association between antemortem diagnosis of CHD and SCD. Compared with the age- and sex-matched controls, the odds of carrying an antemortem diagnosis of CHD among those experiencing SCD was 3.71 (95 percent CI: 2.84, 4.86) for younger women and 2.14 (95 percent CI: 1.76, 2.60) for older men. Relative to their respective controls, both younger men and women with SCD had higher odds of carrying an antemortem diagnosis of CHD than the older decedents. The strength of the association between antemortem diagnosis of CHD and SCD changed marginally during the 20-year period, suggesting a decrease over time in the relative odds of prior CHD among persons experiencing SCD as compared with controls (for the year × prior CHD diagnosis interaction term, \( p = 0.09 \)).

**Proportion of unexpected SCDs.** For all sudden cardiac decedents, the time period covered in the medical record prior to the index death was 42 ± 20 years. Overall, the proportion of unexpected SCDs among all sudden cardiac decedents was 49 percent. Figure 2 shows the proportion of unexpected SCD by year, age, and sex group; it ranged from 66 percent among younger (<75 years) women to 42 percent among older (≥75 years) men.

### TABLE 1. Relative risk of coronary heart disease death in Olmsted County, Minnesota, by age and location of death, 1979–1998

<table>
<thead>
<tr>
<th></th>
<th>RR†</th>
<th>95% CI†</th>
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<tr>
<td><strong>In-hospital death</strong></td>
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<tr>
<td>All ages</td>
<td>0.36</td>
<td>0.30, 0.43</td>
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<tr>
<td>Age 60 years</td>
<td>0.23</td>
<td>0.18, 0.30</td>
</tr>
<tr>
<td>Age 80 years</td>
<td>0.37</td>
<td>0.31, 0.46</td>
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<tr>
<td><strong>Out-of-hospital death</strong></td>
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<tr>
<td>Age 80 years</td>
<td>0.76</td>
<td>0.65, 0.89</td>
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* 1979 was the reference year for each category.
† RR, relative risk; CI, confidence interval.
The proportion of unexpected SCD was higher among persons younger than age 75 years than among those aged 75 years or more (p = 0.0001). For younger age groups, men had a lower prevalence of unexpected SCD than women did (p = 0.02). This sex difference was not observed among older persons (p = 0.47 for persons aged ≥75 years). Over the 20-year period, the proportion of unexpected SCD did not change (p for trend = 0.14). In logistic regression analysis, after adjustment for age and sex, the association between time and prior CHD was modest (p = 0.11). The odds ratios and 95 percent confidence intervals for the association between unexpected SCD and year suggested a marginal increase in the strength of the association between time and unexpected SCD. With 1979–1983 as the reference quartile, the odds ratios were 0.87 (95 percent CI: 0.66, 1.14) for 1984–1988, 0.96 (95 percent CI: 0.73, 1.27) for 1989–1993, and 1.19 (95 percent CI: 0.91, 1.57) for 1994–1998.

**DISCUSSION**

These results indicate that in Olmsted County, during the past 20 years, in-hospital and out-of-hospital CHD mortality declined significantly; however, the magnitude of the decline was significantly greater for in-hospital CHD deaths, and there were marked disparities in the magnitude of the decline according to age. Indeed, the yearly decline in in-hospital mortality was approximately three times that of out-of-hospital mortality, such that, in 1998, residents of...
Olmsted County were more than twice as likely to die outside of a hospital than in a hospital. The relative odds of prior CHD were higher among persons experiencing SCD than among their respective controls, but the magnitude of the association decreased marginally during the 20-year period, which suggests a modest decline over time in the excess risk of prior CHD among sudden cardiac decedents.

Among sudden cardiac decedents, approximately half of the SCDs were truly unexpected, since they were not preceded by a CHD diagnosis, while the other half occurred among persons with overt CHD prior to death. The proportion of unexpected SCDs increased marginally during the 20-year time period, and while both unexpected SCD and SCD with prior CHD declined over time, the magnitude of the decline was less for unexpected SCD than for SCD with prior CHD.

**Trends in out-of-hospital CHD deaths**

Previous reports provided data covering the years 1987–1994 and indicated a larger decline in in-hospital deaths than in out-of-hospital deaths (1, 2). In particular, data from the Atherosclerosis Risk in Communities Study pertaining to the years 1987–1994 and to persons aged 35–74 years indicated 5.3 percent and 3.6 percent per year declines in in-hospital and out-of-hospital CHD deaths, respectively (2). The data presented herein extend these findings by providing information on more recent trends and among all age groups. The lesser declines in both in-hospital and out-of-hospital mortality in the elderly indicate that, during the past two decades, the burden of CHD has shifted towards older age groups (8, 12). Since most of the currently active community surveillance studies do not include persons older than 74 years of age, they cannot by design completely characterize the burden of CHD (2, 13–15). While delaying CHD deaths towards the elderly should be justifiably perceived as an accomplishment, understanding this trend has important implications for prevention.

In Olmsted County, as in the Atherosclerosis Risk in Communities Study, the decline in in-hospital deaths was greater than the decline in out-of-hospital deaths. However, in Olmsted County, the difference in the magnitude of the decline according to location of death was large and highly statistically significant, with the decline in in-hospital deaths markedly exceeding that of out-of-hospital CHD deaths or SCD. In addition, marked differences according to age were noted, with a lesser decline in the risk of SCD among older persons as compared with younger persons. Similar trends in age differences in the decline in in-hospital CHD deaths were noted, although they were not as large as those for SCD. The marked discrepancy in the magnitude of the decline according to the location of death leads to a gradual shift of CHD mortality to the out-of-hospital setting. While the reduction in length of hospital stay for myocardial infarction in particular may contribute to these trends, they underscore the importance of focusing on out-of-hospital CHD deaths to define prevention measures at the population level. However, direction of prevention efforts requires further delineation of the population of persons experiencing SCD according to the presence or absence of prior CHD.

**SCD and antemortem diagnosis of CHD**

Few data are available on the prior diagnosis of CHD among persons suffering SCD at an out-of-hospital location (6, 16, 17). Data from the Framingham Study published more than 20 years ago indicated that 50 percent of SCDs in men and 64 percent of SCDs in women occurred among persons without evidence of prior CHD and thus were unexpected (16, 17). The present study indicates that approximately half of the SCDs occurring in Olmsted County during the subsequent 20-year time period were unexpected in both men and women, and it extends the Framingham findings by indicating that this proportion remained largely constant over two decades marked by the intensification of both primary and secondary prevention efforts. Since unexpected SCD can be conceptualized as reflecting primary prevention, these data underscore the increasing importance of primary prevention in sustaining the decline in CHD mortality.

It is noteworthy that these data are consistent with recent data from the Minnesota Heart Survey, the Atherosclerosis Risk in Communities Study, and Olmsted County indicating modest changes at best in the incidence of hospitalized myocardial infarction over similar time periods. While myocardial infarction incidence data do not account for prior CHD status and therefore may be a less accurate indicator of true primary prevention than unexpected incident cardiac death, myocardial infarction incidence trends are congruent with the findings presented herein and in part convey analogous implications with regard to primary prevention (1, 2, 9, 18). In this regard, recent trends in the prevalence of obesity (19) and diabetes mellitus (20) underscore the need to reduce the population burden of risk factors. Recent data from the Second National Health and Nutrition Examination Survey and prospectively collected cross-sectional data from a population-based Olmsted County sample indicate adverse trends in blood pressure awareness, treatment, and control (21, 22), also conveying the same necessity. Renewed risk factor modification efforts can be expected to have an impact on both unexpected SCD and expected SCD.

**Limitations**

Although these results provide important insights into the determinants of the decline in heart disease mortality, some limitations should be kept in mind.

The use of a death certificate diagnosis of CHD in an out-of-hospital location for the determination of SCD in Olmsted County has been validated and reported (7). The accuracy of death certificate diagnosis of CHD for in-hospital decedents was not determined in the present study; however, other studies have indicated that it is less subject to misclassification than out-of-hospital death because of the availability of the medical record (23, 24).

However, a number of out-of-hospital deaths could be misclassified and represent unrecognized fatal myocardial infarction. The occurrence of fatal unrecognized myocardial infarction, if it were changing over time, could have an impact on the measured trends. To this end, information on the occurrence of unrecognized myocardial infarction is limited. Its identification requires a prospective cohort study.
design with a yearly electrocardiogram, such as the design of the Framingham Study (25) or the Cardiovascular Health Study (26, 27). On the basis of these studies, approximately 25 percent of nonfatal myocardial infarctions are not recognized clinically. Importantly, this proportion appears constant over time, such that the underascertainment of nonfatal unrecognized myocardial infarction does not differ by time. Extrapolating these observations to fatal unrecognized myocardial infarction, one can surmise that these unrecognized myocardial infarctions are unlikely to confound the trends measured herein.

Throughout the 20 years of the study, increased documentation requirements permeated clinical practice, thus potentially subjecting the measurement of prior CHD to ascertainment bias. Furthermore, the increasing availability of more sensitive diagnostic tests would also tend to increase over time the labeling of patients with various symptoms as having CHD. These two temporal trends would be expected to increase the frequency of the diagnosis of prior CHD, and it is possible that the decline over time in the frequency of prior CHD among SCD cases is underestimated. In this case, however, the preventive inference of our data may be greater, such that the implications for primary prevention would be even stronger.

While no population can be representative of the nation as a whole, as is illustrated by the regional variations in heart disease rates observed in the United States (28), the racial and ethnic composition of Olmsted County limits generalization of these data to ethnic groups not adequately represented in the population studied. Differences in SCD according to race and ethnicity have been reported (29). Conversely, unique strengths of the Olmsted County population that are directly relevant to the study hypothesis lie in the ability to measure trends in CHD death and their association with prior diagnosis of CHD in a population that is optimally poised for ascertainment of prior CHD diagnosis because of the availability of longitudinal data spanning more than 40 years prior to death.

**Conclusion**

In Olmsted County, during the past 20 years, both in-hospital and out-of-hospital CHD mortality declined significantly; however, the magnitude of the decline was significantly greater for in-hospital CHD deaths and for younger persons. The relative odds of prior CHD were higher among persons experiencing SCD than among their respective controls, but the magnitude of the association decreased marginally during the 20-year period, which suggests a modest decline over time in the excess risk of prior CHD among sudden cardiac decedents. Since approximately half of the SCDs were unexpected and the incidence of these unexpected SCDs declined less over time than the incidence of SCD with prior CHD, primary prevention is becoming increasingly more important in sustaining the CHD mortality decline.

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