Characteristics and Baseline Clinical Predictors of Future Fatal Versus Nonfatal Coronary Heart Disease Events in Older Adults

The Cardiovascular Health Study

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Background—Although >80% of annual coronary heart disease (CHD) deaths occur in adults aged >65 years and the population is aging rapidly, CHD event fatality and its predictors in the elderly have not been well described.

Methods and Results—The first myocardial infarction (MI) or CHD death among the 5888 adults aged ≥65 years occurring during enrollment in the Cardiovascular Health Study during 1989–2001 was identified and adjudicated. Characteristics measured at examinations before the event were examined for associations with case fatality (death before hospitalization or hospital discharge) and for differences in predictors by demographics or clinical history. During a median follow-up of 8.2 years, 985 CHD events occurred, of which 30% were fatal. Case fatality decreased slightly over time, ranging from 28% to 30% per year in the early 1990s versus 23% by 2000–2001; with adjustment for age at MI and gender, there was a 6% lower odds of fatality with each successive year (odds ratio [OR], 0.94; 95% confidence interval [CI], 0.90 to 0.98). Case fatality was similar by race and gender but higher with age and prior CHD (MI, angina, or revascularization). When considered alone, many subclinical disease measures, such as common carotid intima-media thickness, ankle-arm index, left ventricular mass by ECG, and a major ECG abnormality, and traditional risk factors, such as diabetes and hypertension, were associated with fatality. In multivariable analysis, independent predictors of fatality were prior congestive heart failure (OR, 3.20; 95% CI, 2.32 to 4.41), prior CHD rather than only history of MI (OR, 2.51; 95% CI, 1.84 to 3.43), diabetes (OR, 1.66; 95% CI, 1.10 to 2.31), and age (OR, 1.21 per 5 years; 95% CI, 1.07 to 1.37), adjusted for gender and each other. Prior congestive heart failure, regardless of left ventricular systolic function, age, gender, or prior CHD, conferred a ≥3-fold increased risk of fatality in almost all subgroups.

Conclusions—Among community-dwelling older adults, CHD case fatality remains substantial, with easily identifiable risk factors that may be different from those that predict incident disease. In the elderly in whom the risk/benefit of therapies may be influenced by multiple competing comorbidities and care needs, risk stratification possibly may be improved further by focusing more aggressive care on specific patients, especially those with a history of congestive heart failure or prior CHD.

Key Words: aging ■ coronary disease ■ mortality ■ myocardial infarction ■ prognosis
specific insurance systems, or outcomes based on data gathered at the time of the event. Given the rapidly aging population and expected increased prevalence of CHD, further study on CHD case fatality and its predictors in the community-dwelling elderly is warranted to further improve prognostication and reduce mortality.

We therefore conducted a study using data gathered systematically and prospectively before CHD events to examine acute CHD mortality in a large random sample of community-dwelling elderly with the following objectives: (1) to describe acute CHD events, case fatality, and the characteristics of older adults with events; (2) to identify characteristics associated with acute CHD event fatality and identify the strongest independent predictors of CHD case fatality; and (3) to determine whether these characteristics differ by factors such as age, gender, race, or clinical history.

Methods

Study Setting and Participants

The Cardiovascular Health Study (CHS) is a population-based, longitudinal observational study designed to identify factors related to the onset and course of CHD and stroke in adults aged ≥65 years. Participants were randomly sampled from Medicare eligibility lists in 4 US communities in North Carolina, California, Maryland, and Pennsylvania. Sampled individuals and all household members aged ≥65 years able to give informed consent and expecting to remain in the area for 3 years were eligible. Only individuals who were institutionalized, wheelchair-bound in the home, under hospice care, or under active treatment for cancer were excluded. Recruitment of 5201 participants was completed in 1989–1990, with an additional 687 black subjects recruited by the same sampling methods in 1992–1993. These 5888 study participants (57.3% of those contacted eligible) were enrolled and followed up for CHD events through June 2001. Those who participated were more educated, younger, and more likely to be married than those who did not participate. Details of the design and recruitment experience have been described previously.

Data Collection

At baseline, all participants underwent a home interview by trained interviewers and an extensive examination at the field center clinic for physical examination and testing. Standardized questionnaires assessed CHD risk factors, symptoms, history, and medications. Self-reports of MI, angina, congestive heart failure (CHF), and stroke were confirmed and validated by review of medical records or any other apparent cause of death was found, consistent with standardized consensus guidelines. Participants classified as having prior CHD had a history of MI, angina, percutaneous coronary intervention (PCI), or coronary artery bypass graft (CABG) surgery before CHS enrollment. An MI was considered recurrent if the participant had a definite MI before CHS enrollment. Hypertension was classified as systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or current use of antihypertensives. Diabetes was classified as fasting blood glucose ≥126 mg/dL, and impaired fasting glucose was classified as glucose 110 to 125 mg/dL. Medication use reflected confirmed prescriptions except for aspirin, which included over-the-counter use >7 days in the prior 2 weeks. All characteristics were baseline visit data, except for major ECG abnormality, ECG left ventricular (LV) mass, and forced expiratory volume in 1 second, which were measured at the clinical visit before the event.

Statistical Analysis

After distribution normality was established, characteristics of those with CHD events were compared by age group (age ≥65 versus <65 years), gender (women versus men), race (blacks versus whites), CHD (prior versus no prior CHD), and fatality (fatal versus nonfatal) with the use of χ² tests for the equality of proportions and t tests for the equality of means. Multiple logistic regression models were used to estimate age- and sex-adjusted relative odds of fatality associated with the presence of each characteristic for categorical variables or for each increase in interquartile range for continuous variables. Tests for differing effects over time and among demographic and clinical subgroups were done with models that included an interaction term. Results are presented separately in cases in which significant interactions were found. Independent associations with fatality were estimated with the use of logistic regression with stepwise selection, starting with an empty model with age and sex forced to be retained and all other characteristics competing for entry being added or deleted per step if significant at P<0.01. Models containing the selected variables were then run and validated in the larger data set, in which all participants with available data were included. All analyses were also run separately for out-of-hospital versus in-hospital deaths and are presented separately if a difference was found. STATA 7.0 (Stata Corporation, College Station, Tex) and SAS version 8 (SAS Institute Inc, Cary, NC) were used for data analysis. All probability values represent 2-sided tests with emphasis placed on results with probability values <0.01 for statistical significance given the large number of comparisons.

The authors had full access to the data and take full responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results

CHD Events

Among the 5888 participants, during a median follow-up time of 8.2 years, 985 MIs and CHD deaths occurred at an average of 5.3 years after CHS entry, with a CHD event rate of 19.2 events per 1000 person-years (Figure 1). The majority of events were incident MIs. There were 126 out-of-hospital CHD deaths.

Classification of CHD Events and Variables

The primary outcome in this study was acute CHD event case fatality. All cardiovascular events were identified according to CHS surveillance and ascertainment methods previously described, in which all events were adjudicated by a physician committee using standard protocol and algorithms incorporating cardiac enzymes, symptoms, and ECG changes. For this study, CHD events included the first CHD death or hospitalized MI occurring for each participant after CHS enrollment; events were considered fatal if the participant died before or during the hospitalization for the event. Silent MIs discovered at a subsequent CHS visit were excluded because the precise date the MI occurred could not be determined. Out-of-hospital fatal CHD deaths were considered those that did not meet criteria for MI, but the participant had chest pain within 72 hours of death or history of chronic ischemic heart disease and no other obvious cause of death was found, consistent with standardized consensus guidelines.
Characteristics of Participants With CHD Events

The age of the participants at the time of their CHD event ranged from 66 to 103 years, with a mean of 79±6.1 years (Table 1). Women were older than men at the time of the event (79.6 versus 78.6 years; P=0.01), and therefore subsequent gender differences were examined stratified by age. Women had more traditional risk factors, and men had more evident subclinical disease. Those aged <80 years were more likely to have a history of CHF despite the same prevalence of abnormal LV systolic function, were less likely to smoke or have diabetes, had higher systolic but lower diastolic blood pressures, had lower body mass index (BMI), and had more evident subclinical disease by most measures compared with those aged ≥80 years (all P<0.01). A larger proportion of blacks with events were women compared with whites (54% versus 40%; P=0.003). Blacks were also more hypertensive, had higher BMI, and had more evidence of peripheral vascular disease (all P<0.01). Of those with prior CHD, 46% met those criteria by having had a prior MI, and the other 54% had prior CHD due to a history of angiography or revascularization by PCI or CABG. Those with prior CHD were more likely to have hypertension but had lower blood pressures than those without a history of CHD. They were also more likely to have prior CHF, abnormal LV systolic function, low HDL cholesterol, and more evident subclinical disease by every measure (all P<0.01). Comparisons of characteristics by prior MI as opposed to prior CHD yielded similar results.

Case Fatality

Of the 985 events, 30% (298) were fatal before hospitalization or hospital discharge. An additional 21 deaths occurred between hospital discharge and 28 days after the event. Over time, case fatality ranged from 28% to 30% of events per year in the early 1990s to 23% by 2000–2001 (Table 2). There was no significant difference over time by χ² testing or in unadjusted logistic regression models. However, with adjustment for age at MI and gender, there was a 6% lower odds of fatality with each successive year (odds ratio [OR], 0.94; 95% confidence interval [CI], 0.90 to 0.98) and a 25% lower odds of fatality with each successive 4-year time period (OR, 0.75; 95% CI, 0.62 to 0.91). The most common cause of death was arrhythmia (58%), followed by CHF in 23%.

There was no difference in case fatality by gender or race, but case fatality was higher among those aged ≥80 years compared with those aged <80 years in women and among those with prior disease (MI, CHD, CHF) and many other comorbidities. Of the 797 hospitalized MIs, case fatality was 13.4% (45/335) among women and 14.1% (65/462) among men, and more of the recurrent MIs were fatal than incident MIs (21% [33/156] versus 12% [77/641]; P=0.003). Of the 298 fatal events, 42% (126) were out-of-hospital deaths. There were more out-of-hospital deaths among those with prior CHD (48% versus 29%; P=0.001), with no difference in out-of-hospital deaths by age, gender, or race.

Characteristics Related to Case Fatality

When participants with fatal versus nonfatal events were compared, those with fatal events were older; were more likely to have a history of CHD, MI, CHF, diabetes, and hypertension; and had more evident subclinical disease by most measures compared with those with nonfatal events (Table 3). In logistic regression models predicting fatality within each gender, increased age was a predictor of case fatality among women. No association was seen among men, but the gender interaction term approached but did not reach statistical significance by the criterion of P<0.01. Prior MI, CHD, and CHF were associated with a 2.5- to >4-fold increased risk, and diabetes and hypertension were associated with an almost 2-fold increased risk of fatality among the entire group adjusted for age and sex. Many subclinical disease measures, referring to evidence of atherosclerosis by testing such as common carotid intima-media thickness, were also associated with an increased risk of fatality.

Interaction testing to identify whether there were any differences in associations by subgroup showed no differences in characteristics associated with case fatality that were different by race or prior CHD, and analyses by prior MI as opposed to prior CHD yielded similar results. The risk and interaction for current smoking in blacks (OR, 3.3; 95% CI, 1.1 to 9.7) approached but did not meet our criteria of statistical significance (OR and interaction probability values 0.03), with no association among whites. The only risk that appeared to be different by age group was LV mass associated with increased risk of fatality only in those aged <80 years (OR, 1.6 per 47 g; 95% CI, 1.2 to 2.1; interaction P=0.007), but this was no longer apparent with adjustment for prior CHD. The only risk that appeared to be different by gender was systolic blood pressure, associated with a 29% lower risk of fatality among men for each increase of 30 mm Hg in measure-
ment, even with adjustment for antihypertensive medication. This was not found in women, and the gender interaction term was significant ($P \leq 0.01$). Further investigation revealed that men with fatal events had lower blood pressures than men with nonfatal events (134 versus 139 mm Hg; $P \leq 0.005$); men with prior CHD had lower blood pressures than men without prior CHD (133 versus 141 mm Hg; $P \leq 0.0001$); and, with adjustment for prior CHD, higher systolic blood pressure was no longer associated with a lower risk of fatality.

Independent Predictors of Case Fatality

By stepwise age- and sex-adjusted multivariable analysis with all characteristics as candidates, the independent predictors of fatality were prior CHF, prior CHD, diabetes, and age, all adjusted for the other predictors (Figure 2). Age- and/or gender-adjusted stepwise models run separately within subgroups by gender, age, and prior CHD showed that a history of prior CHF was an independent predictor in all groups, conferring a 3- to 4-fold increased risk of case fatality among those with and without a history of prior CHD or prior CHF, even with adjustment for LV systolic function. In age- and gender-adjusted models stratified by LV systolic function, the independent predictors of case fatality among those with normal systolic function were age (OR, 1.21 per 5 years; 95% CI, 1.05 to 1.40), prior CHF (OR, 3.57; 95% CI, 2.39 to 5.32), and prior CHD (OR, 2.46; 95% CI, 1.70 to 3.54). Among those with abnormal systolic function, prior CHF was the independent predictor, associated with a 3-fold increased risk of fatality (OR, 2.98; 95% CI, 1.55 to 5.73). With stratification by prior MI, the predictors among those without a history of MI were age (OR, 1.22 per 5 years; 95% CI, 1.05 to 1.41), prior CHF (OR, 4.66; 95% CI, 3.17 to 6.86), and diabetes (OR, 1.82; 95% CI, 1.23 to 2.70). Among those with a history of MI, prior CHF again was the independent predictor, associated with a 2- to 3-fold increased risk of fatality among men and both age groups, but not among women. Female gender and diabetes were predictors of increased risk among those aged <80 years. Stepwise models within blacks only revealed no independent predictors. We did not observe any changes in the association between CHD event fatality

### TABLE 1. Baseline Characteristics of Participants With CHD Events, CHS 1989–2001

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All (n=985)</th>
<th>Women (n=210)</th>
<th>Men (n=332)</th>
<th>P</th>
<th>Women (n=196)</th>
<th>Men (n=247)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at MI, y</td>
<td>79.0</td>
<td>74.9</td>
<td>74.3</td>
<td>0.04</td>
<td>*</td>
<td>84.7</td>
<td>84.4</td>
</tr>
<tr>
<td>Race black</td>
<td>11.7%</td>
<td>17.6%</td>
<td>9.9%</td>
<td>0.009</td>
<td></td>
<td>12.8%</td>
<td>8.1%</td>
</tr>
<tr>
<td>Prior CHD</td>
<td>49.0%</td>
<td>41.4%</td>
<td>51.8%</td>
<td>0.02</td>
<td></td>
<td>49.0%</td>
<td>51.8%</td>
</tr>
<tr>
<td>Prior MI</td>
<td>22.5%</td>
<td>19.1%</td>
<td>28.0%</td>
<td>0.02</td>
<td></td>
<td>15.3%</td>
<td>23.9%</td>
</tr>
<tr>
<td>Prior CHF</td>
<td>26.2%</td>
<td>21.0%</td>
<td>22.3%</td>
<td>0.71</td>
<td>*</td>
<td>32.1%</td>
<td>31.2%</td>
</tr>
<tr>
<td>Prior stroke</td>
<td>14.8%</td>
<td>11.4%</td>
<td>14.2%</td>
<td>0.36</td>
<td></td>
<td>19.9%</td>
<td>14.6%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>25.2%</td>
<td>28.9%</td>
<td>29.9%</td>
<td>0.79</td>
<td>†</td>
<td>20.7%</td>
<td>19.4%</td>
</tr>
<tr>
<td>Current smoker</td>
<td>11.9%</td>
<td>17.6%</td>
<td>14.2%</td>
<td>0.28</td>
<td>†</td>
<td>8.7%</td>
<td>6.5%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>82.0%</td>
<td>76.7%</td>
<td>75.3%</td>
<td>0.72</td>
<td></td>
<td>86.7%</td>
<td>74.5%</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>140</td>
<td>141</td>
<td>136</td>
<td>0.004</td>
<td></td>
<td>145</td>
<td>139</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>71</td>
<td>70</td>
<td>73</td>
<td>0.03</td>
<td>†</td>
<td>69</td>
<td>69</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>209</td>
<td>229</td>
<td>200</td>
<td>0.0001</td>
<td></td>
<td>220</td>
<td>197</td>
</tr>
<tr>
<td>LDL cholesterol, mg/dL</td>
<td>131</td>
<td>144</td>
<td>126</td>
<td>0.0001</td>
<td></td>
<td>135</td>
<td>124</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dL</td>
<td>49</td>
<td>55.8</td>
<td>44.3</td>
<td>0.0001</td>
<td></td>
<td>55.4</td>
<td>46.4</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>26.8</td>
<td>27.5</td>
<td>27.2</td>
<td>0.43</td>
<td>†</td>
<td>26.6</td>
<td>26.0</td>
</tr>
<tr>
<td>Ankle-arm index &lt;0.9</td>
<td>24.3%</td>
<td>19.4%</td>
<td>18.7%</td>
<td>0.84</td>
<td>*</td>
<td>30.9%</td>
<td>30.7%</td>
</tr>
<tr>
<td>Internal carotid IMT, mm</td>
<td>1.66</td>
<td>1.52%</td>
<td>1.67</td>
<td>0.003</td>
<td>*</td>
<td>1.60</td>
<td>1.82</td>
</tr>
<tr>
<td>Common carotid maximum, mm</td>
<td>1.14</td>
<td>1.09</td>
<td>1.13</td>
<td>0.07</td>
<td>*</td>
<td>1.10</td>
<td>1.21</td>
</tr>
<tr>
<td>Abnormal LV function</td>
<td>19.2%</td>
<td>12.7%</td>
<td>25.5%</td>
<td>0.001</td>
<td></td>
<td>13.4%</td>
<td>20.4%</td>
</tr>
<tr>
<td>Major ECG abnormality</td>
<td>59.6%</td>
<td>53.3%</td>
<td>56.7%</td>
<td>0.44</td>
<td>*</td>
<td>60.3%</td>
<td>68.5%</td>
</tr>
<tr>
<td>LV mass by ECG, g</td>
<td>168.5</td>
<td>148.0</td>
<td>186.8</td>
<td>0.0001</td>
<td></td>
<td>143.9</td>
<td>181.1</td>
</tr>
<tr>
<td>FEV$_1$, ratio</td>
<td>1.95</td>
<td>1.64</td>
<td>2.31</td>
<td>0.0001</td>
<td>†</td>
<td>1.43</td>
<td>2.13</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>6.4%</td>
<td>4.3%</td>
<td>5.4%</td>
<td>0.55</td>
<td></td>
<td>8.2%</td>
<td>8.1%</td>
</tr>
</tbody>
</table>

Values represent proportion with characteristic or mean measurement among each group. BP indicates blood pressure; IMT, intima-media thickness. $P$ values are from $\chi^2$ tests for the equality of proportions or $t$ tests for the equality of means. *$P<0.01$ for higher mean or proportion age $\geq 80$ vs age 65–79 years. †$P<0.01$ for higher mean or proportion age 65–79 vs age $\geq 80$ years.
and CHF or hypertension over time by interaction testing or with models run in separate time periods. In analyses specifically predicting out-of-hospital death, the independent predictors were also prior CHF and prior CHD.

When we adjusted for treatments received during the event hospitalization (percutaneous transluminal coronary angioplasty, CABG, thrombolytics, aspirin, angiotensin-converting enzyme inhibitors, antiarrhythmics, and nitroglycerin) in models that included all the independent predictors that were identified in stepwise analysis, prior CHF remained the only significant predictor of case fatality (OR, 3.97; 95% CI, 1.95 to 8.08). When these treatment variables were added as actual candidates to the stepwise age- and sex-adjusted multivariable models predicting case fatality, the independent predictors of fatality were prior CHF (OR, 3.45; 95% CI, 1.94 to 6.13), age at MI (OR, 1.31 per 5 years; 95% CI, 1.06 to 1.62), and having received thrombolytic therapy (OR, 3.44; 95% CI, 1.63 to 7.25). Having received aspirin in the hospital was associated with a decreased risk of fatality (OR, 0.40; 95% CI, 0.22 to 0.71).

Discussion

In this population-based prospective study of community-dwelling older adults, case fatality from acute CHD events remains high, with a substantial proportion of out-of-hospital deaths. A few traditional risk factors and many measures of subclinical disease appear to be associated with CHD case fatality in this population; however, preexisting diseases and comorbidities such as prior CHD and CHF appear to be the strongest independent predictors of CHD case fatality, with few differences by age, gender, race, or history of CHD.

Our study definition of case fatality focuses on death before hospital discharge rather than 28- or 30-day fatality, which is also often used. However, a small number of additional deaths occurred within 28 days of the event but after hospital discharge, possibly because of a higher likelihood of being kept in the hospital longer and/or dying sooner after a cardiac event among older persons with MI, making this a relatively short period of time for additional deaths to occur. The hospitalized MI case fatality rates of 13.4% among women and 14.1% among men that we found are comparable to 28-day MI case fatality rates of 9% to 12% reported in surveillance studies of 30- to 74-year-old subjects. The improving trend in age- and sex-adjusted case fatality rates is also consistent with the findings in these studies. However, comparisons of most of our findings with other studies on CHD mortality are limited given that most of the studies on CHD morbidity that we could find focused on overall mortality rates and trends, examined single risk factors, or focused only on comparisons of CVD mortality by particular patient characteristics.

Demographics and Case Fatality

Previous studies that have found higher mortality rates and CHF or hypertension over time by interaction testing or with models run in separate time periods. In analyses specifically predicting out-of-hospital death, the independent predictors were also prior CHF and prior CHD.

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Demographics and Case Fatality

Previous studies that have found higher mortality rates in women have primarily been studies of acute MI in middle-aged cohorts, or the increased risk in women has been found to be greatest in younger women and to gradually decline with increasing age. Other studies that have focused on the elderly, such as ours, have found no significant differences attributable solely to gender, as the association of age with fatality appeared to diminish with adjustment for comorbidities like prior CHD, CHF, and diabetes, suggesting that the relationship of age to CHD fatality may be accounted for primarily by the increased prevalence of these characteristics. However, age was still an independent predictor of fatality even with adjustment for these factors, which suggests that the elderly should not be considered a single group and that continued risk stratification by age may still be useful, especially among older women, in whom almost 20 more events of every 100 are fatal. We found no significant differences in outcomes by race, which is encouraging.
MI29 but not CHD mortality. Other findings in the elderly shown associations of traditional risk factors with incident fatality in any analysis. Prior studies in this cohort have cholesterol levels or BMI did not show an increased risk of were apparent only when considered alone, and higher this population. Other risk factors such as hypertension found to be an independent predictor for case fatality in ST-elevation versus non–ST-elevation MI. 

interpretation of this is limited in this study without this population. An increased risk of fatality associated with normal LV systolic function in importance of CHF with normal LV systolic function in associated with CHD fatality in all analyses and all groups, strongly than history of prior MI alone. Prior CHF was PCI, or CABG, appeared to predict case fatality more details about event presentation and whether the MI was an associated with CHF. Lower blood pressures in older men with CHD may be due to illness from CHD or other unmeasured factors that contribute to mortality. Notably, however, these blood pressures were in the high-normal range, with differences of only a few millimeters of mercury in pressure, which have been associated previously with an increased risk of cardiovascular disease. Systolic blood pressure control and monitoring may need to be more precise and more intensive, especially in elderly men. Subclinical atherosclerotic disease has been associated with prevalent CHD and its risk factors, total mortality, and incident MI in asymptomatic adults. In our study many subclinical disease measures were associated with CHD case fatality when considered alone, even among those with prior CHD. This suggests that these measures, often used to predict incident disease, may also be useful for further risk stratification to identify those with an even higher risk of death, even among those with known CHD.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Nonfatal (n=687)</th>
<th>Fatal (n=298)</th>
<th>P</th>
<th>Women* (n=502)</th>
<th>Men* (n=483)</th>
<th>All† (n=985)</th>
<th>No Prior CHD‡ (n=483)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at MI, y</td>
<td>78.5</td>
<td>80.2</td>
<td>0.0001</td>
<td>1.83† (1.39-2.41)</td>
<td>1.20 (0.96-1.48)</td>
<td>1.40 (1.19-1.67)</td>
<td>1.67 (1.27-2.22)</td>
</tr>
<tr>
<td>Prior MI</td>
<td>18%</td>
<td>33%</td>
<td>0.0001</td>
<td>3.15† (1.80-5.50)</td>
<td>2.25† (1.52-3.32)</td>
<td>2.50† (1.82-3.45)</td>
<td>...</td>
</tr>
<tr>
<td>Prior CHD</td>
<td>40%</td>
<td>69%</td>
<td>0.0001</td>
<td>2.88† (1.82-4.55)</td>
<td>3.83† (2.60-5.64)</td>
<td>3.44† (2.57-4.62)</td>
<td>...</td>
</tr>
<tr>
<td>Prior CHF</td>
<td>17%</td>
<td>48%</td>
<td>0.0001</td>
<td>4.66† (2.86-7.60)</td>
<td>3.99† (2.69-5.91)</td>
<td>4.25† (3.13-5.78)</td>
<td>3.31† (1.87-5.87)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>22%</td>
<td>33%</td>
<td>0.0001</td>
<td>2.67† (1.62-4.40)</td>
<td>1.57† (1.06-2.34)</td>
<td>1.93† (1.42-2.63)</td>
<td>1.54 (0.91-2.61)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>79%</td>
<td>88%</td>
<td>0.0001</td>
<td>1.41 (0.74-2.70)</td>
<td>2.13† (1.27-3.56)</td>
<td>1.87† (1.25-2.80)</td>
<td>1.14 (0.67-1.95)</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>140</td>
<td>138</td>
<td>0.19</td>
<td>1.05 (0.80-1.39)</td>
<td>0.70† (0.55-0.90)</td>
<td>§</td>
<td>0.81 (0.60-1.10)</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>71</td>
<td>70</td>
<td>0.29</td>
<td>1.11 (0.85-1.47)</td>
<td>0.78† (0.62-0.99)</td>
<td>0.91 (0.76-1.09)</td>
<td>1.05 (0.78-1.42)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27.0</td>
<td>26.5</td>
<td>0.13</td>
<td>0.99 (0.80-1.23)</td>
<td>0.82 (0.64-1.03)</td>
<td>0.91 (0.78-1.07)</td>
<td>0.92 (0.72-1.18)</td>
</tr>
<tr>
<td>Impaired fasting glucose</td>
<td>16%</td>
<td>12%</td>
<td>0.19</td>
<td>0.85 (0.42-1.71)</td>
<td>0.77 (0.47-1.27)</td>
<td>0.77 (0.52-1.17)</td>
<td>1.31 (0.73-2.36)</td>
</tr>
<tr>
<td>Ankle-ankle index &lt;0.9</td>
<td>22%</td>
<td>30%</td>
<td>0.04</td>
<td>1.95† (1.19-3.21)</td>
<td>1.27 (0.84-1.91)</td>
<td>1.48† (1.08-2.03)</td>
<td>0.95 (0.54-1.70)</td>
</tr>
<tr>
<td>Internal carotid IMT, mm</td>
<td>1.64</td>
<td>1.72</td>
<td>0.07</td>
<td>1.27 (0.91-1.77)</td>
<td>1.13 (0.88-1.46)</td>
<td>1.18 (0.96-1.44)</td>
<td>0.98 (0.68-1.40)</td>
</tr>
<tr>
<td>Common carotid IMT, mm</td>
<td>1.12</td>
<td>1.17</td>
<td>0.005</td>
<td>1.48† (1.15-1.90)</td>
<td>1.16 (0.95-1.42)</td>
<td>1.27† (1.09-1.48)</td>
<td>0.98 (0.75-1.29)</td>
</tr>
<tr>
<td>LV mass by ECG, g</td>
<td>166</td>
<td>174</td>
<td>0.009</td>
<td>0.99 (0.80-1.23)</td>
<td>0.82 (0.64-1.03)</td>
<td>0.91 (0.78-1.07)</td>
<td>0.92 (0.72-1.18)</td>
</tr>
<tr>
<td>Major ECG abnormality</td>
<td>54%</td>
<td>74%</td>
<td>0.0001</td>
<td>2.56† (1.58-4.14)</td>
<td>2.27† (1.53-3.37)</td>
<td>2.31† (1.71-3.13)</td>
<td>2.00† (1.24-3.24)</td>
</tr>
<tr>
<td>Abnormal LV function</td>
<td>15%</td>
<td>29%</td>
<td>0.0001</td>
<td>2.78† (1.43-5.39)</td>
<td>2.45† (1.62-3.72)</td>
<td>2.58† (1.82-3.67)</td>
<td>2.69† (1.39-5.22)</td>
</tr>
</tbody>
</table>

Values are mean or percentage unless otherwise indicated. BP indicates blood pressure; IMT, intima-media thickness. §Significant gender interaction, P<0.01.

This may be due to the small sample size of blacks in the study or a more similar prevalence of risk factors by race at older ages, as previous studies have suggested.27

**Clinical Characteristics and Case Fatality**

Preexisting CHD and CHF, regardless of etiology, appear to be the strongest independent predictors of CHD event fatality. Prior CHD, which includes history of angina, MI, PCI, or CABG, appeared to predict case fatality more strongly than history of prior MI alone. Prior CHF was associated with CHD fatality in all analyses and all groups, even with adjustment for LV function, supporting the importance of CHF with normal LV systolic function in this population. An increased risk of fatality associated with having received thrombolytic therapy during hospitalization has been noted previously in the elderly,28 but the interpretation of this is limited in this study without details about event presentation and whether the MI was an ST-elevation versus non–ST-elevation MI.

Of the traditional CHD risk factors, only diabetes was known CHD.

weight may actually be a marker of poorer health in older populations.26,30,31 Perhaps the increased risk from factors such as smoking has effects earlier in life, with the possible exception of older blacks, in whom the increased risk may persist. The seemingly contradictory association of higher systolic blood pressure with a lower risk of death has been seen previously in elderly men.32 This did not appear to be a treatment effect but was due to the presence of prior CHD. Lower blood pressures in older men with CHD may be due to illness from CHD or other unmeasured factors that contribute to mortality. Notably, however, these blood pressures were in the high-normal range, with differences of only a few millimeters of mercury in pressure, which have been associated previously with an increased risk of cardiovascular disease. Systolic blood pressure control and monitoring may need to be more precise and more intensive, especially in elderly men.

Subclinical atherosclerotic disease has been associated with prevalent CHD and its risk factors, total mortality, and incident MI in asymptomatic adults.26,29,34,35 In our study many subclinical disease measures were associated with CHD case fatality when considered alone, even among those with prior CHD. This suggests that these measures, often used to predict incident disease, may also be useful for further risk stratification to identify those with an even higher risk of death, even among those with known CHD.
Limitations

Although this is a large population-based cohort, it is a selected sample composed of people who have already survived to age 65 years, and rates seen in our study may have been influenced by selection bias and better care or closer monitoring of patients because of known study participation. They may also be generally healthier than many previously reported samples of the elderly with MI that are collected from more severe or more overt MI cases presenting to tertiary care hospitals. The large number of comparisons and increased risk of type I error may not have been accounted for completely by our more stringent level of 0.01. Smaller sample sizes for subgroup analyses may have limited power for detecting differences, especially racial differences, given the relatively small number of blacks. In addition, there may be many other characteristics not accounted for that likely played a role in influencing outcomes, such as hospitalization and treatment details or code status, and other determinants of overall mortality in the elderly such as functional status. We also did not focus our analyses on trends over time; again, comparisons of our findings with studies on CHD mortality in younger populations are limited because of differences in study focus, with most data focused on overall mortality rates and trends and/or on examining associations of mortality with single risk factors or by particular patient characteristics.

However, this study of older adults in diverse community settings differs from and extends previous CHD mortality studies in a number of ways. We included participants with other fatal CHD events and not only those admitted for acute MI, but many of those who died out of hospital and especially before hospitalization who otherwise would have gone unrecognized. We also included those with prior CHD, given improving MI survival and subsequently high prevalence of a history of MI among older adults today, and we examined demographic and clinical subgroups within this elderly population. Additionally, our study sample was not limited to specific hospitals or subject to strict selection criteria in studies done as part of clinical trials. Finally, our data were systematically and prospectively collected and validated before all coronary events, allowing for prediction of future mortality.

Conclusions

Among older adults, case fatality from acute CHD events remains high, with a substantial proportion of out-of-hospital deaths, and the risk factors that predict fatality may be different than those that predict incident CHD. A history of CHF, regardless of LV systolic function, age, gender, or prior CHD, appears to be one of the strongest independent predictors of CHD case fatality, which supports the importance and need for further study of nonsystolic heart failure in this population. Diabetes is also an important predictor of fatality, as well as prior CHD, which includes a history of angina or prior revascularization, not only history of MI. Subclinical disease measures may have some role in risk stratification, even among those with known CHD. The elderly should not be consider-

Figure 2. Independent predictors of case fatality among participants with CHD events (OR, 95% CI). OR is relative odds of fatality for the characteristic adjusted for age, sex, and the other predictors from stepwise logistic regression models predicting case fatality (death before hospitalization or hospitalization) within each group as indicated, starting with age and gender and all other variables as candidates added or deleted per step if significant at P<0.01. *Model predicting out-of-hospital death specifically. AMI indicates acute MI.
ered a single homogeneous group because although there may be less obvious differences by race and gender in this population, the risk of CHD fatality continues to increase with age, especially among women. The relationship between systolic blood pressure, prevalent CHD, and risk of CHD mortality in older men needs to be clarified further. Finally, although traditional risk factors should continue to be treated aggressively in all patients, in the elderly, in whom the risk/benefit of therapies often must be reconsidered in the presence of multiple competing comorbidities and medical care needs, risk stratification may be improved further by identifying those who are most in need of all available measures and focusing the more aggressive care on those patients with known CHD and those with a history of CHF or diabetes, who may be at the highest risk for fatal CHD events.

Acknowledgments

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Disclosures

None.

References


**CLINICAL PERSPECTIVE**

The majority of coronary heart disease (CHD) deaths each year occur in adults aged >65 years. This high-risk older population currently constitutes less than one fourth of the US population but is projected to double in size within 30 years and to account for half of hospital admissions for acute myocardial infarction. Despite these statistics, the elderly, especially those older than 75 years, have been significantly underrepresented in clinical trials and the published literature. Questions remain about whether findings from middle-aged populations also apply to those aged >65 years or whether might there be different factors that are more important in the older population or more important for predicting fatality from an event rather than predicting incident events, as is often studied. In this prospective cohort study of community-dwelling older adults, 30% of the CHD events were fatal, with a substantial proportion of out-of-hospital deaths. Case fatality decreased significantly over time and was similar by race and gender but increased with age, especially among women. A few traditional risk factors such as diabetes and many measures of subclinical disease were associated with case fatality when considered alone. However, prior CHD and congestive heart failure appeared to be the strongest independent predictors. Prior congestive heart failure conferred a ≥3-fold increased risk of fatality in all subgroups regardless of left ventricular systolic function. Prior CHD (myocardial infarction, angina, or previous revascularization) predicted case fatality more strongly than history of prior myocardial infarction alone. These data may be of value for the clinician in improving risk stratification and identifying those elderly patients at the highest risk for fatal CHD events who are most in need of the most aggressive care with all available preventive measures.
Characteristics and Baseline Clinical Predictors of Future Fatal Versus Nonfatal Coronary Heart Disease Events in Older Adults: The Cardiovascular Health Study
Camille A. Pearte, Curt D. Furberg, Ellen S. O'Meara, Bruce M. Psaty, Lewis Kuller, Neil R. Powe and Teri Manolio

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