Recent Trends in the Prevalence of Coronary Disease

A Population-Based Autopsy Study of Nonnatural Deaths

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Background: Despite increases in obesity and diabetes mellitus, mortality caused by coronary disease continues to decline. Recent trends in coronary disease prevalence are unknown.

Methods: There were 3237 deaths among Olmsted County, Minnesota, residents aged 16 through 64 years during the 1981-2004 period. Of the 515 due to accident, suicide, homicide, or a manner that could not be determined, 425 individuals (82%) had coronary anatomy graded. Pathology reports were reviewed for the grade of coronary disease (range, 0-5) assigned each of 4 arteries: left anterior descending (LAD), left circumflex (LCx), right coronary artery (RCA), and left main artery (LMA). High-grade disease was defined as more than a 75% reduction in cross-sectional luminal area (grade 4) in any of LAD, LCx, or RCA or more than 50% reduction (grade 3) in LMA. Evidence of any disease was defined as a grade higher than 0 in any artery. Calendar-year trends were analyzed as linear and nonlinear functions.

Results: Over the full period (1981-2004), 8.2% of the 425 individuals had high-grade disease, and 83% had evidence of any disease. Age- and sex-adjusted regression analyses revealed temporal declines over the full period (1981-2004) for high-grade disease, any disease, and grade of coronary disease. Declines in the grade of coronary disease ended after 1995 (P = .01 for every artery) and possibly reversed after 2000 (P = .06 for LCx).

Conclusions: Declines in coronary disease prevalence overall (during 1981-2004) reinforce arguments that any increased prevalence resulting from improved survival among persons with disease was offset by reductions in disease incidence. Study findings suggest that declines in coronary disease prevalence have ended. The question of whether recent trends are attributable to increasing obesity and diabetes mellitus awaits further investigation.

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Over the past century, the rate of death due to heart disease in the United States rose until the mid 1960s when it began a steady decline, which continues today (Figure 1). Data from Olmsted County, Minnesota, and elsewhere provide convincing evidence that declines in heart disease mortality were accompanied by declines in the incidence of coronary artery disease (CAD), the most common form of heart disease, as well as improved survival among persons with CAD. The net impact of these opposing trends on the prevalence of nonfatal CAD within the population is less clear. Information drawn from autopsies has been considered the gold standard for case detection and enumeration; it also affords estimates of subclinical disease and disease severity. But to guarantee that autopsy findings mirror trends for the general public, it is essential that autopsy rates are high and that the effect of CAD on the decision to autopsy has remained constant over time. Unfortunately, the national autopsy rate has never been high and declined markedly from 19.1% in 1972 to 9.4% in 1994, when the National Center for Health Statistics stopped collecting national data. A survey of all autopsies conducted in each state by one of us (P.N.N.) found a continuing decline, with the national average in 2003 of only 8.3%. These low and declining rates suggest that potential bias in the decision to autopsy compromises the ability of autopsy data to generate accurate estimates of long-term trends in disease.

Olmsted County has traditionally had autopsy rates across all age groups exceeding national estimates by an order of magni-
tude for older ages. A previous study examined the prevalence of high-grade CAD at autopsy among Olmsted County residents from 1979 to 1994. There was no significant change in high-grade CAD between the 1979-1983 period and the 1990-1994 period overall, but when stratified by ages 20 to 59 years and 60 years or older, younger persons exhibited a significant 37% decline (P = .02) and older persons exhibited a nonsignificant 3% decline (P = .44). Autopsy rates declined from 31% during the 1979-1983 period to 23% during the 1990-1994 period; declines were greatest for older age groups. The decision to autopsy was significantly associated with ante mortem CAD diagnoses (P < .001). There was little evidence of temporal trends in autopsy referral bias; however, it cannot be excluded as an explanation. It is important that the investigation did not extend to recent years, a period characterized by dramatic increases in the prevalence of obesity and type 2 diabetes mellitus, which are both powerful risk factors for CAD. The recent epidemics of obesity and diabetes mellitus have prompted some authors to suggest that declines in heart disease mortality observed over the past half century will soon end and that today's children may be the first generation to experience shorter life expectancy than their parents. However, there is a shortage of data to test these predictions.

This article describes temporal trends in the prevalence of high-grade CAD and lesser forms of CAD for Olmsted County residents aged 16 through 64 years from 1981 through 2004 and tests for nonlinear effects of calendar year. The study uses autopsy data from all county residents whose manner of death was “nonnatural” (ie, accident, suicide, homicide, or a manner that could not be determined). Concerns regarding trends in autopsy referral bias are markedly reduced because the rate of autopsy among nonelderly persons whose manner of death was nonnatural is very high and the decision to autopsy is largely uncorrelated with CAD. Autopsies of individuals whose manner of death was nonnatural thus offer the promise of a relatively unbiased sample of population trends in CAD prevalence. The years under investigation include those during which marked increases in obesity and diabetes mellitus observed nationally were mirrored locally.

METHODS

Longitudinal population-based studies of disease prevalence are facilitated in Olmsted County (population, 124,277 according to the 2000 US census) because Rochester, the county seat, is relatively isolated from other metropolitan areas and is home to one of the world’s largest medical centers, the Mayo Clinic. Essentially, all medical care received by local residents is provided either by the Mayo Clinic and its 2 affiliated hospitals, or a second group practice, Olmsted Medical Center (OMC), and its affiliated hospital. Since 1907, every Mayo Clinic patient has been assigned a unique identifier. Information from every Mayo Clinic contact (ambulatory, hospital, emergency department, and nursing home visits), including pathology reports, copies of death certificates, and autopsy information, is contained within a single dossier for each patient. Diagnoses assigned at each visit are coded and entered into continuously updated computer files. Under the auspices of the Rochester Epidemiology Project, and with continued funding from the National Institutes of Health, the diagnostic index and medical records linkage were expanded to the few other providers of medical care to local residents, primarily OMC.

Death certificates of almost all county residents cared for by Mayo Clinic physicians are completed by the coroner or a Mayo Clinic pathologist. Infrequently, death certificates are completed by oncologists for hospice patients and by internists for nursing home patients. The entire medical record is reviewed; autopsy findings take precedence over clinical information. Death certificates for patients cared for by physicians affiliated with other institutions (eg, OMC) are completed by those physicians. All autopsies have been conducted in Mayo Clinic’s pathology department using a uniform and comprehensive system of autopsy techniques.

SUBJECTS

Approval for the present investigation was obtained from the Mayo Clinic and OMC institutional review boards. Rochester Epidemiology Project resources, including Minnesota State electronic death certificates and death tapes, were used to identify all Olmsted County residents aged 16 through 64 years who died in the county from January 1, 1981, through December 31, 2004. Deaths were categorized as natural or nonnatural according to the check box located on all county death certificates, which queries whether the manner of death was accident, homicide, suicide, or could have been an accident, homicide, suicide, or any other manner of death that was not natural.
DETERMINATION OF CAD

One of us (P.N.N.) reviewed all autopsy records of nonnatural deaths, including the complete pathology reports, and recorded the grade assigned each main coronary artery: left arterial descending (LAD), left circumflex (LCx), right coronary artery (RCA), and left main artery (LMA). The grade ranged from 0 (no reduction in cross-sectional luminal area) through 5, with 1, 2, 3, 4, and 5 defined as more than 0% to 25%, 26% to 50%, 51% to 75%, and 76% to 99%, and 100% reduction, respectively.

STATISTICAL ANALYSIS

Decedent characteristics were summarized using descriptive statistics. Univariate regression was used to test for significant associations between decedent characteristics and year of death (P<.05). For decedents with coronary anatomy graded, logistic regression, adjusted for age and sex, was used to test whether year of death was associated with (1) the presence of high-grade CAD (grade ≥ 4 in any of LAD, LCx, or RCA, or grade ≥ 3 in LMA) and (2) evidence of any CAD (grade >0 in any artery). Ordinal logistic regression, adjusted for age and sex, was used to test whether the year of death was associated with grade of CAD. For each analysis, we considered all 2-way interactions with calendar year.

We then analyzed trends in CAD as a function of calendar year as a possibly nonlinear function based on (1) a wedge-shaped function (linear then flat), with the initial slope and change point (from linear to flat) estimated from the data (2 parameters), and (2) a wedge-shaped function with 2 slopes, neither constrained to be flat, and a change point (3 parameters). When taken as a sequence of models, this is a nested hierarchical sequence. In each case, it was the change in the overall model χ² that was assessed relative to the change in degrees of freedom. All models were ordinal logistic regression and were age and sex adjusted. Any significant improvement in fit with the linear-then-flat function compared with the linear function was interpreted as evidence of slowing of the decline, and the estimated change point as the approximate year that the slowing occurred (P<.05). Any further significant improvement in fit obtained by allowing the second slope to be unconstrained was interpreted as evidence of a reversal of the earlier decline (P<.05).

RESULTS

There were 3237 Olmsted County residents aged 16 through 64 years who died within the county from January 1, 1981, through December 31, 2004. Decedent characteristics are summarized in Table 1, for all years combined and for successive 8-year periods 1981-1988, 1989-1996, and 1997-2004. For all decedents, the mean (SD) age at death was 50 (12) years; 63% were male. The manner of death was nonnatural for 515 (16%). Consistent with patterns observed elsewhere,35,36 decedents whose manner of death was nonnatural were younger (P<.001) compared with decedents whose manner of death was natural.

It is important that 96% of nonnatural deaths among decedents aged 16 through 64 years were autopsied, and 82% had coronary anatomy graded. Of the 68 individuals autopsied whose death was nonnatural and without coronary anatomy graded, 61% had no explanation; the remainder had mention that the heart was damaged at death (4%) or donated for educational or research purposes (35%). Consistent with patterns observed elsewhere,35,36 the proportion of Olmsted County decedents whose death was nonnatural declined over time. There was no change over time in the proportion of those who had experienced nonnatural deaths who were autopsied. There was a statistically significant increase over time in the proportion of nonnatural deaths that went to autopsy and had coronary anatomy graded (P<.001). There

Table 1. Characteristics of Olmsted County Residents Who Died at Ages 16 Through 64 Years in Olmsted County, 1981-2004

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>All deaths No.</td>
<td>3237</td>
<td>932</td>
<td>1083</td>
<td>1222</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>50 (12)</td>
<td>50 (13)</td>
<td>49 (12)</td>
<td>50 (12)</td>
</tr>
<tr>
<td>Males, No. (%)</td>
<td>2036 (63)</td>
<td>557 (60)</td>
<td>684 (63)</td>
<td>795 (65)</td>
</tr>
<tr>
<td>Nonnatural deaths</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. (% all deaths)</td>
<td>515 (16)</td>
<td>180 (19)</td>
<td>162 (15)</td>
<td>173 (14)</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>36 (14)</td>
<td>35 (15)</td>
<td>35 (14)</td>
<td>37 (13)</td>
</tr>
<tr>
<td>Males, No. (%)</td>
<td>387 (75)</td>
<td>126 (70)</td>
<td>123 (76)</td>
<td>138 (80)</td>
</tr>
<tr>
<td>Autopsied, nonnatural deaths</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. (% nonnatural)</td>
<td>493 (96)</td>
<td>173 (96)</td>
<td>153 (94)</td>
<td>167 (97)</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>36 (14)</td>
<td>35 (15)</td>
<td>35 (14)</td>
<td>37 (12)</td>
</tr>
<tr>
<td>Males, No. (%)</td>
<td>368 (75)</td>
<td>121 (70)</td>
<td>115 (75)</td>
<td>132 (79)</td>
</tr>
<tr>
<td>Autopsied, nonnatural deaths with coronary anatomy graded</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. (% nonnatural)</td>
<td>425 (82)</td>
<td>140 (78)</td>
<td>124 (76)</td>
<td>161 (93)</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>36 (14)</td>
<td>36 (15)</td>
<td>37 (14)</td>
<td>36 (13)</td>
</tr>
<tr>
<td>Male, No. (%)</td>
<td>323 (76)</td>
<td>104 (74)</td>
<td>93 (75)</td>
<td>126 (78)</td>
</tr>
</tbody>
</table>

Abbreviation: NA, not applicable.

*P-values are derived from univariate tests of calendar year effect, with calendar year entered as a single year.
TRENDS IN HIGH-GRADE CAD

Over all 24 years combined, only 35 of the 425 decedents with coronary anatomy graded (8.2%) met criteria for high-grade CAD. Figure 2A provides estimates by 4-year periods. Univariate analysis of the effect of calendar year revealed a significant decline over time \( (P = .04) \). Among decedents with high-grade CAD, age at death was unchanged over time \( (P = .19) \); there was a nonsignificant trend toward fewer males in later years \( (P = .08) \). The latter is in the direction opposite that observed for all other categories. Multivariable regression for the outcome of CAD (Table 2) revealed that age was the only variable that reached statistical significance in the main-effects model. In the model that investigated interactions, the significant interactions between calendar year and sex and between calendar year and age revealed that temporal declines in high-grade CAD were greater for males compared with females and for younger individuals compared with those who were older. See Table 2 for \( P \) values.

TRENDS IN ANY CAD

Figure 2B provides estimates by 4-year periods of the proportion of decedents with coronary anatomy graded for whom there was evidence of any CAD. For each artery separately, multivariable logistic regression (Table 2) revealed that, over the full period (1981-2004), the odds of any CAD declined significantly with increasing calendar year; the odds increased with increasing age but did not differ significantly between men and women. There were no significant interactions between calendar year and either age or sex. See Table 2 for \( P \) values.

TRENDS IN THE GRADE OF CAD

Figure 2C provides the annual mean grades for each of the 4 arteries. Table 2 provides results of multivariable ordinal logistic regression for grade of CAD. For each artery, over the full period (1981-2004), the grade of CAD declined significantly with increasing calendar year. For each artery, there was a positive and significant association between age and grade. The CAD grade was higher for males than for females; the difference reached significance for LAD and LCx; there was a nonsignificant trend for RCA and no significant difference for LMA. There were no significant interactions between calendar year and either age or sex. See Table 2 for \( P \) values.

NONLINEAR TRENDS

To explore whether the trends observed were constant over time, we focused on the outcome that afforded the greatest discrimination (ie, the grade assigned each artery). For each artery, both the linear-then-flat model and the reversed-directions model revealed significantly better fits compared with the model that assumed a linear trend. For the linear-then-flat model, the identified change point was 1994 for LAD \( (\chi^2 = 6.43; P = .01) \) and LMA \( (\chi^2 = 11.79; P < .001) \) and 1995 for LCx \( (\chi^2 = 8.54; P = .004) \) and RCA \( (\chi^2 = 6.21; P = .01) \). For the reversed-directions model, the identified change point was 2001 for LAD \( (\chi^2 = 7.40; P = .03) \) and LCx

was no statistically significant change over time in mean age at death, for all decedents \( (P = .84) \), those whose manner of death was nonnatural \( (P = .27) \), those who went to autopsy \( (P = .20) \), or those who had coronary anatomy graded \( (P = .92) \). The proportion of male decedents increased over time for each of these categories; the increase was statistically significant for all but the last category (see Table 1 for \( P \) values).
Finally, we compared the 2 non-linear models with each other. There was no significant improvement in fit for the reversed-directions model compared with the linear-then-flat model for LAD (P = .32), RCA (P = .34), or LMA (P = .18). For LCx, there was a nonsignificant trend (P = .06), suggesting that declines in grade of CAD have not only ended, they may have reversed.

We investigated temporal trends in the prevalence of CAD at autopsy among Olmsted County residents aged 16 through 64 years whose manner of death was nonnatural. Over the full study period (1981-2004), there were declines in the proportion of decedents with high-grade coronary artery disease.

**Table 2. Logistic Regression Investigating the Effect of Calendar Year of Death**

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>β Coefficient</th>
<th>SE</th>
<th>OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High-Grade CAD</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at death</td>
<td>0.1079</td>
<td>0.0188</td>
<td>1.11 (1.07-1.16)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>−0.2969</td>
<td>0.4308</td>
<td>0.74 (0.32-1.73)</td>
<td>.49</td>
</tr>
<tr>
<td>Calendar year</td>
<td>−0.0427</td>
<td>0.0274</td>
<td>0.96 (0.91-1.01)</td>
<td>.12</td>
</tr>
</tbody>
</table>

**Evidence of Any CAD**

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>β Coefficient</th>
<th>SE</th>
<th>OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at death</td>
<td>0.0867</td>
<td>0.0137</td>
<td>1.09 (1.06-1.12)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>0.5168</td>
<td>0.3138</td>
<td>1.68 (0.91-3.10)</td>
<td>.10</td>
</tr>
<tr>
<td>Calendar year</td>
<td>−0.0500</td>
<td>0.0208</td>
<td>0.95 (0.91-0.99)</td>
<td>.02</td>
</tr>
</tbody>
</table>

**Grade of CAD**

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>β Coefficient</th>
<th>SE</th>
<th>OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at death</td>
<td>0.0895</td>
<td>0.0081</td>
<td>1.09 (1.08-1.11)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>0.5925</td>
<td>0.2242</td>
<td>1.81 (1.16-2.81)</td>
<td>.008</td>
</tr>
<tr>
<td>Calendar year</td>
<td>−0.0552</td>
<td>0.0137</td>
<td>0.95 (0.92-0.97)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

**Abbreviations:** CAD, coronary artery disease; CI, confidence interval; LAD, left anterior descending; LCx, left circumflex; LMA, left main artery; NA, not applicable; OR, odds ratio; RCA, right coronary artery; SE, standard error.

a Calendar year of death was defined as 1 for 1981 through 24 for 2004.
b High-grade CAD was defined as more than 75% reduction in cross-sectional luminal area (grade 4 or greater) in any of LAD, LCx, or RCA or more than 50% reduction (grade 3 or greater) in LMA.
c The interactions were such that the odds of high-grade CAD associated with each increasing calendar year were 0.78 for 30-year-old males, 0.90 for 30-year-old females, 0.98 for 60-year-old males, and 1.13 for 60-year-old females.
d Evidence of any coronary disease was defined as grade higher than 0 in any artery.
e Modeled using ordinal logistic regression.
CAD, more so for males compared with females and younger decedents compared with those who were older. As detailed in Table 2, over the full study period, there were also significant declines both in the proportion of decedents with evidence of any CAD and in the grade of CAD. Notably, among these nonelderly individuals whose manner of death was nonnatural, declines in the grade of CAD ended after 1995, and there is suggestive evidence that the grade of CAD may have increased since 2000.

Declines in CAD prevalence over the full period (1981-2004) are consistent with National Health and Nutrition Examination Survey (NHANES) reports of marked declines in self-reported myocardial infarction among white male and female participants between 1971-1975 and 1988-1994. Our study has advantages over NHANES comparisons in that subclinical disease is included and temporal changes in disease definitions and detection are minimized. Declines in the prevalence of high-grade CAD over the 1981-2004 period are consistent with declines among nonelderly decedents found in the previous Olmsted County autopsy study that included calendar years 1979 to 1994, all ages, and all manner of deaths. Our study addressed concerns with autopsy referral bias in the previous study by focusing on nonelderly adults whose manner of death was nonnatural (ie, decedents for whom the autopsy rate is consistently very high and the decision to autopsy is largely unaffected by ante mortem diagnoses).

A few other studies have similarly focused on nonnatural deaths to investigate temporal trends in CAD among US subjects. With one well-designed exception, analyses of time trends were limited to comparisons of published estimates drawn from different populations in different geographic locations, under different autopsy conditions. To our knowledge, all US comparisons were limited to males, and none included deaths after 1995. Our study has advantages in that measurements were obtained for both sexes and for residents of the same geographically defined population over a continuous period, with a consistent institutional protocol for conducting autopsies. The present study extended beyond 1995 through 2004.

This study has several limitations. The investigation was conducted in a single county. Compared with the United States, Olmsted County has a higher percentage of non-Hispanic white individuals. Except for a greater proportion of health care workers and higher education level, Olmsted County resident characteristics are similar to those of US white individuals. Generalizability to other ethnic groups and other geographic regions cannot be assessed. It is also unknown whether temporal trends in relevant characteristics among decedents whose manner of death was nonnatural reflect those for all Olmsted County residents of similar age distribution. Between-group comparisons for temporal trends in CAD risk factors would necessitate labor-intensive effort beyond the scope of the present study. It is also unclear whether trends for nonelderly individuals reflect those for elderly individuals, for whom the rate of autopsy, even among nonnatural deaths, is unfortunately lower. The precision of the nonlinear analyses regarding cut points and individual slopes was limited by the number of cases. The sample sizes also did not afford investigation of birth cohort effects separate from period effects. The grades assigned each coronary artery were those recorded by the pathologist conducting the autopsy. Although the autopsy protocol was consistent over time, there were some changes among personnel performing the autopsy. A previous Olmsted County study compared coronary artery grades reported at autopsy with repeated review of specimens; the agreement indices for “no high-grade disease” ranged from 0.79 to 0.88. The previous study and our study overlapped in calendar years and consisted of the same core of pathologists; the agreement observed in that study likely applies to our study.

Declines in the prevalence of CAD at autopsy over the 1981-2004 period taken as a whole reinforce the argument that 4 decades of declines in heart disease mortality (Figure 1) largely reflect reductions in disease incidence (ie, reductions in CAD incidence more than offset any rise in prevalence from improved survival among persons with CAD). Our finding that temporal declines in the grade of CAD at autopsy have ended, together with suggestive evidence that declines have recently reversed, provides some of the first data to support increasing concerns that declines in heart disease mortality may not continue. The extent to which recent trends are attributable to the epidemics of obesity and diabetes mellitus awaits further investigation.
Nemetz PN, Beard CM, Ballard DJ, et al. Resurrecting the autopsy: benefits and limitations.


References


