Mortality From Pulmonary Embolism in the United States: 1962 to 1984*

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To examine the effect of advances in the prevention of and therapy for PE, we reviewed mortality for PE in the United States from 1962 to 1984. Age-adjusted PE mortality increased by 67 to 100 percent between 1962 and 1974 for white and non-white men and women. From 1975 to 1984, these rates declined by 20 to 25 percent. Non-white PE mortality was greater than white PE mortality; men had a greater risk of PE death than women. Age-specific patterns (more than 40 years of age) of PE mortality followed those of the age-adjusted death rates, with increases noted in all groups between 1962 and 1974 and declines during the 1975-1984 period. These patterns might reflect improved ascertainment of cases and better prevention of disease. The magnitude of the rates suggests that the list of indications for prophylactic anticoagulation should be reexamined for possible expansion. (Chest 1990; 98:1067-72)

Pulmonary embolism is a common cause of morbidity in the United States. In 1986, it accounted for at least 59,000 hospitalizations and 19,000 days of inpatient care. A variety of conditions, such as the postoperative period, pregnancy and post-trauma, can result in increased blood coagulability and, therefore, elevated risk of PE.

These conditions may be viewed as components of the classic triad of hypercoagulability, damage to blood vessels and stasis. Although this triad was synthesized by Virchow for deep venous thrombosis, it also applies to PE, which is frequently viewed as a complication of deep venous thrombosis. The high fatality rate associated with PE has prompted research inquiries into the treatment of this condition. The epidemiology of PE has not, however, been as well investigated. Strategies for the prevention of the disease are limited to the use of anticoagulants, leg vein compression and early ambulation following surgery.

The review of mortality patterns is one way to develop hypotheses for possible risk factors. Also, mortality trends for PE could provide insight into whether anticoagulants have been used in a broad enough manner to prevent the disease from occurring in the population. In this article, we report the results of our review of trends in the United States for mortality from PE during the 1962-1984 period.

Materials and Methods

The US NCHS routinely collects individual death certificates for all United States residents. Through a collaborative arrangement between the University of Pittsburgh and the NCHS, data tapes of all deaths in the United States between 1962 and 1984 were made available for this investigation. We reviewed these data for deaths in which the underlying cause was PE (for 1962-1967, ICD-7 rubric 465; for 1968-1978, ICD-8 rubric 450; and for 1979-1984, ICD-9 rubric 415.1). In each such instance, the demographic characteristics of the deceased were abstracted. These data were tabulated into age, sex- and race-specific strata and were aggregated into five time periods: 1962 to 1964, 1965 to 1969, 1970 to 1974, 1975 to 1979 and 1980 to 1984.

For population estimates in 1960, 1970 and 1980, age-, sex- and race-specific census data were used. For the intercensal years, the NCHS provided estimates of the age-sex-race-specific populations. For each of the five time periods, average annual age-sex-race-specific PE mortality rates were calculated.

Average annual age-adjusted sex-race-specific PE death rates were calculated using the method of Lilienfeld and Lilienfeld, with the 1960 United States population as the standard. The Cochran-Armitage test for linear trends was used to assess the statistical significance of temporal changes in the rates.

Results

Age-Adjusted Mortality

The average annual age-adjusted United States PE mortality rates for 1962 to 1984 for white men, white women, non-white men and non-white women are shown in Table 1. The average annual age-adjusted PE death rate in white men increased by 67 percent between 1962 and 1974. The rate remained stable through 1979, after which it declined by 20 percent.
Table 1—Average Annual Age-Adjusted Death Rate per 100,000 Population from PE in the United States by Race and Sex, 1962 to 1984

<table>
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</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>3 (6,475)*</td>
<td>4 (17,472)</td>
<td>5 (23,396)</td>
<td>5 (22,583)</td>
<td>4 (19,904)†</td>
</tr>
<tr>
<td>Women</td>
<td>2 (5,550)</td>
<td>3 (16,404)</td>
<td>4 (23,410)</td>
<td>3 (24,171)</td>
<td>3 (22,411)†</td>
</tr>
<tr>
<td>Non-white</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>5 (1,154)</td>
<td>8 (3,178)</td>
<td>9 (4,418)</td>
<td>8 (4,400)</td>
<td>7 (4,021)†</td>
</tr>
<tr>
<td>Women</td>
<td>4 (943)</td>
<td>6 (2,993)</td>
<td>7 (4,290)</td>
<td>6 (4,366)</td>
<td>5 (4,128)†</td>
</tr>
</tbody>
</table>

*Figures in parentheses are the total numbers of deaths for the entire time period.
†p<0.05 in Cochran's test for trends.

For white women, a similar pattern in age-adjusted PE mortality is seen. The death rate doubled between 1962 and 1974 and then declined by 25 percent between 1974 and 1979. It remained at that level through 1984.

The age-adjusted PE death rates for non-white subjects followed temporal patterns similar to those for white subjects. Among non-white men, average annual age-adjusted PE mortality increased by 80 percent during the 1962-1974 time period. From 1975 to 1984, though, it declined by 22 percent. Similarly for non-white women, age-adjusted PE mortality increased by 75 percent for the 1962-1974 period, after which it declined by 25 percent.

For men, age-adjusted mortality for PE was greater among non-white than among white subjects in each time period. This excess ranged from 42 to 100 percent, with no temporal pattern apparent. For non-white women, age-adjusted mortality was uniformly greater than that among white women in each time period by a factor of approximately two. For both white and non-white subjects, PE mortality was greater in men than in women. However, this excess was small, ranging between 25 and 50 percent.

Age-Specific Mortality

The average annual age-specific mortality rates for PE for white men, white women, non-white men and non-white women during 1962 to 1984 are shown in Figures 1 through 4. For all four demographic groups, in each time period PE mortality increased with age. Among white men, annual age-specific PE mortality among those less than 40 years old was generally low throughout the 23 years of observation. For middle-aged white men, the magnitude of the increase in mortality due to PE from 1962 to 1974 was associated with advancing age. However, by 1984, much of this elevation had disappeared (Table 2). For elderly white
men, PE mortality increased 69 and 103 percent between 1962 and 1974, after which it declined somewhat. Nonetheless, notable increases for the 1962-1984 time period can be seen.

Among white women, age-specific mortality from PE followed a pattern similar to that seen in white men. Average annual age-specific PE death rates increased during 1962 to 1974 about 50 to 100 percent in both middle-aged and elderly white women. They then declined by approximately 20 percent from 1975 through 1984. Despite the decline, notable increases in age-specific mortality due to PE during the 23 years of observation can be discerned. Annual average age-specific mortality in non-whites follows the pattern noted for whites, with sizeable increases occurring between 1962 and 1974, followed by moderate de-
clines.

Among both men and women, PE mortality among non-white subjects was similar to that in white subjects. The exception was for the middle-aged, among whom non-white subjects' mortality from PE was 50 percent greater than that for white subjects. For both white and non-white subjects, men had higher PE mortality rates than women by approximately 20 percent.

Discussion

The examination of temporal trends in PE occurrence was first considered by Coon and Willis. They reviewed the prevalence of PE at autopsy in their institution. These findings were extrapolated to national vital statistics, suggesting that 47,000 PE deaths had occurred in 1959 in the United States. Other investigators have used similar approaches to examine the number of such deaths for more recent time periods (Table 3). Based on these estimates, there has been a quadrupling of PE mortality in the United States between 1959 and 1982. While such an increase could reflect the aging of the population, it is unlikely that it could be accounted for in its entirety by increased longevity.

The increase in the estimated frequency of PE deaths could be of great significance in that it suggests that the range of individuals who should receive anticoagulants (to prevent the disease) may be overly constrained. Research into the possible expansion of the indications for prophylactic anticoagulation should be considered. On the other hand, with the advances in diagnostic technology that have occurred in the 1959-1982 time period, coupled with a declining autopsy rate, it also is possible that these estimated increases could be erroneous. Also, the increased attention that PE received in the medical literature in the 1960s and the 1970s, coupled with the therapeutic advances in the treatment of the disorder, could explain much of the observed temporal mortality.

Table 2—Relative Change in Age-Specific PE Mortality Rate in the United States, 1962 to 1984, by Race and Sex

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Race, Sex</th>
<th>30-34</th>
<th>35-39</th>
<th>40-44</th>
<th>45-49</th>
<th>50-54</th>
<th>55-59</th>
<th>60-64</th>
<th>65-69</th>
<th>70-74</th>
<th>75-79</th>
<th>80-84</th>
<th>85+</th>
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<tbody>
<tr>
<td>White</td>
<td>Men</td>
<td>43*</td>
<td>23†</td>
<td>25‡</td>
<td>14‡</td>
<td>37‡</td>
<td>36‡</td>
<td>21‡</td>
<td>32‡</td>
<td>36‡</td>
<td>50‡</td>
<td>56‡</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>1‡</td>
<td>10‡</td>
<td>43‡</td>
<td>75‡</td>
<td>49‡</td>
<td>44‡</td>
<td>49‡</td>
<td>48‡</td>
<td>37‡</td>
<td>42‡</td>
<td>58‡</td>
<td>66‡</td>
</tr>
<tr>
<td>Non-white</td>
<td>Men</td>
<td>44</td>
<td>20*</td>
<td>50*</td>
<td>41‡</td>
<td>29‡</td>
<td>50‡</td>
<td>48‡</td>
<td>16‡</td>
<td>19‡</td>
<td>31‡</td>
<td>103‡</td>
<td>65‡</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>12‡</td>
<td>2‡</td>
<td>40‡</td>
<td>12‡</td>
<td>12‡</td>
<td>21‡</td>
<td>46‡</td>
<td>54‡</td>
<td>72‡</td>
<td>71‡</td>
<td>54‡</td>
<td>79‡</td>
</tr>
</tbody>
</table>

*p<0.05 (Cochran-Armitage test).
†p<0.01 (Cochran-Armitage test).
‡p<0.005 (Cochran-Armitage test).
changes. Compounding such efforts is the apparent variability in the skill and persistence of the pathologists who conduct the autopsies upon which the estimates are premised.

During the past decade, Goldhaber and Hennekens used National Hospital Discharge Survey data to establish that the case fatality rate for PE fell markedly during the 1970s, concurrent with an increase in the frequency of the condition's occurrence as noted by Coon.15 Additional survivorship analyses by Goldhaber et al23 and by Lilienfeld et al27 suggest that this decline did not continue during the early 1980s. Weaknesses in these data include both under- and over-diagnosis of the disease.19,10 The effect of these biases on the case fatality rate for PE is not known.

Our data suggest that prior to 1974, mortality from PE increased notably among both the middle-aged and the elderly. The increase was consistent in all four demographic groups examined, suggesting that this rise may have been reflective of mortality patterns for PE and not the result of changes in cause-of-death coding practices nor of changes in the physician's customs in the attribution of the cause of death.6 Similar mortality patterns have been reported recently in Canada.20 It would be useful to examine PE mortality in the context of all causes of death and not only as an underlying cause.21 Such investigations could establish whether either phenomenon contributed to these trends.

The effect of improved diagnostic techniques that were introduced between 1962 and 1984 is difficult to discern in these data. We think it is likely that such improvements account for much of the increase. The diagnostic difficulties that attend using PE mortality data have been investigated by Dismuke and Vander Zwaag.22 Dismuke and Vander Zwaag also reviewed autopsy diagnoses of PE as compared to the death certificate statement and found only "fair" agreement between the two. However, there are selection biases inherent in using autopsy data.6 Nonetheless, this study reinforces the need for caution in analyzing PE mortality data.

In Great Britain, the Office of Population Census and Surveys sampled the deaths in the United Kingdom and found that 21,000 individuals had died of a PE.2,23 However, fewer than 5,000 of the death certificates listed this condition. (No rates were provided.) If this ratio were constant over time, though, the analysis of mortality trends based on death certificates could be used as a proxy for actual PE mortality trends. Similar survey data for the United States are not available. Investigations of such phenomena on a national scale are, however, needed.

It should also be noted that analyses of PE mortality trends have been undertaken for countries outside North America. In both Switzerland and Great Britain, for example, PE mortality has increased.24,25 Examination of the increases in the United States, Canada, Great Britain and Switzerland might suggest which specific groups were at increased risk of the condition. In Britain, the increase in mortality apparently followed a rise in incidence (at least through 1968).25

The decline in United States PE mortality observed since 1974 may indicate the impact either of a decline in case-fatality for a decrease in the incidence of the condition. Case fatality for PE declined notably during the 1970s, but it did not change markedly in the early 1980s.17,24,26 A recent report by Dismuke and Wagner suggested that the incidence of the disease in the United States is in decline.27 Further investigation of trends in incidence, prevalence and case fatality for PE in the United States in the early 1980s are now needed to study the possible effect of such changes.

Three demographic contrasts also are apparent in our data. First, men more than women are at increased risk of death from PE. This elevated risk is present in all five time periods. It is particularly notable in the age-specific rates after age 49 years in both white and non-white subjects. This increased risk may reflect a greater case fatality rate or it may indicate a higher incidence of the disease. The elevated risk of coronary heart disease for middle-aged men is well-established. There are a variety of risk factors that could contribute to the male-female differential. It is possible that such thrombogenic factors could lead to the development of a fatal embolus. Nonetheless, the United States experience contrasts with that for Switzerland and for Britain. In Switzerland, men and women have had similar age-adjusted PE mortality rates for much of the past two decades.24 Age-specific PE mortality data for the Swiss have not, however, been analyzed. In Britain, women have an age-adjusted deathrate from PE that is twice that for men.29 This difference has persisted for at least two decades. As with the Swiss data, though, age-specific data for the British have not been analyzed. Comparisons of Swiss and British age-sex-specific PE death rates with those for the United States, coupled with analyses of surgical procedure

<table>
<thead>
<tr>
<th>Investigators</th>
<th>Year</th>
<th>Estimated Annual No. of Deaths</th>
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<tbody>
<tr>
<td>Coon and Willis*</td>
<td>1959</td>
<td>47,000</td>
</tr>
<tr>
<td>Soloff and Rodman*</td>
<td>1967</td>
<td>&gt;50,000</td>
</tr>
<tr>
<td>Hume, et al*</td>
<td>1970</td>
<td>142,000</td>
</tr>
<tr>
<td>Alpert and Dalen*</td>
<td>1975*</td>
<td>193,790</td>
</tr>
<tr>
<td>Hume*</td>
<td>1976</td>
<td>189,000</td>
</tr>
<tr>
<td>Bell and Simon*</td>
<td>1982</td>
<td>214,440</td>
</tr>
</tbody>
</table>

*Based upon underlying cause of death data.  †Based upon multiple causes of death data.
rates, anticoagulant utilization rates and other phenomena that might impact on the occurrence of PE might provide some insight into this sex differential.

Second, non-white subjects are at increased risk of PE death compared with white subjects. The reasons for this differential are not clear. Although white and non-white subjects have experienced different accessibility to health care, it does not appear that such a contrast would contribute to the observed differential. This rate differential may therefore reflect differences in the occurrence of the disease for reasons that are not clear. Further inquiry into this differential might provide much information on the etiology of PE.

Third, older individuals are at greater risk of death from a PE than are younger individuals. Yet, Goldhaber et al did not find age to be a risk factor for PE in the Framingham cohort.6 Other investigators have, however, found age to be a prominent risk factor for PE mortality.20,23,27 The reasons for this effect have not been established.

There is much opportunity for epidemiologic work on the etiology of PE. The mortality data that we have reported should provide a basis for these epidemiologic endeavors to go forward. Until the epidemiologic picture of this disease is further developed, efforts aimed at its prevention will be difficult to design.

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13 Coon WW, Willis PW III. Deep vein thrombosis and pulmonary embolism. Am J Cardiol, 1959; 4:611-21