Progress in Stroke Research

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Roger M. Greenhalgh & F. Clifford Rose, *Editors*

PROGRESS IN STROKE RESEARCH: 1

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Foreword

Professor A. J. Harding Rains

In terms of benefit to the patient, the centre of our medical universe, much has taken place with regard to strokes in the past 25 years. Progress has been possible through development in scientific effort through measurement, technological advances and a continued and high standard of the clinical art. Especially significant is the coming together in academic and clinical linkages of those in the different disciplines of medicine who are devoted to a subject such as this. What is particularly encouraging also is the coming together of pure scientists with clinicians and those in professions allied to medicine. Furthermore it is realised that progress is also being made through an international effort.

It is right that we should question any progress claimed in terms of gain versus risk. Does progress offer gain in understanding of causes, gain in knowledge of pathology and physiology, gain in assessment techniques especially those which are non-invasive, gain in methods of treatment and rehabilitation, and does it offer reduction of risks inherent in such progress?

I welcome this opportunity of publicising the contribution of this book to a wider international audience, relating as it does the progress that is being made for the patient's sake and stimulating continuing effort towards progress in the future.

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Part I Pathophysiology of Stroke

Chapter 1

EPIDEMIOLOGICAL ASPECTS OF STROKE

S Haberman, R Capildeo and F Clifford Rose

Introduction

One in three persons will develop cerebrovascular disease. It is the third most frequent cause of death in England and Wales, and the probability of ultimate death from it is 1 in 8 [1].

We shall discuss the trends in mortality rates for England and Wales since 1958 (when the Seventh Revision of the WHO International Cause of Death Classification was introduced), with a view to answering the following questions:

(a) Have the mortality rates for cerebrovascular disease, overall and subdivided by age, sex and pathology, changed, and if so to what extent?
(b) What are the possible explanations for such changes, and, in particular, is there any relationship with the corresponding trends for hypertensive disease and ischaemic heart disease?

Method

The main source of data in this review is the officially published mortality statistics for England and Wales, for the years 1958 to 1975 [2,3]. Where possible, information from OPCS Quarterly Monitors [4] was used to provide information relating to 1976. The official 'cause of death' statistics are derived from the underlying causes as stated on the death certificate by the certifying physician.

When comparing the mortality rates for any two years by a single-figure index, the effect of the difference in the age and sex structures of the two populations must be eliminated. This is achieved by calculating age- and sex-adjusted mortality rates, rather than crude rates. The England and Wales population for 1973 has been used as the standard (the male population to standardize the male rates, and the female population for the female rates). The 1973 population has been used so that reference can be made to results recently published [5].

For measuring the significance of time trends in mortality rates, Kendall's rank correlation coefficient, T, between the rate and the year of occurrence has been calculated. Allowance was made for tied ranks by using the tables published by Sillitto [6].

An alternative approach to estimating the significance of trends in age- and sex-specific mortality rates is to fit a straight line of the form:

$$\log_e(\text{mortality rate}) = \alpha + \beta t \text{ where } t = \text{calendar year.}$$

The fit was made using a least-squares approach. Tests may then be performed to ascertain whether the estimate of a particular slope, $\hat{\beta}$, is significantly different from zero, and whether the difference between the estimate of two slopes, $\hat{\beta}$, is significantly different from zero (in particular, this second test may be applied to corresponding male and female trends).

Accuracy of the Data

The official mortality statistics for England and Wales are well presented, but the accuracy of the data cannot be accepted without reservation. Thus, in a study of the accuracy of death certification, the diagnoses before and after autopsy for a group of cerebrovascular disease deaths in England and Wales showed wide disagreement [7].

There are at least six potential sources of bias impeding the use of mortality statistics for epidemiological analysis [8,9], viz:

(a) Diagnostic difficulty
Since cerebrovascular disease involves an interference with neurological function, a diagnosis of stroke is usually straightforward.

(b) Lethality of the disease
When the case fatality rate is less than 100% (as with cerebrovascular disease), the question arises of how the survivors compare with those who die. If cerebrovascular disease were an illness of short duration with an inevitably fatal outcome, then the diagnosis of cerebrovascular disease would invariably appear on the death certificate. But most stroke patients do not die within a short period [10], survivors dying from myocardial infarction, pneumonia or other unrelated illnesses. For this reason, cerebrovascular disease may not appear on the death certificate. This feature depends to some extent on the severity and persistence of residual signs.

(c) Contributing causes
Possible errors in estimating the numbers of deaths attributable to a particular cause arise because that cause may frequently be listed on the death certificate as a *contributory* cause rather than an *underlying* cause of death. This was found in the US study of multiple causes of death – in 1955, cerebrovascular disease was stated as an underlying cause of death in only 57.1% of the cases where it was mentioned on the certificate [11].

The source of this error is the variability between certifying doctors in choosing cerebrovascular disease as an underlying cause of death when there are multiple pathologies present.

(d) Statistical processing
The problems of statistical processing include:
(i) changes in the rules and procedures for the classification of causes of death;
(ii) changes in the classification code of causes of death, and their misinterpretation.

To avoid such heterogeneity, we have considered a period that spans only one revision of the WHO International Cause of Death Classification (1967).

The effect of the 1967 Revision on numbers of cerebrovascular disease deaths has been estimated by the Registrar General [12] as decreasing the numbers of deaths by 0.2% for both sexes. Clearly, this is not an important effect.

For the major pathological types of cerebrovascular disease, the Registrar General does not produce revised estimates of the numbers of deaths before 1968, so that it is only possible to discuss the trends for these subgroups from 1968.

(e) Reporting of age at death
This is not thought to be significant. The use of age-groups eliminates any potential error from this factor.

(f) Calculation of total population numbers
The computation of mortality rates involves using for the denominator census totals or estimates of the population total in non-censal years. Errors arise in making such intercensal estimates, but they are not thought to be significant for England and Wales, which has an accurate and complete system of vital registration. Thus, Cox [13] reports a 0.008% error in the estimate of the 1931 population, when compared with the census total.

Of these six potential errors, two, (b) and (c), are thought to be important for cerebrovascular disease. If the errors are constant in magnitude between years, and the subgroups of the population under consideration are homogeneous, then mortality data may furnish valuable epidemiological information. The epidemiological value of mortality statistics depends on how clearly they estimate the underlying incidence of disease in the population. The most important consideration is not whether the mortality rates tend to underestimate the actual disease frequency, but whether the differences in mortality by various population characteristics (e.g., age, sex, race) tend to reflect similar differences in the frequency of the disease.

Despite the limitations listed above, the analysis of mortality statistics provides for many purposes an inexpensive and convenient means of obtaining clues to aetiological hypotheses, determining consistency between hypotheses and indicating the frequency of specific diseases in the population [9].

With this justification, many studies have used mortality statistics as a means of approaching the epidemiology of cerebrovascular diseases in England and Wales, US and elsewhere [5,8,14–24]. We propose to apply such an analysis to the statistics for a recent period for England and Wales.

Results

Under the latest revision of the International Cause of Death Classification deaths from cerebrovascular disease are assigned to rubrics 430–438. Each rubric in this group corresponds to a different diagnostic type of cerebrovascular disease. Table I shows the frequency distribution of deaths from cerebrovascular disease between these diagnostic types for 1974 and 1975 [3]; the figures have been rounded to the nearest integer. It is clear that certifying physicians allocate about 50% of cerebrovascular disease deaths to cerebral haemorrhage and cerebral thrombosis, and about 40% to the ill-defined rubrics 436, 437 and 438. Cerebral embolism and transient cerebral ischaemia are rarely used as a cause of death. In view of this concentration of the numbers of deaths and the statistical unreliability