Changes in Survival Following Stroke in Five North Carolina Counties Observed During Two Different Periods

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We evaluated survival following stroke for patients from a five-county area of rural North Carolina enrolled in either of two community hospital-based stroke survey programs. In this area, the first program enrolled 843 stroke patients between 1970 and 1973 and the second program enrolled 786 stroke patients between 1979 and 1980. One-year survival increased from 49% in the first program to 62% in the second for all stroke patients, from 54% to 68% for patients with cerebral infarction, and from 18% to 55% for patients with cerebral hemorrhage. While other reports have attributed declining stroke mortality to a decline in the incidence of stroke, our study suggests that increased survival after stroke may account for a large portion of the decrease in stroke mortality. (Stroke 1989;20:345–350)

There has been a well documented and dramatic decline in stroke mortality1-5 since 1914 as well as much speculation regarding its cause(s). Declining stroke mortality must result from lowered stroke incidence and/or improved survival following stroke. Whisnant4 demonstrated a decrease in stroke incidence in Rochester, Minnesota, that he attributed to advances in antihypertensive therapy. In reviewing Whisnant’s report, Hachinski6 agreed that the decline in mortality could be explained by a decrease in incidence but questioned whether more effective and widespread treatment of hypertension was the singular cause of the decline.

The extent to which incidence studies conducted in “special” communities such as Rochester, Minnesota, or Framingham, Massachusetts, are representative of the US population may be debated. For example, Whisnant4 noted that “antihypertensive treatment was used rather frequently in Rochester after 1955...”, a situation that clearly did not reflect practices in average health care. Dyken7 noted that the relatively small improvement in acute stroke survival in Rochester (from 80% in 1945–1949 to 82% in 1970–1974) may indicate a higher quality of medical care earlier. Because a high standard of health care has been the norm in these special communities, improvements in their case fatality rates may not be representative of the situation for the nation as a whole.

Nationwide, survival after stroke has also apparently been improving in both acute and long-term studies.7 Despite problems of comparing studies performed in different geographic/medical settings, Dyken7 has observed that in studies completed before 1965 acute survival (38–63%) was much lower than in studies completed after that date (70–81%); he also noted similar improvements in long-term survival. Increased survival may be more important to declining stroke mortality nationwide than is apparent in either Rochester or Framingham.

Expected survival after stroke has profound implications, not only for the patient and his or her care, but also for planners of health care systems. Previous studies of survival following stroke8-12 have identified numerous factors related to survival after stroke, including stroke severity, age, history of previous stroke, presence of cardiac disease, diabetes mellitus, and hypertension, and consciousness level at admission. However, the calendar year of
Subjects and Methods
Two large-scale community hospital-based stroke survey programs have been conducted in North Carolina: the North Carolina Comprehensive Stroke Program and the Community Hospital-Based Stroke Program. These two programs will be referred to as the old and new programs, respectively.

The old program recruited 2,519 patients from 25 community hospitals in 20 rural counties between 1970 and 1973. Health professionals from individual hospitals (counties) in the program were recruited and trained over a 3-year period, from 1969 to early 1972. Hence, periods of active accrual of patients varied across the counties from 1 to 4 years. The old program was designed to evaluate the magnitude of the stroke problem and to train health professionals in the care of stroke patients. Extensive data were collected using an observational study design. Follow-up was performed on a regular basis for 5 years.

The new program recruited 1,447 patients from 15 rural counties between 1979 and 1980. For all five counties in this report, recruitment began in December 1978 and ended in January 1980. The new program’s goal was to determine if there was an improvement in patient prognosis attributable to coordinated care of stroke patients. The new program was a case-control study; case counties had coordinated stroke care, while control counties did not. A 1-year follow-up was available for these patients, and 1-year survival rates did not differ significantly between case and control counties.

Stroke patients from Cumberland, Scotland, Moore, Harnett, and Richmond (relatively rural eastern North Carolina) counties participated in both programs. In this five-county area, there were 843 patients in the old and 786 patients in the new program. Based on the 1970 and 1980 US census data for these five counties, recruitment averaged 0.176 patients/100,000 population-days ([number of patients×100,000 population-days]÷[days of participation×population of county]) in the old and 0.237 patients/100,000 population-days in the new program.

We report the survival of all stroke patients (regardless of stroke category) and the survival rate of two subgroups: patients who had suffered cerebral infarction and those who had suffered cerebral hemorrhage. Since follow-up in the new program was only 1 year, we compared 1-year survival. Univariate differences were examined using Kaplan-Meier estimation techniques with log-rank testing, and multivariate adjustment for demographic factors and concurrent diseases was examined using proportional hazards techniques (Cox regression). The hazard is a function of time, representing the instantaneous probability of death at a given time, conditional on survival to that time. The hazard ratio estimates the relative strength of prognostic factors (including differences between the two programs) and is the hazard of one group of patients (say those in the new program) relative to the hazard of another group of patients (say those in the old program).

Results
US vital statistics and census data indicate that the cerebrovascular mortality rate in the five-county area was 89 deaths/100,000 in 1970 and 68 deaths/100,000 in 1980, a 24% decline. There were also decreases in coronary mortality, from 375 to 332/100,000 (an 11% decline) and total mortality, from 761 to 691/100,000 (a 9% decline).

A description of the patients in the two programs is provided in Table 1. Although there were no significant differences between the programs’ age/race/sex composition, the new program had a significantly larger proportion of patients reporting concurrent diseases, including previous stroke, cardiac disease, diabetes mellitus, and hypertension. The proportion of patients conscious at admission was also significantly greater in the new program.

Figure 1 shows the Kaplan-Meier survival curves for the old and new programs. Mean±SEM 1-year survival was 49±2% for patients in the old program and 62±2% for patients in the new program, a significant improvement (p=0.0001). With no other covariates in the model, the hazard in the new program was estimated to be 0.64 times that in the old. To examine whether differences in survival were attributable to other factors, we also performed proportional hazards analysis adjusting for the significant covariates race, age, history of diabetes or hypertension, and consciousness level at admission.
admission. The results are presented in Table 2. The effect of program remained significant \((p=0.0002)\), with an estimated hazard in the new program 0.66 times that in the old. Hence, the covariate adjustment increased the estimated hazard ratio (new:old program) from 0.64 to only 0.66.

Figure 2 shows the Kaplan-Meier survival curves for patients diagnosed as having a cerebral infarction. Mean±SEM 1-year survival was 54±2% in the old and 68±3% in the new program. The univariate hazard in the new program was estimated to be 0.64 times that in the old. Table 2 also reports the proportional hazards analysis for patients suffering cerebral infarction. After adjustment for other significant covariates (age, history of diabetes or hypertension, and consciousness level at admission), the effect of program was still (marginally) significant \((p=0.0175)\). The covariate adjustment increased the estimated hazard ratio by 12%, to 0.72.

Figure 3 presents Kaplan-Meier survival curves for patients with cerebral hemorrhagic events. Mean±SEM 1-year survival for patients in the old program was only 18±4% compared with 55±8% in the new program. The proportional hazards estimate of the univariate hazard in the new program was 0.33 times that in the old. Multivariate proportional hazards analysis for patients with cerebral hemorrhages (Table 2) showed that after covariate adjustment for other significant factors (history of cardiac disease and consciousness level at admission), the hazard ratios are as follows: Race (nonwhite:white); Age ([age+1]:age); Cardiac disease, Diabetes mellitus, Hypertension, and Unconsciousness (yes:no); and Program (new:old).

<table>
<thead>
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<th>Factor</th>
<th>All strokes</th>
<th>Infarctions</th>
<th>Hemorrhages</th>
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<tr>
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<td>Proportional hazards coefficient</td>
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<td>Hazard ratio</td>
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<tr>
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<td>—</td>
<td>—</td>
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<tr>
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<td>0.0252</td>
<td>1.28</td>
</tr>
<tr>
<td>Hypertension</td>
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<td>0.0046</td>
<td>0.78</td>
</tr>
<tr>
<td>Unconsciousness</td>
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<td>0.0001</td>
<td>3.04</td>
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<tr>
<td>Program</td>
<td>−0.415</td>
<td>0.0002</td>
<td>0.66</td>
</tr>
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</table>

Hazard ratios are as follows: Race (nonwhite:white); Age ([age+1]:age); Cardiac disease, Diabetes mellitus, Hypertension, and Unconsciousness (yes:no); and Program (new:old).
Follow-up Time (Months)

Figure 3. Kaplan-Meier survival after cerebral hemorrhage in five North Carolina counties. Old program, dashed line; new program, solid line.

Discussion

Between the 1970s and 1980s, we observed a large reduction in case mortality following stroke in the five-county area. The 1-year survival rates for all strokes improved from 49% in the old to 62% in the new program. One-year survival rates for patients diagnosed as having suffered a cerebral hemorrhage increased dramatically, from 18% to 55%, whereas 1-year survival rates for patients diagnosed as having had a cerebral infarction increased from 54% to only 68%. Survival rates for the categories of stroke should be regarded with caution since the clinical diagnosis of hemorrhage versus infarction may be subject to substantial errors. Previous reports have estimated that as many as 24% of hemorrhages would be mislabeled as infarction by clinical diagnosis. Differences between programs were apparent in the frequency of hemorrhage, infarction, and nonspecific diagnoses, which we attribute to the diligence of a single clinical neurologist who personally reviewed the medical records of all patients in the old program.

Initially, we considered changes in the patient profile (demographic factors, concurrent diseases, and consciousness level at admission) as explanations for the differences in survival rates. However, there were no significant differences in the age/race/sex profiles of these two patient populations, characteristics that we are confident were measured consistently across programs.

A significant decline in the proportion of patients unconscious at admission was evident (42% in the old compared with 28% in the new program). Whisnant\textsuperscript{4} also noted a similar decrease over time in the percent of unconscious patients, which he attributed to the mislabeling of small intracerebral hemorrhages before the era of computed tomography. Because of the rural setting of the hospitals in these programs, few patients in either program received CT scans; hence, we are reluctant to attribute the decrease in the proportion of patients unconscious at admission to improved diagnostic criteria.

Evaluation of the consciousness level at admission does allow for differences in operational definitions. However, it seems unlikely that such a large discrepancy in the proportion of unconscious patients admitted would result from changes in the operational definition of consciousness levels alone. Regardless, statistical adjustment for the consciousness level at admission could not explain the differences in survival between the two programs (unconscious as well as conscious patients had improved survival in the new program).

The reported rate of concurrent diseases was higher in the new than in the old program. We suspect that this increase is due to increased awareness of health conditions and not to a real increase in the prevalence of concurrent diseases. Again, statistical adjustment for the reported incidence of concurrent diseases could not explain the differences in survival between the two programs.

As with any observational study, other sources of potential bias might have influenced the differences in the reported survival rates. These include referral patterns, ability to diagnose stroke, caseness ascertainment, and risk factors.

Referral patterns could have changed over time, with an increased proportion of patients with severe strokes being referred to regional medical centers. This hypothesis could explain the new program's having a larger proportion of patients with less severe strokes, but this is not supported by the increase in accrual per population-day of exposure compared with the old program. If patients with severe strokes in the new program were more likely to be transferred to regional medical centers, then we would anticipate a decrease in accrual rates. We believe that a substantial change in referral patterns between 1970 and 1980 is unlikely for several reasons: 1) both programs included all hospitals in the five-county area, 2) stroke patients in rural areas tend to be admitted initially to a local hospital (these counties were chosen in part because of their relative remoteness from medical centers; none of the five counties were contiguous with a county containing a teaching medical center), 3) both programs registered and followed even patients who were admitted for only a brief stay in the community hospital before transfer to a larger facility (such as a
medical center), and 4) we could ascertain no major intervention during the decade that would have affected referral patterns.

The clinical and technical ability to diagnose stroke could have improved, again allowing for the identification and inclusion of a larger proportion of patients with milder strokes in the new program. Admittedly, this hypothesis is supported by the increase in accrual per population-days of exposure. However, our attempt to control for differences in stroke severity by including consciousness level at admission as a covariate failed to account for the differences in survival between the two programs. It is possible that, within each consciousness level, the new program contained patients with milder strokes; that is, among unconscious patients the new program’s patients had milder strokes than those of the old, and similarly among conscious patients; we have no data to address this concern. However, only to the extent that differences exist within consciousness levels between programs could differences between stroke severity act as a factor leading to the observed differences in stroke survival.

Case ascertainment may have differed as a result of the (somewhat) different protocols of the two programs, and the prevalence of important but unmeasured risk factors such as smoking may have changed over time.

In spite of these factors, we believe there are several reasons why the comparison of these two programs offers the opportunity for cautious evaluation of the changes in stroke survival rates over time.

Patients in both studies represent (primarily) clinically diagnosed strokes in a rural section of North Carolina. The absence of a high rate of CT scanning in the new program allows for a more substantial comparison as identification of strokes in both programs was primarily based on clinical criteria.

The goal of both programs was to record and document all stroke patients hospitalized during the recruitment periods. In both programs, the primary screening was prospective; therefore, not all stroke admissions may have been initially documented. Both programs, however, supplemented the prospective screening with an additional retrospective review of patients hospitalized with strokes.

The factors known to be most predictive of survival after stroke (age, sex, and consciousness level at admission) represent objective measures that allow for greater consistency across studies. After statistically controlling for these factors, the differences between the two programs remain. That is, the survival of patients of the same age and sex and with the same consciousness level at admission was improved in the new program.

Even the most carefully controlled longitudinal studies are subject to bias resulting from changing definitions, personnel, and technologies. It is not clear that the differences between these two programs are necessarily greater than those that occur in other prolonged longitudinal studies.

The improvement in survival following stroke during the 1970s in rural North Carolina might have resulted from:

1. Better medical control of risk factors. More efficacious and widespread treatment of risk factors such as hypertension could reduce the severity of strokes. This hypothesis is consistent with the reduction in the proportion of comatose patients admitted to the new program and to the increase in reported hypertension.

2. Improved emergency medical care. Prompt and aggressive patient care before admission could be a factor in the reduction of the proportion of unconscious patients admitted. However, this could also lead to an increase in stroke mortality by allowing patients with poor prognoses for survival to be admitted to the new program, whereas these patients would have died before hospitalization in the old program.

3. Improved in-hospital care. The largest improvement in case mortality was for patients with cerebral hemorrhage. These are the patients in whom death most often occurs shortly after the event, usually in the hospital. Improved in-hospital patient care could substantially contribute to improving the prognosis of this group.

The impact of an increase in survival on stroke mortality rate can be estimated as follows. During 1970 there were 89 stroke deaths/100,000 residents. Let us assume that all deaths directly attributable to stroke occur in the first year after the stroke. This assumption appears to be reasonable as 576 of the 589 deaths attributed to a stroke in the old program occurred during the first year; these 576 deaths represent 54% of the 1,063 first-year deaths. Hence, let us assume that 54% of all deaths during the first year following a stroke are attributable to cerebrovascular diseases.

Under these assumptions, the observed stroke mortality rate of 89/100,000 in 1970 corresponds to an all-cause mortality rate of 164/100,000 (89+0.54) during the first year following stroke. The estimated 1-year survival of stroke patients in the old program was 49%; hence, stroke mortality was 51% and the number of strokes (incidence) in 1970 may be estimated as 322/100,000 (164+0.51). Assuming no change in stroke incidence from 1970 to 1980, the all-cause mortality rate using the 1980 1-year stroke survival rate of 62% and hence stroke mortality rate of 38% would be 122/100,000 (322×0.38). Again assuming that 54% of all deaths during the first year were directly attributable to stroke, this would correspond to a stroke mortality rate of 66/100,000 (122×0.54), which is only marginally smaller than the 68/100,000 stroke mortality rate estimated from the 1980 vital statistics in these five counties. Under these assumptions, the decline in stroke mortality may be completely explained by changes in stroke survival.

We do not suggest that the entire decline in stroke mortality was due to improved stroke survival. In
fact, we doubt that the sustained decline in stroke mortality, persisting since at least 1914, is due to any single cause (incidence or survival). However, increased survival does appear to have been a major component in the declining stroke mortality rates during the 1970s in rural eastern North Carolina.

References
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