Original Contributions

Secular Trends in Stroke Incidence and Mortality

The Framingham Study

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Background: **The reduction in US stroke mortality has been attributed to declining stroke incidence. However, evidence is accumulating of a trend in declining stroke severity.**

Methods: **We examined secular trends in stroke incidence, prevalence, and fatality in Framingham Study subjects aged 55–64 years in three successive decades beginning in 1953, 1963, and 1973.**

Results: **No significant decline in overall stroke and transient ischemic attack incidence or prevalence occurred. In women, but not men, incidence of completed ischemic stroke declined significantly. Stroke severity, however, decreased significantly over time. Stroke with severe neurological deficit decreased in later decades, with a fall in rates of severe stroke cases in which patients were unconscious on admission to the hospital. There was no substantial change in the case mix of infarcts and hemorrhages and no decline in hemorrhage to account for the decline in severity. The proportion of isolated transient ischemic attacks increased significantly over the 30 years studied, yielding an apparent and significant decline in case–fatality rates in men only.**

Conclusions: **Secular trends in stroke incidence and fatality did not follow a clear or definite pattern of decline. While a significant decline in stroke severity occurred over three decades, incidence of infarction fell only in women. The decline in total case fatality rates occurred only in men and resulted largely from an increased incidence of isolated transient ischemic attacks. The severity of completed stroke was significantly lower in the later decades under study. (*Stroke* 1992;23:1551–1555)**

KEY WORDS • **epidemiology** • **incidence** • **mortality**

Mortality rates for stroke in the United States have declined steadily since 1915, averaging 1% per year until the mid-1960s. In the 1970s, the decline accelerated to approximately a 7% per year pace,[1] but in recent years the pace of decline has slowed.[2,3] There is little doubt that this decline is real and not an artifact of reporting or death-certificate coding; the decrease in death from stroke has occurred in both sexes, in whites and blacks, in all regions of the United States, and over several revisions of the ICDA (International Classification of Diseases Adapted for use in the United States). Furthermore, death from stroke has declined coincident with diminishing total death rates, led chiefly by falling cardiovascular disease death rates.[1,2]

The key element in the decline is thought to be a fall in stroke incidence, a consequence of the successful nationwide program to identify and treat hypertension.[1,4] However, there has been a decrease in stroke case–fatality rates, resulting either from improved treatment of stroke patients or a decrease in stroke severity,[5–7] although not all studies have noted this decrease in case–fatality rates.[8] To determine the basis of these trends in stroke deaths, incidence, and severity, secular trends in stroke were examined in the general population sample in Framingham, Mass. Members of the Framingham cohort who were 55–64 years of age at the start of three successive decades beginning in 1953 were studied.

Subjects and Methods

The Framingham cohort of 5,070 men and women, aged 28–62 years and free of cardiovascular disease at entry to the study in 1948–1951, has been evaluated by means of biennial examinations. Surveillance has been maintained for the development of cardiovascular disease, including completed stroke and transient ischemic attack (TIA). Methods of recruitment, examination and follow-up, and criteria for diagnosis have been reported.[9,10] Since 1968, a study neurologist has evaluated the subjects in the hospital at the time of stroke to document the event and to determine the specific stroke subtype. In recent years, at least one computed tomo-

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TABLE 1. Secular Trends in Stroke and Transient Ischemic Attack Over Three Decades

	Prevalence at start of decade		10-Year incidence rate			1-Year case–fatality rate	
	n	%	*n*	KM rate (%)	SE (%)	*n*	%
Men 55–64							
Decade 1	8/586	1.4	29/578	5.6	1.0	10/29	34
Decade 2	14/613	2.3	38/599	7.2	1.1	9/38	24
Decade 3	22/714	3.1	47/692	8.0	1.1	6/47	13
Test for trend	$p=0.048$			$p=0.15$		$p=0.034$	
Women 55–64							
Decade 1	8/732	1.1	38/724	5.5	0.9	8/38	21
Decade 2	11/838	1.3	34/827	4.5	0.7	13/34	38
Decade 3	15/893	1.7	40/878	5.1	0.8	7/40	18
Test for trend	$p=0.31$			$p=0.54$		$p=0.76$	

KM rate, Kaplan-Meier estimate rate; SE, standard error.

graphic (CT) scan of the brain has been obtained in most stroke cases. Using this detailed clinical and CT scan information, it has been possible to classify stroke cases according to mechanism: atherosclerotic brain infarction (ABI), including large-vessel atherothrombotic and lacunar infarction; solely TIA (isolated TIA); cerebral embolus from a documented cardiac source (CE); intracerebral hemorrhage (ICH); subarachnoid hemorrhage (SAH); and other miscellaneous causes. In addition to this surveillance, TIAs were ascertained prospectively by systematic questioning since biennial exam 12 in 1972.

The clinical records of each of the 226 incident stroke and TIA cases were reviewed by a neurologist and classified according to two measures of stroke severity on admission to the hospital: level of consciousness and severity of the neurologic deficits. Stroke severity at the time of hospitalization was graded as follows: none, no deficit; mild, a deficit was present in visual, communication, motor and/or sensory realms, but the patient was independent in performance of the activities of daily living; moderate, the deficit was severe enough that the patient required assistance in any one of these spheres; and severe, the patient was functionally dependent on others in two or more spheres. Follow-up has been good; only 7% of the cohort has been lost to follow-up or death after 36 years.

Statistical Analysis

Three cohorts were examined. For computation of incidence, the study group comprised 1,869 men and 2,429 women who were aged 55–64 years and free of stroke at the beginning of biennial examinations 3, 8, and 13, corresponding to three decades beginning approximately in 1953, 1963, and 1973. Stroke incidence during each period was computed as the Kaplan-Meier estimate at 10 years, considering deaths and subjects lost to follow-up as censored observations. The log-rank test, using decade number as an ordered variable and covarying for age at the beginning of the decade, was used to test for trends in incidence rates across the decades.[11]

Stroke prevalence was computed as the percentage of all subjects alive at the beginning of each period who had previously experienced a stroke. The 1-year case–fatality rates were computed as the percentage of 10-year-incidence case patients dying within the year after the event. Trends in prevalence and 1-year incidence case–fatality rates were tested by logistic regression, using decade number as an ordered variable and covarying for age at the beginning of the decade. The Mantel-Haenszel χ^2 statistic was calculated to test the association between stroke severity and decade number.[12,13]

Results

Fatality, Incidence, and Prevalence

During the three decades, 226 initial strokes and isolated TIAs occurred: 114 in men and 112 in women. Secular trends in 1-year case–fatality rates, incidence, and prevalence were similar in the two sexes (Table 1). In men, for all stroke types combined, 1-year case–fatality rates fell substantially and significantly from 34% in decade 1 to 24% in decade 2 to 13% in decade 3 (Table 1). Prevalence rates rose significantly from 1.4% to 2.3% to 3.1% in successive decades. Incidence of initial stroke events did not decline; in fact, 10-year incidence of stroke increased steadily from 5.6% to 7.2% to 8.0%, a trend that was not statistically significant. In women, the 1-year case–fatality rate rose then fell. Prevalence rose from 1.1% to 1.3% to 1.7% (Table 1). Ten-year incidence rates did not change appreciably; none of the trends in women were statistically significant (Table 1).

To assess the possibility that a change in mechanisms of stroke might explain these patterns, strokes were tabulated according to subtype by sex in each of the three decades (Table 2). Stroke resulting from hemorrhage was relatively infrequent, accounting for 10% of the total. However, because case–fatality rates for stroke secondary to hemorrhage are substantially greater than those for infarction, the proportion of stroke from intracranial hemorrhage was compared in the three decades. During the 30-year period, there

TABLE 2. Cerebrovascular Disease in Three Successive Decades According to Stroke Subtype

Type	Decade 1		Decade 2		Decade 3	
	n	%	*n*	%	*n*	%
Men 55–64						
ABI	19	66	19	50	21	45
CE	4	14	4	11	10	21
ICH	2	7	3	8	2	4
SAH	1	3	2	5	1	2
Other	2	7	2	5	0	0
Isolated TIA	1	3	8	21	13	28
Total	29		38		47	
Women 55–64						
ABI	23	61	16	47	15	38
CE	9	24	8	24	10	25
ICH	1	3	1	3	1	3
SAH	3	8	4	12	2	5
Other	1	3	1	3	1	3
Isolated TIA	1	3	4	12	11	28
Total	38		34		40	

ABI, atherosclerotic brain infarction; CE, cerebral embolus; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage; TIA, transient ischemic attack.

were 23 hemorrhages in all; seven ICHs and four SAHs in men and three ICHs and nine SAHs in women. Because the numbers were small, intraparenchymatous and subarachnoid hemorrhages were combined. The proportion of stroke from hemorrhage did not change substantially in men and was 10% in decade 1, 13% in decade 2, and 6% in decade 3. In women, the proportion from hemorrhage followed the same trend: 11% in decade 1, 15% in decade 2, and 8% in decade 3. These changes were not statistically significant in either sex.

Transient ischemic attacks followed by stroke were classified according to completed stroke type, not as TIAs. The proportion of cerebrovascular events that were manifested solely as TIAs increased substantially in the latter two decades. In men, only 3% occurred in decade 1; in decades 2 and 3, isolated TIAs accounted for 21% and 28% of all stroke events, respectively (Table 2). In women, the trend was similar; isolated TIAs accounted for 3% of stroke events in decade 1, 12% in decade 2, and 28% in decade 3 (Table 2). If isolated TIAs are removed, the proportion of completed strokes categorized as ABI was nearly the same in the three decades: 68%, 63%, and 62% in men and 62%, 53%, and 52% in women. The trend toward a decline is no longer apparent. Furthermore, the proportion attributed to CE rose in decade 3 in both sexes. None of these trends were significant; however, we may have lacked the power to detect a trend due to the limited number of events.

After excluding these isolated TIA cases, secular trends in incidence and case–fatality rates were not significantly altered in women. In men, the trend toward increasing incidence is no longer seen, incidence rates are flat across the three decades, and the decline in case–fatality rates no longer reaches statistical significance (Tables 1 and 3). Due to the limited number of cases, analysis of secular trends of specific stroke subtypes could be done only for brain infarction. While the overall pattern was similar to that seen for all completed stroke combined, in women the decline in incidence became statistically significant (Table 4).

TABLE 3. Secular Trends in Completed Stroke Over Three Decades (Isolated Transient Ischemic Attack Excluded)

	10-Year incidence			1-Year case–fatality	
	n	KM rate (%)	SE (%)	*n*	%
Men 55–64					
Decade 1	28/578	5.4	1.0	10/28	36
Decade 2	30/599	5.7	1.0	9/30	30
Decade 3	34/692	5.8	1.0	6/34	18
Test for trend		$p=0.87$		$p=0.14$	
Women 55–64					
Decade 1	37/724	5.4	0.9	8/37	22
Decade 2	30/827	3.9	0.7	13/30	43
Decade 3	29/878	3.7	0.7	7/29	24
Test for trend		$p=0.07$		$p=0.75$	

KM rate, Kaplan-Meier estimate rate; SE, standard error.

Stroke Severity

To assess the possibility that secular trends in stroke severity were responsible for the trends in prevalence and fatality, stroke severity and level of consciousness on admission to the hospital of the 226 stroke incidence cases were compared over the three decades (Tables 5 and 6). Retrospective estimation of stroke severity on admission to the hospital could be made in all but seven stroke cases in men and 11 in women and was depen-

TABLE 4. Secular Trends in Atherothrombotic Brain Infarction Over Three Decades

	10-Year incidence			1-Year case–fatality	
	n	KM rate (%)	SE (%)	*n*	%
Men 55–64					
Decade 1	19/578	3.7	0.8	4/19	21
Decade 2	19/599	3.6	0.8	2/19	11
Decade 3	21/692	3.6	0.8	3/21	14
Test for trend		$p=0.83$		$p=0.41$	
Women 55–64					
Decade 1	23/724	3.4	0.7	4/23	17
Decade 2	16/827	2.1	0.5	6/16	38
Decade 3	15/878	1.9	0.5	1/15	7
Test for trend		$p=0.048$		$p=0.53$	

KM rate, Kaplan-Meier estimate rate; SE, standard error.

TABLE 5. Stroke Severity on Admission to Hospital for Completed Strokes (Isolated Transient Ischemic Attack Excluded)

	Decade 1		Decade 2		Decade 3	
	n	%	*n*	%	*n*	%
None/mild	9	15	14	25	24	44
Moderate	29	48	22	40	22	40
Severe	22	37	19	35	9	16
Unknown	5		5		8	
Total	65		60		63	
Test for trend over decades			$p<0.001$			

dent on the information available in the clinical record. Cases of isolated TIA were not included in this severity analysis. For men and women combined, there was a significant increase in the frequency of mild deficits and a marked decline in severe deficits, particularly from decade 2 to decade 3 (Table 5). The prevalence of stroke patients unconscious on admission to the hospital rose slightly from decade 1 to decade 2, then fell significantly from decade 2 to decade 3 in both men and women ($p=0.04$ for men and women combined) (Table 6).

Discussion

Over three successive decades, the prevalence of all stroke events, including isolated TIA, rose, and case-fatality rates fell significantly in 55–64-year-old men; incidence rates rose, but this change was not statistically significant. In women, incidence and case-fatality rates were flat while prevalence rose, but none of the trends were statistically significant. The proportion of cerebrovascular disease events that were isolated TIAs changed substantially over the three decades studied. In both men and women, isolated TIAs as a proportion of total cerebrovascular events rose from 3% in decade 1 to 28% in decade 3. This dramatic increase is more likely to be apparent than real and is probably a consequence of heightened awareness of the importance of these transient events as a harbinger of stroke. It is possible that trends in detection and treatment of hypertension and other risk factors may have exerted a salutary impact on stroke severity, leading to more TIAs than completed strokes. Evidence to support this latter explanation is not available. However, when trends in incidence of completed stroke and brain infarction were examined, a definite decline was seen in women, with rates generally flat and unchanging in men over three decades.

There was a significant decline in the severity of the neurological deficit from stroke, including a reduction in the prevalence of unconsciousness on admission to the hospital in both sexes. The lessening in the severity of the stroke was evident only in the most recent decade, from 1973 to 1983, and resulted from an increase in the proportion of cerebrovascular events due to isolated TIAs and to a real reduction in the severity of completed stroke. Because the number of strokes due to intracerebral and subarachnoid hemorrhage was small, secular trends in stroke severity were largely due to a decrease in the severity of ischemic stroke.

TABLE 6. Percentage of Stroke Patients Unconscious on Admission to Hospital for Completed Strokes (Isolated Transient Ischemic Attack Excluded)

	Decade 1		Decade 2		Decade 3	
	n	%	*n*	%	*n*	%
Men	5/26	19	7/29	24	3/30	10
Women	4/34	12	6/26	23	2/25	8

$p=0.04$ for decade 2 versus decade 3 (sexes combined) by χ^2 test.

In Rochester, Minn., incidence of stroke declined steadily from 1950 to 1979 in women; incidence rates remained flat in men until the 1970–1974 time period when incidence fell in men as well. In Rochester, incidence rates have risen in the most recent quinquennium (1980–1984).[2] Stroke severity has also fallen dramatically in Rochester, where there was a significant ($p<0.001$) reduction in the 30-day case-fatality rates (from 33% during 1945–1949 to 17% during 1980–1984[2]); the 1980–1984 quinquennium coincided with the availability of head CT scan. This trend of falling stroke severity has also been noted in other populations. In a study of stroke outcome in Allegheny County, Pa., age-adjusted mortality rates declined significantly from 1971 to 1980 for four sex-race groups. In addition, hospital case-fatality rates also decreased significantly, from 19.6% to 11% during 1971–1980.[14] The decline in death rates corresponded to a reduction in the severity of stroke. Fewer stroke patients were comatose, and this reduction in the prevalence of coma was thought to reflect the decrease in stroke severity, which the authors found was responsible for more than 80% of the decline in case-fatality rates.

Survival after stroke improved in a five-county rural area of North Carolina, where two community-based stroke survey programs were in operation.[5] The authors compared survival of approximately 800 stroke patients in each of two time periods, 1970–1973 and 1979–1980, and found improved survival (from 49% to 62% overall), with the most striking improvement in survival rate after cerebral hemorrhage (from 18% to 55%). The significant decline in stroke severity and in case-fatality rates accounted for a substantial portion of the improved survival rate after stroke.[5] The decline in death rates, 24% from 1970 to 1980, corresponded to US vital statistics and census data reports for the same five-county area. The authors concluded that the decrease in deaths from stroke mortality resulted not solely from a decrease in incidence but in substantial measure from improved survival after stroke.[5]

A recent report of survival of an age- and sex-adjusted 50% sample of hospitalized stroke patients in the Minneapolis–St. Paul, Minn., metropolitan area in 1970 was compared with that in 1985.[15] Hospitalized stroke 28-day case-fatality rates fell from 27.9% in 1970 to 18.1% in 1985 in men ($p=0.01$) and from 24.0% to 14.9% in women ($p<0.05$). Thus, decreased death rates resulted not from reduced incidence but from improved survival in this metropolitan area between 1970 and 1985, probably as a result of improved medical care of the acute stroke patient.[15]

It seems likely that a number of mechanisms have contributed to the decline in stroke severity. First, increased awareness and recognition of TIAs on the part of the general population and physicians must

explain some portion of the increase in prevalence of these events. This increased recognition would tend to increase the incidence of total cerebrovascular events while reducing the case-fatality rate.

Second, reduction in severity might result from a differential decline in the incidence of specific stroke subtypes with high case-fatality rates, such as intracerebral and subarachnoid hemorrhage. In the Rochester, Minn., population, a decline in intracerebral hemorrhage incidence occurred over 25 years, 1945–1979.[16] It was estimated that 24% of hemorrhages in the years before the advent of the CT scan had incorrectly been attributed to cerebral infarction and that these hemorrhages tended to be smaller and less severe.[15] There has been a clear decline in case-fatality rates for intracerebral hemorrhage in Hisayama, Japan, due in part to a decrease in the incidence of massive ganglionic hemorrhages from 1961 to 1983 in the two cohorts studied in that area of Japan.[17] In addition, decreased case-fatality rates after subarachnoid hemorrhage have been reported in the period 1975–1984 in Rochester and for white men and women in the United States.[18]

The third major factor responsible for the apparent reduction in case-fatality rates is the widespread availability of the head CT scan during the latter half of the 1970s. The resultant improvement in diagnostic sensitivity has probably increased the apparent incidence of stroke by detection of milder cases. Although case ascertainment methods have not changed and clinical criteria for the diagnosis of stroke in Framingham have been constant over more than 20 years, the CT scan has undoubtedly had an impact. Improved diagnostic sensitivity afforded by the routine availability of CT scan in Framingham since 1978 could have had an impact on the second half of the third decade (1973–1983), enhancing detection of milder stroke events. This diagnostic tool may also have contributed to the increase in incidence and the commensurate decline in stroke severity over time. The increased use of CT scan in the late 1970s has been related to an increase in the rate of hospitalization nationwide, with a concomitant decline of in-hospital case-fatality rates.[6] A similar pattern has been reported in Rochester, with an increase in incidence and a decline in severity from stroke overall and according to specific stroke subtype.[3] However, in a study of secular trends in all cardiovascular disease (including coronary heart disease) in the Framingham cohort, the decline in mortality resulted primarily from improved case-fatality rates, with no substantial change in disease incidence.[19]

It has been suggested that the improved survival of coronary heart disease patients has resulted in a group at increased risk for stroke, which might account for the increase in stroke incidence in Rochester in the years 1980–1984.[20] Whether this explanation applies in Framingham is unclear. The complete picture is undoubtedly related to the interplay of a number of factors, including the following: an increase in patients susceptible to stroke, resulting from improved survival of coronary disease patients; a decline in the incidence of severe stroke; decreased stroke case-fatality rates resulting from improvements in medical care; increased awareness of transient neurologic symptoms as harbingers of stroke; and improved technology resulting in increased diagnostic sensitivity. Although there were clear improvements in control of hypertension and reduction of cigarette smoking and serum total cholesterol levels in recent years, no convincing decline in stroke incidence was seen in the Framingham cohort.[19] For the most part, the decline in stroke mortality in Framingham has resulted from a decline in stroke severity, not incidence.

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