Precipitating Factors, Prognosis, and Demography of Cerebrovascular Disease in an Indiana Community: A Review of All Patients Hospitalized from 1963 to 1965 With Neurological Examination of Survivors

BY MARK L. DYKEN, M.D.*

Abstract: Precipitating Factors, Prognosis, and Demography of Cerebrovascular Disease in an Indiana Community: A Review of All Patients Hospitalized from 1963 to 1965 with Neurological Examination of Survivors

As an initial step in studying the characteristics of cerebrovascular disease in a geographically limited segment of population, the hospital records of 285 patients coded as "CNS vascular" in the Elkhart General Hospital (Indiana) were reviewed for the years 1963, 1964 and 1965 by a team of neurology residents, under the supervision of the author. Information from examination of almost half the group by a team of neurologists and data from relatives, family physicians, hospital records and death certificates concerning the remainder led to the conclusion that the original diagnosis of "CNS vascular" could not be substantiated in 25 patients (9%), was cerebral infarction in 125 (53%), cerebral hemorrhage in 40 patients (14%), subarachnoid hemorrhage in 21 patients (7%), generalized atherosclerosis in 24 patients (8%), and transient focal cerebral ischemic attacks in 25 patients (9%).

Disorders such as diabetes, hypertension, heart disease, myocardial infarction, auricular fibrillation and genitourinary disease were significantly more frequent in patients with cerebral infarction than in a group of similar age and sex patients collected from the same hospital in an attempt to form a "contrast group." However, hypertension was the only disorder significantly more often associated with cerebral hemorrhage.

Cigarette consumption was increased at a highly significant level in the males who had infarction and the prognosis was, in general, unfavorably affected by older age, further cerebrovascular events, and abnormal electrocardiograms. Eighty-three percent of the patients with cerebral hemorrhage died during initial hospitalization.

Introduction

The purpose of this report is to describe the types, characteristics, and three-year course of all patients with cerebral vascular disease admitted during the years 1963, 1964 and 1965 to the only hospital for a well-defined community of approximately 42,000 people in Indiana. This study is unique for the following reasons: (1) The patients were the entire diagnosed cerebral vascular disease population from the only hospital serving a community of approximately 42,000 people. (2) The medical staff and the hospital were highly regarded.
and patients tended to stay in the community for diagnosis and treatment. (3) Sixteen medical specialties were represented, but not neurology or neurosurgery, which might attract special referrals. (4) An independent examination of charts, informants and survivors was performed under the direction of a neurologist who was based in a medical center 150 miles from the community, so that he had no influence upon the initial referral, treatment or progress of the population. (5) Very few patients were lost during the follow-up period. (6) Comparisons were made with a population of control patients matched by sex, age, race and year of admission.

Methods

All admissions to the Elkhart General Hospital were reviewed for the years 1963, 1964 and 1965 by trained social workers, and charts with a diagnosis coded “CNS vascular” were identified. A team of neurology residents, under the supervision of the author, evaluated each case and confirmed or appropriately changed the diagnosis. Once these “CNS vascular” patients had been identified, patients diagnosed as having “trauma” during that year were selected as controls and matched for age, sex, race and time of admission. Although it is well known that patients with trauma may have characteristics different from the general population, the control patient had to have been hospitalized. If we had excluded cardiovascular disease, and matched only by age and sex, our controls would have consisted largely of patients with malignancies or other chronic debilitating illnesses. Patients with trauma were the only large group that most closely resembled the general population.

When a “CNS vascular” patient survived the identifying hospitalization, the field workers used all available community resources to locate him or, in case of his demise, an informant. If he died later, relatives, friends, family physicians, hospital records, and death certificates were reviewed to answer questions as reliably as possible. Of the 102 living patients, 97 (95%) were examined.

In the material that follows and in the tables, when a significance level is given it is obtained by either Chi square test or a t test for significance of difference between two samples for independent samples or nonindependent samples. In all cases, a ± sign stands for one standard deviation.

Results

Of the total 285 patients initially identified as having cerebrovascular disease, 221 were from the city of Elkhart and 60 were from Elkhart.
CEREBROVASCULAR DISEASE IN AN INDIANA COMMUNITY

County and several communities in Michigan on the Indiana-Michigan border. Only four (2%) were not from the geographical area.

The diagnosis was changed to "definitely not cerebral vascular disease" in 13 (5%) of this total (table 1). In an additional 12 (4%), not enough information was available either to identify the patient as having cerebral vascular disease or to rule out this possibility. Twenty-four had had multiple episodes over many years and were admitted for progressive mental deterioration or associated disease with organic sensorial defects. As table 1 summarizes, a firm diagnosis of ischemic cerebral infarction (infarct) was made in 150 cases, of cerebral hemorrhage (hemorrhage) in 40, of subarachnoid hemorrhage (SAH) in 21, and of transient ischemic attacks (TIA) in 25.

The nonwhite population of Elkhart was 5.3% in 1960 and was higher at the time of this study; however, it was a very young nonwhite population, whose members had not reached the age to contribute significantly to this cerebral vascular disease group. Of the total patients, only seven were nonwhite.

Males outnumbered the females 122 to 114. The number in each subgroup is listed in table 2.

The average age of males in the cerebral infarction group was 68.4 years, which was significantly younger than the 73.0 of females (P < 0.02), and in both the male and female populations those who survived were significantly younger than those who died. The mean age of 60 years of the males with cerebral hemorrhage was also significantly less than the mean age of 70 years of females (P < 0.02).

No significant differences in income, type of work, or education were noted in comparisons either of the subgroups or patients and their controls.

A statistically significant increase of cerebral vascular disease in relatives (mother, father or siblings) of patients with infarction (P < 0.005) and transient ischemic attacks (P < 0.005) was noted, but no significant differences were present in those with hemorrhage or subarachnoid hemorrhage.

Although a small proportion of admissions to Elkhart General Hospital were for cerebral vascular disease, the percentage of the deaths in the hospital was about the same as

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<td>Sex</td>
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<td>SAH</td>
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<td>TIA</td>
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<td>Previous CVAs</td>
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*Previous CVAs vs. none.
that reported for the entire city of Elkhart (1960 to 1965), or about 12%. Autopsies were performed on 26% of the total patients who died, but only upon 16% of the cerebrovascular patients who died with cerebrovascular disease.

In only 61% of the patients with cerebral infarction who died in the hospital was cerebrovascular disease listed as the cause of death, and of those who died after discharge from the hospital, it was so listed in only 25%.

The average time of hospitalization was much longer in those who survived in the cerebral vascular groups than in the general hospital patients. The length of time was directly proportional to the severity of the illness (mean: 10.4 days in the TIA group to 37.5 days in the hemorrhage group).

# Predisposing or Contributing Factors

The number of patients engaging in moderate or vigorous exercise at the time of onset of symptoms in the cerebral hemorrhage group was significantly higher ($P < 0.02$) than in the infarction group.

The patients with cerebral infarcts and with TIAs had significantly more previous cerebral vascular episodes than did their controls (table 3).

Related illnesses were higher in the cerebral infarction patients ($P < 0.001$) and the hemorrhage groups ($P < 0.05$) than in controls (table 4). Specifically related diseases that were significantly increased in the cerebral infarction group were diabetes mellitus ($P < 0.005$), hypertension ($P < 0.001$), heart disease ($P < 0.001$), myocardial infarction ($P < 0.005$), auricular fibrillation ($P < 0.005$), and genitourinary disease ($P < 0.005$). Women with cerebral infarction had a mean of 3.5 children compared to 2.1 of the controls (significant $P < 0.01$). No other group demonstrated any significant differences.

Height was compared to that of controls in all subgroups and no differences of significance were present, nor were there significant differences in weight except in females with cerebral infarction. Those who died during the initial admission were compared to their controls and were, on the average, 18 lbs heavier ($P < 0.05$). Those who died following hospitalization were 35.6 lbs heavier ($P < 0.001$). The living female
patients averaged 12 lbs heavier than their controls, but this difference was not significant.

Although cigarette consumption was low in both the cerebral infarction and control groups, the males who had infarction smoked significantly more than did their controls (P < 0.005).

Cerebral hemorrhage related mainly to hypertension, as this was the only individual disease that seemed to be significantly different in the controls than in the study patients (P < 0.01). The patients in the SAH and TIA groups did not have a significantly higher incidence of related diseases than did their controls.

A large number of abnormal electrocardiograms were obtained in both patients and controls. The patients with cerebral infarcts who died after surviving their initial hospitalization had a higher percentage of abnormal electrocardiograms (79%) than did those patients who were living at the time of follow-up (44%).

A significantly higher percentage of those who died after discharge (29%) went to a nursing home than did those who are still living (9%).

Ninety-one percent of the cerebral infarct patients who are still living and 54% of those who died after discharge were able to ambulate in some fashion at the time of discharge. This difference is highly significant (P < 0.005).

**Survival Characteristics**

Patients with cerebral infarcts or with TIAs had significantly more cerebral vascular events than their controls after discharge. Those in the infarct group who died after discharge had more interim cerebral vascular accidents than those who are still living. Of the 25 patients with TIA, ten continued having transient ischemic attacks, three had infarction, two had a combination of infarction and transient ischemic attacks, and ten were completely free of all cerebral vascular symptoms.

In the cerebral infarct group of patients who died after discharge, 71% needed partial to complete care (table 5). This contrasted with 26% of those who were still living. This difference is highly significant. On the basis of the follow-up examination, it was the examiner's opinion that only 20% of the living patients needed partial to complete care and that 80% could either completely care for
themselves or return to some type of occupation (table 5). The actual functional level was far below the functional potential because of the age group. Most of these patients were retired and many lived with children who insisted upon caring for them.

In those with transient ischemic attacks all survived the initial hospitalization. During the 3.13 years of follow-up of this group, seven patients died. In five, the matched control was alive. In one instance the patient died before the control, and in one instance after. Five of the controls for the surviving 18 patients with cerebral infarction died during the time interval studied. Therefore, mortality was exactly the same in both groups. Of the 18 survivors, 16 were capable of returning full time to their previous occupations.

Discussion

Of the 285 patients having coded diagnoses on their charts of "CNS vascular," 12 (4%) had poorly defined phenomena and were classified as indeterminate diagnosis. An additional 13 (5%) did not have cerebrovascular disease as determined by follow-up information or examinations. Of the total group, 53% had cerebral infarction (9% due to embolus), 14% had cerebral hemorrhage, 7% had subarachnoid hemorrhage, 9% had transient ischemic attacks, 8% had generalized atherosclerosis, 4% had an indeterminate diagnosis, and 5% did not have cerebral vascular disease. The stroke population described by Eisenberg et al. in the Middlesex County study was composed of 48% "thrombotic infarctions," 2% embolus, and 36% cerebral hemorrhage (both cerebral hemorrhage and SAH); in 14% the "diagnosis was undetermined." In the Framingham study, 63% of the patients had cerebral infarction due to thrombosis, 18% had subarachnoid hemorrhages, 15% had cerebral embolism, and 4% had intracerebral hemorrhage. Of the patients reported by Marshall and Shaw, 3% had cerebral hemorrhage, 67% had "cerebral thrombosis," and 31% had diffuse cerebral vascular disease. From the available data the reasons for these differences in percentage of diagnostic categories cannot be determined.

Since 221 patients came from the city of Elkhart (population 42,000), a hospitalized cerebrovascular disease incidence rate was calculated at 176 per 100,000 per year. This is similar to other studies; the Middlesex incidence rate was 220 per 100,000 population age-adjusted to the United States population to 170 per 100,000, and the Rochester, Minnesota incidence rate was 174 per 100,000.

The diagnosis in the 150 cases of cerebral infarction was well established. In this group, 13 cases (9%) had cerebral embolism. Other patients may have had embolism, but not enough information was available to make this distinction. The Middlesex County study and the Worcester, Massachusetts study were analyzed and comparisons of mortality were made with our population (table 6). The mortality was higher in Middlesex County and much lower in Worcester than in our population.

Of the Elkhart group, 58% of the cerebral infarctions occurred in males and 42% in

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<td><strong>Comparison of Mortality and Survival in Patients with Ischemic Infarctions</strong></td>
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<tr>
<td>Elkhart</td>
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<tr>
<td>Died in hospital</td>
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<td>Died after discharge</td>
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<td><strong>Comparison of Sex Incidence in Patients with Ischemic Infarctions</strong></td>
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<tr>
<td>Elkhart</td>
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<td>Male</td>
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females. Table 7 compares these figures to those of the Worcester study,\textsuperscript{7} the Middlesex study,\textsuperscript{8} and the Framingham study.\textsuperscript{4} In each of these, the females far outnumbered the males. In the Elkhart study, however, there was no significant difference between the sex composition of the groups who died in the hospital, died after hospitalization, or were still living. Marshall and Shaw,\textsuperscript{9} in their surviving patients, reported 160 males and 91 females, McDowell et al.\textsuperscript{8} 72 males versus 25 females, and David and Heyman\textsuperscript{8} 26 males and 10 females. These data suggest that there are differences in different regions and hospitals in the sex incidence of patients with cerebral infarction.

The average age in Elkhart patients is much higher than the 59 years reported in the Framingham study\textsuperscript{4} but approximates the 74.5 years seen in the Middlesex study.\textsuperscript{8} The wide variation in ages reported in various hospital studies may be related to selection, geographical variation, or the percentage of males versus females. Our males were significantly younger than the females, and in both male and female populations those who survived were significantly younger than those who died. The older age of the females probably reflects the increased number of females living at risk in this age group. Numerous investigators have noted decreased mortality in lower age groups.\textsuperscript{10-12} The increase in all related illnesses listed in table 4 compared to controls must be analyzed with caution as most are interrelated; for example, diabetes mellitus, hypertension, heart disease, previous myocardial infarctions, and auricular fibrillations all may be interrelated.

The mean height was not significantly different from that of the controls. Females who died weighed significantly more than their controls. In addition, women with cerebral infarction had more children than their controls. Women who have had two or more children may differ in other aspects. For instance, Humerfelt and Wedervang\textsuperscript{13} described a significantly lower systolic blood pressure in this group. It is conceivable that women who have more children tend to gain more weight, which may be related to cerebral vascular disease. However, Baker et al.,\textsuperscript{14} in their studies on the role of nutritional factors in cerebral vascular disease, concluded that obesity played no role in cerebral atherosclerosis. The Framingham study\textsuperscript{4} also revealed no significant increased incidence of stroke related to obesity. It may well be that multiparity may be related to increased weight, and the increased weight may be related to some other factor which has a direct effect on cerebral atherosclerosis. Another possibility is that trauma patients in the control group weigh less than similar groups in the general population. This seems unlikely, as all the women who had infarctions were far above the upper limits, and the controls were within the limits of desirable weight as listed by the Metropolitan Life Insurance Company.\textsuperscript{15}

Low cigarette consumption was noted in all groups, but males who had cerebral infarctions smoked significantly more than their controls. Crofton and Crofton\textsuperscript{16} found no apparent relationship to smoking. Kannel et al. reported in the Framingham study that excess development of thrombotic brain infarction appeared to be associated with cigarette smoking but that the numbers were not large enough to be statistically significant.\textsuperscript{4}

Twenty-six (54\%) of the patients who ultimately died had at least one additional cerebral vascular event. Fifteen (25\%) of those who were still living had at least one additional cerebral vascular insult. A high likelihood of further cerebral ischemia or infarction exists following an initial infarction, and this is higher in those who died within three years than in those who survived three years.

When the total cerebral infarction population was compared to the control population, the increased mortality was highly significant. However, when only the patients who survived hospitalization were compared to their controls, the difference was not significant at a 0.05 level. The increased mortality in those patients surviving hospitalization is not nearly as apparent when matched to controls as it is when one looks at raw data.

Thirty-three patients (83\%) with cerebral hemorrhage died during initial hospitalization, and only four survived to the time of follow-up. The seriousness of this condition is stressed by the brief average time of admission to death (2.3 days), the long average hospitalization for the survivors (37.5 days), and the rapidity of hospitalization after insult (2.3 hours). The total population consisted of 17 males and 23 females. The patients with hemorrhages had a significant incidence of hypertension as com-
pared to their controls. This association has been almost universally pointed out.

Only 21 patients had subarachnoid hemorrhage, making reliably significant comparisons impossible.

The incidence of cerebral vascular disease in relatives of the patients with transient ischemic attacks was significantly higher than in the controls. This was calculated at a probability of less than 0.005 despite the small series.

A significantly higher percentage of previous cerebral infarction or ischemia was reported in the TIA group than in the controls, but 13 (54%) had had no previous attacks of any kind. This would support the contention that this group was selected and that frequently the patients were admitted after the first attack to verify the diagnosis. The TIA group had more subsequent cerebral vascular events than their controls. Ten patients continued to have transient ischemic attacks, three had cerebral infarctions, two had an infarction and transient ischemic attacks, and ten were completely free of all cerebral vascular disease in the follow-up period.

The mortality rate in the TIA group was exactly the same as that in the control group. In this small series, the diagnosis of transient ischemic attacks did not contribute significantly to mortality when matched with control patients of the same age and sex.

Summary

The hospital records of 285 patients coded as "CNS vascular" were studied. Of 102 living patients, 97 (95%) were re-examined by a team of neurologists. Information concerning the 188 patients not examined was collected from relatives, family physicians, hospital records and death certificates. The period of follow-up was three years.

Diagnosis could not be substantiated as some form of cerebrovascular disease in 25 patients (9%). One hundred-fifty patients (53%) had cerebral infarction, 40 (14%) had cerebral hemorrhage, 21 (7%) had subarachnoid hemorrhage, 24 (8%) had generalized atherosclerosis, and 25 (9%) had transient ischemic attacks.

Disorders such as diabetes, hypertension, heart disease, myocardial infarction, auricular fibrillation and genitourinary disease were significantly more frequent in patients with cerebral infarction than in the control patients. However, hypertension was the only disorder significantly more often associated with cerebral hemorrhage.

Prognosis was unfavorably affected by older age, further cerebrovascular events, abnormal electrocardiograms and the type of cerebrovascular disease; 83% of patients with cerebral hemorrhage died during the initial hospitalization.

Women with cerebral infarction were significantly heavier than their controls and had more children.

Cigarette consumption was increased at a highly significant level in the males who had cerebral infarction.

The ultimate survival in the patients who had transient ischemic attacks was identical to that of the controls. Sixteen of the 18 patients who survived were capable of functioning full time in their previous occupations.

Acknowledgments

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