Epidemiologic Features of Isolated Syncope: The Framingham Study

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SUMMARY To obtain epidemiologic information regarding syncope, 2336 men and 2873 women aged 30 to 62 years at entry to the study were evaluated for syncope. During 26 years of surveillance, evidence of cardiac or neurologic morbidity and mortality was also recorded. At least one syncopal episode was reported by 71 (3.0%) of the men and 101 (3.5%) of the women during the course of the study.

Criteria for isolated syncope (i.e., transient loss of consciousness in the absence of prior or concurrent neurologic, coronary, or other cardiovascular disease stigmata) were met by 56 (79%) of the 71 men and by 89 (88%) of the 101 women with syncope. During 26 years of follow-up isolated syncope was not associated with any excess of stroke (including transient ischemic attack) or myocardial infarction. Similarly, isolated syncope was not associated with any excess of all-cause or cardiovascular mortality (including sudden death).

SYNCOPE has been described as a relatively common, potentially dangerous problem that often remains unexplained despite extensive clinical evaluation. The possibility that syncope might at times represent an isolated manifestation of cerebrovascular disease has been raised. A recent one year prospective study of patients with syncope revealed a high overall mortality. An excess of sudden death was found among subjects with syncope with mortality rates ranging from 3 to 24% in one year depending on patient subgroup. The excess mortality was found in patients with evidence of underlying cardiovascular or life-threatening non-cardiovascular illnesses. There was no evidence of excess mortality (including cardiovascular and cerebrovascular mortality) in patients with syncope of unknown etiology and no other major illnesses.

Other retrospective and cross-sectional studies of syncope in patients and highly selected study groups have been reported. More generalizable epidemiologic information regarding syncope from a large well-defined free-living population with selective bias minimized would help to clarify the significance and prognostic meaning of this apparently common symptom. Twenty-six year follow-up of 5209 subjects evaluated biennially in the Framingham Study provides such information on syncope.

The objective of this report is to examine the prevalence, morbidity and mortality associated with isolated syncope (i.e., transient loss of consciousness in the absence of prior or concurrent neurologic, coronary, or other cardiovascular disease stigmata).

Methods

Patients

The Framingham Study has involved 2336 men and 2873 women examined biennially for signs and symptoms of cardiovascular disease (including transient ischemic attacks and stroke) since the initial examinations which took place from 1948 to 1952. These subjects ranged in age from 30 to 62 years (mean 46) in 1950.
Detailed criteria for coronary disease, transient ischemic attack, stroke, sudden and other cardiovascular mortality have been reported elsewhere. Descriptions of the sampling procedures have also been detailed elsewhere. Follow-up has been excellent with less than 5% of the cohort totally lost to follow-up. Information obtained from all available sources including medical records, death certificates, interviews with relatives and postmortem examinations were evaluated by a panel of physicians. These data were used to supplement biennial evaluations to establish the presence or absence of morbidity and to assign a cause of death.

For stroke, including transient ischemic attacks, surveillance was maintained with daily monitoring of all admissions to the only general hospital in Framingham. If a stroke was suspected, the patient was seen in the hospital by the study neurologist. Neurologic signs or symptoms noted by study physicians at a biennial examination were followed by a detailed evaluation in the neurology clinic. Stroke morbidity included acute brain infarctions, embolic strokes and transient ischemic attacks.

Age at the first episode of syncope was solicited from subjects to assess whether the initial episode preceded entry into the study. Eight subjects (including 7 women) gave the age of “childhood” as the time of the initial episode of syncope. Their age at initial episode was approximated at age 15 years. Only subjects with incident cases of syncope reported after entry into the study (i.e., described at the second or later examination) were considered as having syncope in the analyses of morbidity and mortality. In addition (because of the extreme rarity of stroke prior to age 60 years), subjects were excluded from follow-up analyses of isolated syncope if they were less than 35 years of age at entry to the study and, thus, less than 60 years of age after 26 years of follow-up.

Age-decade (and sex-) specific as well as age-adjusted analyses were used to compare morbidity and mortality between subjects with and without isolated syncope.

The basic unit of time in the Framingham Study is an exam cycle, i.e., two years. Each subject is reevaluated for disease status and for a standard set of characteristics every two years. To use this information, we treated each subject’s data at each examination as a separate observation. Thus, a person could contribute data to different categories at various examinations. For incidence data the rates are reported as two year rates. Although these rates are often divided by two and the resultant statistics termed “average annual incidence,” this procedure involves a questionable extrapolation which we chose not to use. Two-year age-adjusted stroke and myocardial infarction rates were of course based only on those subjects who were free of such morbidity at the beginning of each two year interval.

Records of persons with syncope were reviewed by a neurologist (LC) and a cardiologist (DDS) to assure that the criteria for syncope were met. The neurologist and cardiologist who made decisions about the criteria for syncope being met, were unaware of the outcomes (stroke, death, etc.) in these subjects. The study statistician (DLM) was responsible for deriving the outcome information from the computerized follow-up data.

**Results**

**Prevalence of Syncope**

In the course of 13 biennial examinations, 71 (3.0%) of the 2336 men and 101 (3.5%) of 2873 women reported at least one syncopal episode during their lifetime. Fifteen men and 12 women who reported syncope had prior or concurrent cardiac or neurologic stigmata (coronary heart disease N = 21, stroke N = 4, other N = 2). Criteria for isolated syncope were met by 56 (79%) of the 71 men and 89 (88%) of the 101 women. Two of the 56 men were excluded from further analyses because of their young age at entry to the study (less than age 35 years — see Methods). However, inclusion of these two men in the analyses would not be expected to significantly change the results. The distribution of ages at the initial episode of isolated syncope is plotted in figure 1. The mean age at initial episode for men was 52 years (15–78 years) and for women was 50 years (13–87 years).

Nearly all of the men and most of the women had their initial episode of syncope as adults. That is, 50 (98%) of the 54 men and 79 (89%) of the 89 women had their initial episode of syncope when they were 20 or more years of age. More than one episode of syncope was reported by 16 (30%) of the 54 men and 24 (27%) of the 89 women.

Prevalence estimates for isolated syncope by age and sex are given in figure 2. As expected, there was a significant gradient with age in both sexes with prevalence in men ranging from about 7 per 1000 person-exams in men age 35 to 44 to about 56 per 1000 person-exams in men 75 and older. Prevalence estimates were similar in women except in the 75 and older group where men were significantly more likely than women to give a history of isolated syncope (56 versus 36 per 1000 person-exams for men and women, respectively).

![Figure 1. Age at initial episode of isolated syncope, men and women, the Framingham Study. 26 year follow-up.](image-url)
Morbidity and Mortality with Isolated Syncope

Two year age-adjusted stroke and myocardial infarction rates per 1000 person-exams are shown in figure 3. There was no substantial or statistically significant difference in stroke or myocardial infarction rate in those who had isolated syncope compared to those who did not.

Two-year age-adjusted rates for all-cause and cardiovascular mortality as well as sudden death are shown in figure 4. Again, there were no significant differences in any of these categories of mortality for those with and without isolated syncope.

Similarly, age-group (and sex-) specific comparisons revealed no significant differences in these categories of morbidity and mortality between those with and without isolated syncope, with one borderline exception. In the female 35–44 year age group, one (2%) of 49 women with isolated syncope subsequently had a stroke compared to three (0.05%) who had strokes among 5564 (N inflated by “person-exams” approach) without isolated syncope (chi square, 6.25).

Discussion

This study indicates that syncope, in the absence of prior or recurrent neurologic, coronary, or other overt cardiovascular disease stigmata, is not associated with increased morbidity or mortality. This is consistent with the prospective clinical study of Kapoor et al which indicated that patients with syncope secondary to a noncardiovascular or unknown cause are not necessarily at increased risk of sudden death if they do not have severe underlying, life-threatening illnesses. Neither study suggests that isolated syncope is a frequent indication of covert cerebrovascular disease or risk of stroke.

The current study is consistent with clinical studies that have shown that patients with isolated syncope make up a large proportion of patients with syncope. More than 75% of Framingham Study subjects with syncope had isolated syncope. This is apparently true even when the initial episode of syncope occurs in adulthood. The studies cited combined with the current study suggest that a careful history and physical examination can be used to identify most of the subjects with this low-risk form of syncope.

Three major categories of syncope based on pathophysiology have been described. They include: 1) acute reduction in cerebral blood flow, as in vasovagal faints, cardiac disorders, pulmonary vascular outflow obstruction, failure of venous return, loss of peripheral vascular tone, and/or cerebrovascular disease; 2) chemical aberration of the blood flowing to the brain, as in hypoglycemia, hypopcapnea, or hypoxia; and 3) neural and/or psychologic causes as in nonconvulsive seizures, hysteria, or the cerebral type of carotid sinus syncope. The category of acute reduction in blood flow in general, and vasovagal faints in particular, presumably makes up the largest proportion of isolated syncopal episodes. In the majority of subjects
in the general population such episodes of syncope occur only once. The relatively benign course of syncope noted in this general population-based sample should not obscure the potential for a malignant course and need for careful evaluation with appropriate therapy in individual settings. This appears particularly true when there is evidence of a cardiac cause.9

References

Progression of Stroke After Arrival at Hospital
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SUMMARY In order to investigate the frequency, extent and importance of progression of stroke symptoms after arrival at hospital, 402 consecutive patients were studied. Speech ability, extremity and facial pareses were evaluated and graded on four occasions during hospitalization. Deterioration was noted in 43% of the patients; it was fairly marked in 25%. The frequency among the few patients with cerebral haemorrhage was much the same as in those with infarction. Limb motor function was affected in most cases. Half of the progressions occurred within the first 24 h after admission. Patients with progression stayed longer in hospital, were more disabled at discharge and more often needed further institutional care than those without progression, although the initial dysfunction was similar in the two groups. No characteristics were found that would help to identify a risk of deterioration. Thus, progression of stroke symptoms after arrival at hospital is a common and serious problem, whose solution calls for vigorous research.

STROKE PROGRESSION has attracted very little attention. In textbooks, the type, frequency and prognosis of progression are simply ignored.1 2 Reviewing the literature, Jones and Millikan found no account of the natural history; they reported deterioration in 23-46% of their brain infarction patients.3 4 As these figures probably include progression from the case history, they do not indicate the proportion of patients who deteriorated after they came under observation and therapeutic assessment. At the Salzburg meeting in 1980 Hachinski and Norris5 reported that in as many as 29-33% of their patients with ischemic lesions, deterioration was noted after arrival at hospital. However, since the evaluations were based on a score, the Toronto Stroke Scale, a worsening picture might reflect complications in some cases rather than progress of specific stroke symptoms. Neither of these reports touched on the outcome or patient characteristics. Nor did they mention whether admission had been selective. We therefore wanted to study the extent and frequency of progression of pareses and speech disorders among unselected stroke patients after arrival at hospital. Also we wanted to know whether any differences could be found between patients with haemorrhage and those with infarction. Was the deterioration temporary or of importance for the degree of recovery? Could patients at risk for progression be identified by any characteristics?

Material and Methods
During the period 1976-79, 402 stroke patients were cared for in the non-intensive Stroke Unit of the Serafimer Hospital, serving a defined area of Stockholm with 120,000 inhabitants. All persons seeking acute medical advice were referred to that hospital. Stroke cases, including TIA, were transferred to the Stroke Unit if beds were available. The unit treated about half, and a representative part, of all stroke cases admitted to the hospital.6 Furthermore, the patients mean age, the distribution of previous diseases and
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