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Mortality in the First 30 Days Following Incident Acute Symptomatic Seizures

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Summary: *Purpose:* Very little is known about short-term mortality after acute symptomatic seizure. One study found an increased mortality in the first year after acute symptomatic seizure, like mortality following acute symptomatic status epilepticus.

Methods: We studied mortality in the first 30 days after an acute symptomatic seizure in two cohorts. In Washington Heights, New York City, we reviewed the medical records of all adults aged 20 years and older seen at Columbia Presbyterian Medical Center from January 1, 1990 through December 13, 1994 to identify incident acute symptomatic seizure. In Rochester, Minnesota, the medical records of all Rochester residents were reviewed to identify incident acute symptomatic seizure from January 1, 1965 through December 31, 1984. Case fatality (CF) and standardized mortality ratio (SMR) were calculated for deaths in the first 30 days.

Results: A total of 323 adults were identified in Washington Heights and 428 in Rochester. The CF was 20% in both cohorts. CF was greatly increased in the people aged 65 years and older (28.4% in Washington Heights and 40.5% in Rochester) versus younger individuals (17.7% in Washington Heights and 11.2% in Rochester). In both cohorts, the SMR was greatly increased overall (102.1 in Washington Heights and 149.4 in Rochester), and separately for males, females, all etiologies except head trauma in Washington Heights, and younger individuals. In older individuals, the SMR was increased in Washington Heights but not in Rochester.

Conclusion: Acute symptomatic seizures are associated with increased mortality in the first 30 days. It is unknown how seizures contribute to this mortality or whether mortality is due solely to the underlying medical condition. **Key Words:** Acute symptomatic seizure—Mortality.

Very little is known about mortality following an acute symptomatic seizure. One study in Bordeaux (1) found that mortality was increased in the first year following an acute symptomatic seizure (SMR = 10.3, 95% CI 8.3–12.7). Data on mortality following acute symptomatic status epilepticus also show an increased mortality (2–6).

METHODS

We undertook a study of mortality in the first 30 days after an acute symptomatic seizure in two cohorts: a multiethnic population from Washington Heights, New York; and an ethnically homogeneous population from Rochester, Minnesota. Acute symptomatic seizures were defined as a seizure in "close" temporal association with an acute CNS insult or transient systemic disturbance (7). These seizures were presumed to be an acute manifestation of the insult. Insults included CNS infection, cerebrovascular disease, brain trauma, primary or metastatic CNS tumor, eclampsia, acute toxic insults, alcohol or drug withdrawal, metabolic disorders, encephalopathy, "unknown" cause (extremely ill people with electrolyte imbalances), and two or more causes (e.g., uremia and hypocalcemia).

Washington Heights Cohort

To identify cases with incident acute symptomatic seizures, we reviewed the medical records of all adults aged 20 years and older seen at Columbia Presbyterian Medical Center with an ICD-9 discharge diagnosis indicating seizure or status epilepticus (780.3, 345.0–345.9). Patients were ascertained over the period January 1, 1990 through December 13, 1994.

Rochester, Minnesota Cohort

The medical records of all Rochester, Minnesota, residents with a diagnosis of seizure, convulsion, epilepsy, or conditions known to be related to seizures were reviewed in order to ascertain patients with incident acute symptomatic seizures (7). Patients were ascertained through the records-linkage system of the Rochester Epidemiologic Project from January 1, 1965 through December 31, 1984.

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TABLE 1. *Distribution of cause of seizures among deaths in the first 30 days following acute symptomatic seizure in Washington Heights, New York City and Rochester, Minnesota*

Cause of seizure	Proportion of deaths (%) in Washington Heights (68 deaths in the first 30 days)	Proportion of deaths (%) in Rochester (82 deaths in the first 30 days)
Cerebrovascular disease	26.4	31.7
Encephalopathic	19.2	23.2
Metabolic	26.4	8.5
CNS infection	11.8	3.7
Trauma	1.5	9.8
Toxic	5.9	3.7
Neoplastic	2.9	8.5
Unknown	–	6.1
2+ causes	–	4.9

Analysis

We calculated the overall case fatality (CF) for death in the first 30 days following acute symptomatic seizure and by gender and age.

We calculated the proportion of deaths by etiology of the acute symptomatic seizure, separately for the two cohorts.

The standardized mortality ratio (SMR) was used to compare the observed deaths to those expected. The standard for the SMR were the death rates in the U.S. population for 1990 for the Washington Heights cohort and the death rates in Southeastern Minnesota for 1969 and 1979 for the Rochester cohort.

RESULTS

A total of 323 adults with an incident acute symptomatic seizure were identified in Washington Heights, New York City, and 428 cases in Rochester, Minnesota.

Short-term Mortality

The overall CF was 21.1% in Washington Heights and 19.2% in Rochester. CF did not differ by gender in either cohort. However, the CF was far greater in the people aged 65 years and older (28.4% in Washington Heights and 40.5% in Rochester) than in younger individuals (17.7% in Washington Heights and 11.2% in Rochester).

Among the deaths, the most common cause of acute symptomatic seizure was cerebrovascular disease in both cohorts (26.4% in Washington Heights and 31.7% in Rochester; see Table 1). Metabolic cause was also important in Washington Heights (26.4%) but not in Rochester (8.5%). Encephalopathic cause of the acute symptomatic seizure was also associated with a high proportion of deaths in both cohorts (19.2% in Washington Heights and 23.2% in Rochester).

We calculated the SMR for early mortality overall and by age, gender, and etiology (Table 2). In both cohorts, the SMR was greatly increased overall, and separately for males, females, and younger individuals. Results differed for older individuals: the SMR was increased in Washington Heights (SMR = 51.6, 95% CI 34.5–72.1) but not in Rochester (SMR = 1.3, 95% CI 0.96–1.7). The SMR was greatly increased for early death in all etiologies of acute symptomatic seizure, but most markedly for acute symptomatic seizure due to anoxic encephalopathy (SMR = 170.5 in Washington Heights and 1,357.1 in Rochester). In the Washington Heights cohort, only the SMR for brain trauma was not significant (SMR = 39.1, 95% CI 0.1–153.2).

DISCUSSION

We found a 20% CF for deaths during the first 30 days following acute symptomatic seizure. There was no

TABLE 2. *Standardized mortality ratios for early deaths following acute symptomatic seizure in Washington Heights, New York City and Rochester, Minnesota*

Group	Washington Heights, New York City, SMR (95% CI)	Rochester, Minnesota, SMR (95% CI)
Overall	102.1 (79.3–127.8)	149.1 (119.0–184.7)
Males	120.0 (86.1–159.6)	192.7 (145.2–249.3)
Females	83.2 (54.8–117.6)	105.5 (71.0–148.0)
<65 yr	376.0 (267.2–503.2)	364.6 (252.2–493.1)
≥65 yr	51.6 (34.5–72.1)	1.3 (0.96–1.7)
Etiology		
CNS infection	143.1 (61.1–259.5)	73.2 (12.6–175.2)
Brain trauma	39.1 (0.1–153.2)	102.5 (42.5–183.2)
Cerebrovascular disease	81.1 (47.9–122.8)	159.5 (104.1–226.8)
Toxic	149.8 (39.0–332.7)	96.8 (16.7–231.7)
Metabolic	140.7 (83.2–213.2)	184.2 (69.1–337.3)
CNS tumor	26.7 (2.5–76.4)	280.0 (104.5–512.7)
Anoxic encephalopathy	170.5 (90.4–275.8)	1,357.1 (835.5—2,067.3)
Two or more causes	NA	222.2 (57.8–499.4)
Systemic	89.9 (23.4–199.6)	NA
Unknown cause	NA	147.1 (49.8–297.4)

SMR, standardized mortality ratio; CI, confidence interval.

difference in CF for males and females, although CF was greater for older individuals than for individuals younger than 65 years. This likely reflects the tendency for older people to die at a higher rate than younger people, regardless of their underlying disease process.

Among people with acute symptomatic seizure who die in the first 30 days, cerebrovascular disease and anoxic encephalopathy predominate as causes of the seizure. Metabolic causes of acute symptomatic seizure were commonly found among deaths in the Washington Heights cohort but not in the Rochester cohort. This may be due to the differences between the two populations: Washington Heights is an ethnically diverse population of low socioeconomic status with a relatively high prevalence of HIV infection; and Rochester is an ethnically homogeneous population (96.7% white non-Hispanic) of middle to high socioeconomic status with a low prevalence of HIV infection. Interestingly, no deaths occurred during the first 30 days among people with seizures due to eclampsia or drug/alcohol withdrawal.

Observed deaths greatly exceeded expected deaths overall and for males, females, young, and old. Additionally, observed deaths exceeded expected deaths for all underlying causes of acute symptomatic seizure. These results are consistent with data on 5-year mortality following acute symptomatic seizure from Southwest France (1).

The question remains: what, if any, is the contribution of seizure to the short-term mortality observed following acute symptomatic seizure? Most of the underlying causes of acute symptomatic seizure are themselves strongly associated with death (e.g., cerebrovascular disease, anoxic encephalopathy, brain trauma, brain neoplasm). The occurrence of a seizure during the acute phase of these conditions may be a sign of impending death or an accompaniment to severe illness without any effect on mortality. Studies are needed to unravel these competing explanations for the high mortality in the first 30 days following acute symptomatic seizure. These studies should follow individuals with the underlying illness to examine risk factors for the development of acute symptomatic seizure and to elucidate risk factors for death among individuals with acute symptomatic seizure compared to those without such seizures.

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