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Sudden Unexpected Death in Epilepsy: Finding the Missing Cardiac Links

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Introduction and Objectives: Sudden unexpected death in epilepsy (SUDEP) is a significant cause of mortality in patients with refractory epilepsy, accounting for up to 17% of all deaths in epilepsy, and exceeding the expected rate of sudden death in the general population by nearly 24 times.

Most of the identified SUDEP risk factors are unavoidable, and patients with refractory epilepsy currently face a lifelong SUDEP risk as high as 1% per year. Elucidating the mechanisms of this devastating condition might offer an opportunity for preventive measures, and therefore could have significant implications in reducing mortality in this patient population.

One commonly postulated mechanism is cardiac arrhythmia precipitated by seizure discharges acting via the autonomic nervous system.

Project Goals: Our long-range goal is to allow early identification of patients at risk for SUDEP so that appropriate preventive and protective interventions can be instituted.

The specific aims of this pilot study are the following:

(1) To evaluate the interictal (between seizures) and ictal (during seizures) cardiac rhythm characteristics of patients with SUDEP compared with the general population and other patients with epilepsy.

(2) To study the cardiac and neurologic clinical characteristics of patients with SUDEP compared with the general population and other patients with epilepsy

(3) To evaluate the interictal and ictal electroencephalographic characteristics of patients with SUDEP in relation to any identified interictal and ictal cardiac rate/rhythm changes.

Results: We identified 3,852 patients who were evaluated in the epilepsy monitoring unit between 1995 and 2005.

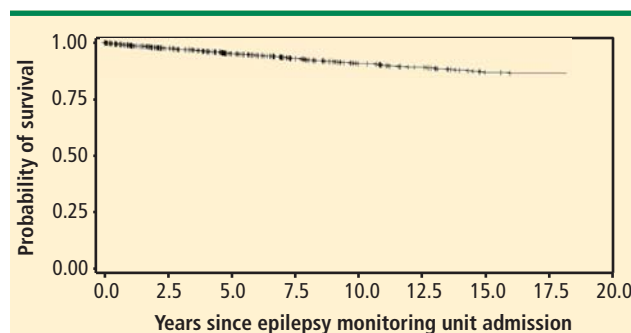


FIGURE. Survival curve.

Among those, we identified 301 deaths based on the Social Security Death Index database. The overall survival curve is shown in the **Figure**. Of those who died, 237 (77%) had epilepsy, 41 (13%) had nonepileptic seizures, and 29 (9%) had both recorded. Mean age at death was 49.9 years (18.6–99.6 years; SD, = 17.9). The cause of death was identified in 211. The death certificates need to be obtained for the remainder.

SUDEP accounted for 21% of the deaths in our cohort with epilepsy.

Identified Characteristics of SUDEP Cases: Significant differences were observed in the mean epilepsy duration and mean monthly seizure frequency between SUDEP and controls: 22.9 ± 2.3 years epilepsy duration in SUDEP versus 13.7 ± 1.5 years in controls; $P = .005$; and 31.3 ± 16.9 seizures per month in SUDEP versus 1.4 ± 0.7 in controls; $P = .005$. Patients with SUDEP were more likely to have been discharged from the epilepsy monitoring unit on valproic acid. Valproic acid was only used in controls on admission. In SUDEP cases, it was used 50% of the time on admission only, 33% on admission and discharge, and 17% on discharge only [$P = .01$]. The risk for SUDEP was independent of epilepsy type or localization.

Our current data collection efforts are now focused on obtaining the cardiac data elements and obtaining the remaining death certificates to identify the remaining SUDEP cases.

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