

## EDITORIAL

# Because scientists are unable to explain the unexplained, screening for cardiovascular abnormalities is a good method to protect against sudden unexpected death in patients with epilepsy

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According to Professor Gutgesell, sudden and unexpected deaths in young athletes and celebrities elicit intense media coverage, often accompanied by the questions, “Why did he die?” and “Why could not this have been prevented?” (1). Interestingly, these two important questions are also asked by the relatives of patients with epilepsy who die suddenly. In the field of epilepsy, how can we elucidate these issues?

Regarding the first question, in the vernacular of the epilepsy world, the patient suffered what is called “sudden unexplained death in epilepsy” (SUDEP). SUDEP is a leading cause of mortality in patients with epilepsy (2) and is defined as sudden, unexpected, witnessed or unwitnessed, non-traumatic, and non-drowning deaths in patients with epilepsy. It occurs with or without evidence of a seizure, excluding documented *status epilepticus*, when the post-mortem examination does not reveal a toxicological or anatomical cause of death (3). The reported incidence of SUDEP is variable, largely due to the differences in patient populations, study designs, and the criteria used for defining the condition (2). In fact, results from a US population-based study indicate that the risk of sudden death in people with epilepsy is estimated to be as much as 20 times higher than that of the general population (4). In general terms, SUDEP is responsible for 7.5% to 17% of all deaths in patients with epilepsy and has an incidence between 1:500 and 1:1,000 patient-years among affected adults (5). Concerning risk factors, a number of associated factors have been reported, but the results are not consistent between studies. To date, several studies have identified factors that potentially correlate with an elevated risk of SUDEP, such as the refractoriness of the epileptic condition, presence of generalized tonic-clonic seizures, early onset of epilepsy, antiepileptic medication (polytherapy with antiepileptic drugs), young age, and duration of the seizure disorder (2,6,7). Although the cause of SUDEP is still unknown, one of the main mechanisms of SUDEP is autonomic dysregulation (i.e., cardiac abnormalities during and between seizures) (6-8).

To address the second question (“Why could not this have been prevented?”), although progress has been made relating to SUDEP over the last decade, it remains somewhat of a ‘black box’ phenomenon (6). Thus, predicting and preventing SUDEP are challenging tasks (6). Although we still are unable to prevent the onset of epilepsy or to reverse an established clinical picture, preventive measures in clinical practice have been proposed to minimize the occurrence of SUDEP: 1) good seizure control; 2) stress reduction; 3) participation in physical activities and sports; 4) supervision at night; 5) educating family members regarding cardiopulmonary resuscitation (CPR) techniques and the basics of defibrillator use; and 6) dietary management (i.e., omega-3 supplementation) (9). However, we agree with Shorvon and Tomson (10) that because there are no data on the effectiveness of any particular clinical strategy, these suggestions are merely speculative. However, based on the reported evidence, we believe that reducing the occurrence of tonic-clonic seizures, exercising caution when changing antiepileptic drugs, and improving post-ictal surveillance are likely to be beneficial (10).

From a cardiovascular perspective and because the mechanism for the occurrence of SUDEP in people with uncontrolled seizures could be of cardiac origin, (6-8) it seems obvious that a true convergence of clinical neurology and cardiology should be adopted to attempt to minimize the occurrence of sudden cardiac death in individuals with epilepsy. Thus, some primary and secondary preventive measures should be evaluated in people with refractory epilepsy.

Similar to individuals in the general population, all people with epilepsy should regularly take part in important primary preventive measures. We must remember that because sudden cardiac arrest is often linked with coronary artery disease, the same factors that put a patient at risk of coronary artery disease may also put them at risk for sudden cardiac arrest. These factors include a family history of coronary artery disease, smoking, high blood pressure, high blood cholesterol, obesity, diabetes, and a sedentary lifestyle.

Concerning secondary preventive measures, individuals with epilepsy that are also at a high risk for SUDEP should receive additional tests. Because identifying cardiovascular abnormalities may help prevent episodes of cardiac arrest, the recommended tests include blood tests (lipid, enzymatic, hormone, and electrolyte profiling) and electrocardiography. In addition, imaging tests are suggested to screen for cardiac dysfunction, such as chest X-rays, nuclear scans, and echocardiograms.

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Finally, we completely support the suggestion (11) that if there is a reasonable chance of preventing SUDEP, it must be discussed with patients with epilepsy who are at the highest risk of SUDEP. With this goal in mind, the physician can explain possible strategies that people with epilepsy and their families can take to reduce their SUDEP risk. As all of the risk factors, mechanisms, and specific methods to prevent SUDEP are not yet completely understood, caution remains prudent and necessary.

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