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**INCIDENCE AND RISK FACTORS OF THE SUDDEN UNEXPECTED
DEATH IN EPILEPSY**

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Sudden unexpected death is one of the most common fatal complications of epilepsy. It is sudden, unexpected, witnessed or unwitnessed, death in patients with epilepsy in reasonable state of health, in whom postmortem examination does not reveal an alternative structural or toxicologic cause for death. Sudden unexpected death in epilepsy (SUDEP) was first recognized as a mortal complication of epilepsy by medical examiners, reaching the scientific community through reported autopsy series.

SUDEP accounts for 5% to 30% of deaths in people with epilepsy. Thus, it is a major cause of death in patients with epilepsy. Particularly this is true for the 20- to 40-year-old patients with chronic epilepsy which is refractory for medical treatment. SUDEP is related to all forms of epilepsy, including focal or generalized, idiopathic or symptomatic, regardless of etiology. The results of a recent metaanalysis sponsored by the American Academy of Neurology showed that overall incidence of SUDEP was 0.58/1000 patient-years. Children with epilepsy have a risk of SUDEP of 0.22/1000 patient-years. In adults this risk increases to 1.2/1000 patient-years.

The main risk factor is generalized tonic-clonic seizures, especially if they occur more than 3 times a year. Patients with such seizures were found to have a 10-fold higher risk of SUDEP compared with patients who did not have them. In addition, patients with 3 or more generalized tonic-clonic seizures per year have a risk of SUDEP 15 times higher than patients with less than 3 generalized tonic-clonic seizures per year.

Other risk factors include older age, sleeping in prone position, absence of attendance, male sex, noncompliance with medical treatment, polytherapy with antiepileptic drugs, and chronic alcohol or anxiolytic use. It should be mentioned that SUDEP is not associated with the use or toxicity of any specific antiepileptic medication. But from the other hand in women the risk of SUDEP may be increased in association with oxcarbazepine, carbamazepine, and lamotrigine use. In children and adolescents intellectual disability, structural brain changes and neurological deficit increase the risk of SUDEP.

Preliminary data show that the duration of postictal EEG suppression may be correlated with an increased risk of SUDEP but its clinical significance and role as a predictor are controversial. Interictal biomarkers of cardiac rhythms can identify sympathovagal disequilibrium. Heart rate variability, a measure of differences between interbeat intervals, in people with epilepsy reflects decreased parasympathetic activity. Antiepileptic treatment tends to further decrease parasympathetic activity, factors that have been attributed to increased cardiovascular morbidity and mortality in the general population.

Recent studies also revealed potential structural neuroimaging biomarkers on magnetic resonance imaging in people who subsequently died of SUDEP. In 1 study, voxel-based morphometry demonstrated increased gray matter volume in the right anterior hippocampus/amygdala and parahippocampus in people with SUDEP, as well as decreased gray matter volume in the posterior thalamus. The right medial temporal lobe changes may be associated with increased autonomic outflow, resulting in cardiac tachyarrhythmias.

Thus, awareness about risk factors of SUDEP and proper assessment of medical history and medical records will allow a forensic pathologist to choose a proper forensic autopsy strategy, correctly interpret autopsy findings, make correct diagnosis and argument conclusions in case of sudden, unexpected death of the person who suffered from epilepsy.