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Letter to the Editor

To Detect Differences between SUDEP and SUD Cases, Comprehensive Examinations of these patients are Required

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Letter to the Editor

We read with interest the article by Palsoe *et al*. comparing cases of sudden unexpected death in epilepsy (SUDEP) (n=84) with cases of sudden unexplained death (SUD) without epilepsy (n=393) in terms of demographics, circumstances, comorbidities, autopsy findings, postmortem toxicology, and prescribing practices [1]. SUDEP cases were associated with unwitnessed deaths, living alone, psychiatric comorbidities, and a low prevalence of cardiac hypertrophy [1]. Pro-arrhythmogenic drug prescriptions and pro-arrhythmogenic drugs post mortem were more common in SUDEP cases than in SUD cases without epilepsy [1]. It was concluded that SUDEP cases are often unwitnessed, affect patients living alone, and are associated with psychiatric comorbidities [1]. The study is noteworthy, but some points should be discussed.

The first point is that the study was retrospective in design, extracted data from electronic records, and relied heavily on ICD codes. Retrospective designs have several disadvantages [2]. Compared to prospective studies, they have a lower level of evidence, are susceptible to memory bias or misclassification, cannot establish causality but only associations, some important statistics cannot be calculated, temporal relationships are often difficult to assess, and they require large sample sizes when the outcomes are rare [2].

The second point is that even if a patient died suddenly and suffered from prevalent epilepsy according to the ILAE classification, this does not necessarily mean that this patient died of SUDEP. Even patients who meet the definition of prevalent epilepsy can die from causes other than seizures, such as malignant ventricular arrhythmias, pulmonary causes, sepsis, or cerebral causes unrelated to epilepsy and antiepileptic drugs.

The third point is that patients classified as SUD were not systematically subjected to a brain autopsy. In order to rule out acute ischemic stroke, subarachnoid hemorrhage, intracerebral hemorrhage with or without ventricular rupture, venous sinus thrombosis, meningitis, encephalitis, meningeal carcinomatosis, tumor, or abscess formation, a brain section would have been mandatory, especially in cases without cardiovascular risk factors, without a history of malignancy, or without signs of acute infection prior to SUD.

The fourth point is that Takotsubo syndrome (TTS), also known as stress cardiomyopathy, was not considered as a cause of SUD or SUDEP. TTS is defined as acute, usually reversible heart failure without coronary artery disease. TTS occurs most frequently in postmenopausal women and manifests in about half of patients with ST-elevation, elevated creatine kinase and troponin levels, and cardiovascular complications (heart failure, malignant arrhythmias, cardioembolism) [3]. Therefore, postmortem histological abnormalities indicative of TTS should be sought [4].

The fifth point is that we disagree with the statement in the “Methodology” section that Danish death certificates are an ideal screening tool for sudden deaths [1]. If the police do not order a forensic autopsy, how can a Danish doctor know what a person died of if he was not present at the time of death, no autopsy was performed, and no toxicological examination took place? His assessment depends on what any witnesses tell him, and if there are no witnesses, he has to rely on the available data from the patient's medical history. However, the medical history and witness statements do not necessarily guarantee that the exact cause of death can be determined. Were all included patients subjected to a forensic autopsy?

The sixth point is that it is not clear why an autopsied sudden cardiac death (SCD) was defined as sudden death due to cardiac or unknown causes [1]. If the cause is unknown, why is it referred to as SCD? It should be classified as SUD rather than SCD.

In summary, to determine reliable differences between SUDEP and SUD, a prospective design should be chosen that includes an autopsy of the brain and examination of the myocardium for traces of TTS.

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References
1. Palsøe MK, Hansen CJ, Torp-Pedersen C, Linnet K, Kløvgaard M, Tfelt-Hansen J, *et al*. Sudden unexplained death in individuals with and without epilepsy. Seizure, Aug 7, 2025; 131:361-368. Doi: 10.1016/j.seizure.2025.08.007
2. Tofthagen C. Threats to validity in retrospective studies. J Adv Pract Oncol, May 2012; 3(3):181-183.
3. Manolis AA, Manolis TA, Melita H, Manolis AS. Takotsubo Syndrome and Sudden Cardiac Death. Angiology, Feb 2023; 74(2):105-128. Doi: 10.1177/00033197221105757
4. Grassi S, Campuzano O, Cazzato F, Coll M, Puggioni A, Zedda M, *et al*. Postmortem diagnosis of Takotsubo syndrome on autoptic findings: is it reliable? A systematic review. Cardiovasc Pathol, Jul-Aug 2023; 65:107543. Doi: 10.1016/j.carpath.2023.107543