

Sudden neurological death misclassified, underestimated

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UC San Francisco researchers have devised a new term, "sudden neurological death," to describe apparent sudden cardiac deaths that actually were due to neurological causes, such as stroke, aneurysm or epilepsy, and estimate that 10,000 to 25,000 of these deaths may go undetected each year.

The finding could impact overall estimates of cardiac and neurological disease burden. They also suggest that apparent sudden cardiac deaths could be misclassified in cardiovascular clinical trials, which might change our understanding of the risks and benefits of cardiovascular treatments such as blood thinners. The study appears in the Sept. 16 online issue of *Neurology*, the medical journal of the American Academy of Neurology.

The researchers said many of these deaths may be missed because out-of-hospital sudden deaths are often assumed to be cardiac, which can only be verified via a detailed postmortem investigation. Less than 15 percent of sudden deaths that occur outside a hospital lead to an autopsy.

"Our data suggests that low prevailing autopsy rates may contribute to a systematic misclassification of sudden neurological deaths as sudden cardiac deaths," said senior author Zian H. Tseng, MD, MAS, a UCSF Health cardiac electrophysiologist. "This has the potential to impact overall event rates of sudden cardiac deaths and neurological emergencies in the general population, as well as hemorrhage outcomes in large cardiovascular clinical trials, which often rely on the



overburdened existing coroner and medical examiner infrastructure to determine assumed cause of <u>death</u> for study participants."

By common epidemiologic definitions, a <u>sudden cardiac death</u> is a sudden, unexpected death occurring within an hour of symptom onset for witnessed events or within 24 hours of being observed symptom-free for unwitnessed events. There are an estimated 184,000-450,000 annual sudden cardiac deaths in the United States, with more than 90 percent occurring outside the hospital.

In this study, Tseng and his colleagues used data on the incidence and causes of sudden neurological deaths they compiled in the ongoing POST SCD (POstmortem Systematic invesTigation of Sudden Cardiac Death) study.

POST SCD is a comprehensive study of out-of-hospital sudden deaths in the City and County of San Francisco that is funded by the National Heart, Lung, and Blood Institute. It aims to discover the true causes of sudden cardiac death, why it is more prevalent in some demographic populations and whether it is too often inaccurately cited as a cause of death.

All of the deaths reported in the *Neurology* study met the widely accepted World Health Organization criteria for sudden cardiac death. Following a systemic evaluation of 352 consecutive sudden cardiac deaths reported to the San Francisco Medical Examiner between 2011 and 2013 – including a full autopsy and detailed evaluation of the heart and cranial vault in 95 percent of cases (335) – the researchers found that 5.4 percent of these deaths (18) should have been classified instead as a sudden neurological death.

At 5.4 percent, this could mean that between 10,000-25,000 annual sudden cardiac deaths in the United States actually could be sudden



neurological deaths.

Further, Tseng and his colleagues found that 14.9 percent of all non-cardiac sudden deaths during this two-year period were due to a neurological cause such as aneurysmal subarachnoid hemorrhage or sudden unexpected death in epilepsy. It was the most common non-cardiac cause of sudden death after drug overdose.

"If even half of the brain hemorrhages that we observed in this study would have been missed with prevailing autopsy rates, this would mean that we are underestimating the risk of fatal brain aneurysms by 25 to 30 percent," said study lead author Anthony Kim, MD, MAS, medical director of the UCSF Stroke Center.

"Also, the lower risk of sudden neurological death compared to sudden cardiac death among males and whites, and a corresponding trend toward increased risks in women and the fast-growing population of Asians and Hispanics, may justify follow-up studies to evaluate whether greater vigilance is warranted for specific demographics," continued Kim, an associate professor of neurology at UCSF.

A failure to identify sudden neurological deaths, particularly among those at high risk for sudden cardiac death, has potential implications for interpreting the results of large cardiovascular trials, said Tseng, who is the Murray Davis Endowed Professor in the Cardiology Division and Cardiac Electrophysiology Service at UCSF. Specifically, it could shift the balance of the relative risks and benefits of blood thinners, particularly among patient populations that have a higher risk for neurological than <u>cardiac conditions</u>.

More information: Anthony S. Kim et al. Sudden neurologic death masquerading as out-of-hospital sudden cardiac death, *Neurology* (2016). DOI: 10.1212/WNL.0000000000003238



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