Sudden unexplained death (SUD) of the young is the term used for sudden deaths occurring before the age of 40 years, which remain unexplained despite analysis of all available antemortem information (usually because the victims had no family history of heart disease or warning symptoms) and a postmortem examination that was unrevealing or was not performed. For the surviving family members, the fact that the tragic death of a previously healthy relative remains unexplained only adds frustration and confusion to grief. Furthermore, because arrhythmic death in the young is often caused by familial diseases, reaching the correct diagnosis is important for those left behind, who may then receive appropriate prophylactic measures. Therefore, it is good clinical practice to systematically evaluate families of SUD victims in attempts to minimize the unexplained. Having said that, it is also important that family members considering screening be aware of the potential negative consequences associated with the diagnosis of an asymptomatic inheritable disease. Unjustified remorse or recrimination may torment parents of a deceased child, whereas unforeseen anxiety or disqualification from sports or life insurance policies may become problematic for asymptomatic, yet affected, siblings. A 1%/year risk of sudden death, as currently estimated for asymptomatic individuals with Brugada syndrome discovered through screening, may be perceived as reassuring by some but may be terrifying to others.

Evaluation of SUD families should begin with a meticulous review of available data concerning the index SUD victim. The circumstances of death are important: sleep-related death favors long-QT syndrome (LQTS) or the LQT3 type, short-QT syndrome, or Brugada syndrome (if male); sudden death during stress favors coronary disease (congenital coronary anomalies or premature atherosclerosis), cardiomyopathies, catecholaminergic polymorphic ventricular tachycardia (CPVT), or LQTS, whereas unexplained drowning favors LQT1 and CPVT. Favoring a diagnosis by no means establishes the same; sleep-related death by no means excludes CPVT.

Every effort should be made to retrieve all the medical tests performed by the SUD victim. A report of normal ECG should not be taken at face value because too many physicians will not recognize a long-QT interval and because, until recently, traces with short-QT interval were defined as normal simply because the QT was not prolonged. On the other hand, not all forms of ECG abnormalities retrospectively identified in an SUD victim should be automatically assumed to be the cause of death. Early repolarization, for example, is an ECG finding that is strongly associated with idiopathic ventricular fibrillation but is also prevalent among healthy individuals. Except for cases where the arrhythmias pathognomonic of idiopathic ventricular fibrillation are recorded, caution should be exercised before an SUD case is diagnosed as an early repolarization syndrome, solely on the basis of retrospective ECG interpretation. This point is especially important because early repolarization is a familial trait, regardless of the presence or absence of arrhythmic disease. Consequently, if early repolarization is present on the ECG of an SUD victim, his/her siblings are twice as likely to display the same ECG variant even if this finding has nothing to do with the victim’s death.

In countries where forensic examination of sudden death cases is not mandatory, relatives may refuse authorization of the examination for a variety of reasons, including religious principles. They are likely to regret this decision years down the road, when symptoms or ECG findings in other family members raise concerns about possible familial syndromes. A well-performed forensic examination, including a toxicology screen, may establish the diagnosis in cases of traumatic, toxic, noncardiac, or some forms of cardiac death (eg, cardiomyopathies, coronary anomalies), whereas a negative pathological examination, as happens in 30% of young SUD cases, will favor a primary electric disease or channelopathy. Postmortem radiology, with computed tomography coronary angiography, should be proposed when forensic examination is refused. Importantly, blood should be collected in EDTA (the purple-top tube) to enable DNA extraction, which should be stored for a molecular autopsy (ie, screening the DNA of the SUD victim for known genetic diseases). It should be emphasized, however, that the list of genetic diseases potentially leading to SUD is long and that for each disease several genotypes exist. Therefore, wide-spectrum screening of all possible arrhythmogenic genetic disorders is too expensive to be practical at the present time. Instead, screening should be selectively directed at candidate genes based on a comprehensive evaluation of the SUD victim and the surviving siblings. Genetic results, however, should not be accepted as gospel truth because distinguishing disease-causing mutations from innocent genetic variants requires expertise.

Several series report on the yield of systematically evaluating family members of SUD victims. In these studies, 100 to 260 surviving relatives (of 32–57 index SUD victims) were evaluated with an ECG, echocardiogram, exercise testing, and Holter monitoring; additional tests, such as cardiac magnetic resonance imaging or challenges with sodium channel blockers.

The opinions expressed in this editorial are not necessarily those of the editors or of the American Heart Association.

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Evaluation of SUD is an art, best performed at referral centers; it involves detective-like investigation of the victim’s data and systematic evaluation of the surviving relatives. The evidence supporting the diagnosis should be carefully weighted when selecting therapy. For example, the long-term risk for asymptomatic family members with Brugada syndrome is lowest when the characteristic ECG is only revealed by a drug challenge with a sodium channel blocker. In a similar fashion, asymptomatic SUD relatives with mild QT prolongation and abnormal epinephrine test are probably at low risk because the duration of the QT interval is the strongest prognostic factor in asymptomatic, genetically confirmed, LQTS. Avoidance of potentially proarrhythmic medications (http://www.brugadadrugs.org/ and www.gtdrugs.org) may be the only therapeutic intervention needed for such patients.

Disclosures

None.

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