EDITORIAL

Investigating sudden cardiac death – A new paradigm

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It is as simple as this: “Death is inevitable, and what better way to die than suddenly. This statement is applicable to the elderly, but sudden death in a young person not only is a tragedy for the victim but also has a devastating effect on parents, spouses, and the victim’s children.”

However, in many well-resourced countries around the world, sudden unexplained death victims, sudden cardiac arrest survivors, and their relatives are still not routinely examined as we approach the end of 2020. Autopsy, family tracing of relatives at risk, genetic testing, and follow-up strategies are often missing.

The 2020 APHRS/HRS expert consensus statement on the investigation of decedents with sudden unexplained death and patients with sudden cardiac arrest, and of their families, has the quality and strength to enhance the conditions for sudden cardiac arrest survivors and their relatives as well as for relatives of sudden unexplained death victims.

The expert consensus statement is comprehensive, is meticulously written, covers all aspects of this serious condition, and provides a straightforward and operational approach to future initiatives.

This statement paper provides a very important framework for the investigation of (1) patients with sudden cardiac arrest, (2) decedents with sudden unexplained death, and (3) families of both sudden cardiac arrest survivors and sudden unexplained death victims, since many conditions responsible for the cardiac arrest or unexplained death may be inherited in the family.

While this document provides clinicians with practical recommendations for evaluating patients with sudden cardiac arrest, decedents with sudden unexplained death, and their families, the best approach will vary with the situation and can be influenced by the subject’s age and results of initial testing, among other factors. Some of the recommendations do specify an age cutoff, which is somewhat arbitrary and may not always be appropriate for the disease investigated for or the demographics of the patient’s country. In cases where an age cutoff is specified in a recommendation, it has passed the consensus voting among members of the writing group. Still, such a cutoff should be considered with caution, taking into account the clinical situation of the individual patient and family.

It is recommended to refer sudden cardiac arrest survivors and their family members for evaluation in centers with experienced multidisciplinary teams, since this can facilitate navigation of these complexities and organize interval follow-up. The disciplines of cardiology, pediatrics, radiology, pathology, counseling, psychology, and genetics have to be involved in this process. Therefore, in centers responsible for such investigations, the establishment of multidisciplinary teams is essential to provide a complete service to such patients and their families.

It is recognized that not all investigative modalities recommended will be available in all circumstances, and it is pointed out that this document is an attempt to outline an approach to which the clinician should aspire.

The consensus statement provides a comprehensive “Top 10” of important messages, which in short express the following:

1. Put more focus on sudden cardiac death as an important public health issue.
2. Establishment of multidisciplinary teams is central for an appropriate investigation of survivors of sudden cardiac arrest, victims of sudden unexplained death, and their relatives in search of a diagnosis.
3. During the investigation and search for a diagnosis, the psychological care of families affected by sudden unexplained death and survivors of sudden cardiac arrest and their families should be remembered.
4. A detailed personal and family history is essential in investigating sudden unexplained death, focusing on sentinel symptoms during life such as syncope or seizures, witness accounts, premorbid investigations, and inspection of any heart rhythm monitoring around the time of death.
5. A comprehensive autopsy is an essential part of the investigation, and tissue suitable for genetic analysis should be ensured.
6. For victims of sudden cardiac death or cardiac arrest survivors with a known phenotype, genetic testing of the proband focused on likely candidate genes, along with clinical evaluation of family members, contributes in identifying family members at risk.
7. For victims of sudden cardiac death or survivors of cardiac arrest where the phenotype is not known, arrhythmia syndrome–focused genetic testing may be appropriate to help arrive at a definite diagnosis, whereas wider testing is not recommended.
8. In sudden cardiac arrest survivors, detailed personal and family history, witness accounts, physical examination, multiple electrocardiograms, and cardiac imaging are essential.

9. Genetic investigation of sudden cardiac arrest survivors is best undertaken at a center with a multidisciplinary care infrastructure and should focus on likely well-described candidate genes.

10. In families of victims of sudden unexplained death and survivors of sudden cardiac arrest, evaluation should include clinical and, if known, genetic cascade testing.

Future directions suggested
The authors of this consensus statement paper have a number of valuable contributions to future directions in this field. Correctly, they state that “many of the recommendations in this document seem intuitive, obvious, and straightforward; however, much of what is being recommended within this document is seldom routinely performed even in well-resourced countries.” The question is, why isn’t this happening? The answer is complex. The recommendations in sudden unexplained death cannot be followed if there is no autopsy. Further, if the organization and procedures to perform evaluation of first-degree relatives is lacking, it is a major obstacle to proceed into the new recommended paradigm. Autopsy and evaluation of first-degree relatives is challenged by many medico-political barriers that obstruct and delay best medical practice. In addition, funding is another issue. Allocating the necessary funding is key. Along with the authors, we hope that the consensus statement will empower those who wish to change things for the better by implementing the recommendations. Achievement of a new paradigm is determined by a series of steps. Firstly, it is important to gain knowledge of the precise prevalence, epidemiology, and etiologies of sudden unexplained death and sudden cardiac arrest in the young part of the population in different countries. Secondly, all communities, states/provinces, and countries must advocate for and expect a comprehensive autopsy, including postmortem genetic testing, to be performed whenever a sudden unexplained death occurs in a young person. Thirdly, classification of the living, whether a sudden cardiac arrest survivor or first-degree relative of a sudden unexplained death victim or a sudden cardiac arrest survivor, must become standard of care. Predisposing inherited cardiac disease will be exposed after initial cardiac evaluation including clinical examination, electrocardiography, echocardiography, and stress test. More advanced investigations such as sodium channel drug provocation tests, advanced cardiac imaging such as magnetic resonance imaging, and genetic testing require further studies in this context. This pertains also to the recommended interval for a repeat cardiologist evaluation of the first-degree relatives when their first evaluation is either normal or inconclusive.

Finally, studies aiming to minimize the collateral damage from uncertain clinical findings and genetic “variants of uncertain significance” are needed. We must avoid the premature and erroneous diagnosis owing to excessive confidence in or over-interpretation of clinical or genetic findings of uncertain significance, as this can cause remarkable harm.

This consensus statement is an important step on the road to achieve changes, and we hope that its recommendations will be considered and incorporated into clinical practice throughout the world.

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