Sudden cardiac death: what should we tell the family?

R.J de Winter

The sudden unexpected death of a child or a young person can have enormous implications for the surviving family members in addition to the immediate shock, sadness and sense of loss. The sudden loss of a sibling without any prior medical history may confront the family members with the question whether the sudden death was caused by a genetic condition and the fear that other family members may suffer the same fate. Increased awareness of these inherited cardiovascular conditions and the availability of genetic testing in the clinical arena make it possible to identify genetically affected individuals before they have symptoms or experience sudden cardiac death. In particular, when routine cardiovascular autopsy findings do not provide a diagnosis, molecular testing is advocated. The development of such tests has been paralleled by the emergence of preventative treatments, which provide a rationale for active screening of relatives of sudden or unexplained cardiac death victims in order to either confirm or exclude the presence of potentially lethal genetic disorders, the most important of which are cardiomyopathies and primary arrhythmia disorders.

Approximately 150 young individuals are victims of sudden cardiac death in the Netherlands each year. Excluding premature atherosclerosis and acute coronary syndromes as the potential cause of sudden cardiac death, an inherited cardiomyopathy or primary arrhythmia may explain 10 to 40% of cases.¹⁻³ Most inherited cardiac diseases show an autosomal dominant pattern of inheritance, and first-degree relatives of SCD victims have a 50% risk of being a carrier of an inherited cardiac disease.

Thus, several hundred family members annually may be confronted with the sudden loss of a relative and may be candidates for genetic screening and counselling.

In 2007, the Heart Rhythm UK (HRUK) Familial Sudden Death Syndromes Statement Development Group issued recommendations for genetic testing in familial sudden cardiac death syndromes on the basis of information available at that time.⁴ Depending on the findings at autopsy of the SUD victim, clinical assessment using ECG, echocardiogram, Holter monitoring, exercise testing and/or the use of genetic screening are recommended. In this statement, particular attention is drawn to the sensitivity and specificity of clinical and genetic testing. Expert clinical and detailed family assessment is recommended. This may exist in a number of settings but will involve a multidisciplinary team including a cardiologist with specialist experience in the management of these conditions and individuals with specific clinical genetics training and expertise. Thus, familial syndromes can be identified in a substantial minority of autopsy-negative sudden death victims using a combination of clinical and genetic screening.^{4,5}

In this issue of the Netherlands Heart Journal, Hendrix et al. describe the rationale and design of the CAREFUL study, cardiogenetic screening in first-degree relatives of sudden and unexplained cardiac death victims <45 years.⁶ In this study, regional organisation of autopsy in sudden or unexplained cardiac death victims and the diagnostic yield of genetic screening and counselling in family members is compared between two intervention regions and two control regions. In a prospective population-based follow-up study, a comprehensive intervention (stimulate autopsy and DNA storage of victims and the referral of first-degree relatives for cardiogenetic evaluation) is applied in a 'top down' and 'bottom up' mode. In each region, young sudden death victims are registered and for all cases performance of autopsy and evaluation of relatives in a cardiogenetics outpatient clinic will be determined. The primary outcomes are the pro-

R.J. de Winter

Department of Cardiology, Academic Medical Center, University of Amsterdam, Amsterdam, the Netherlands

Correspondence to: R.J. de Winter
Department of Cardiology B2-137, Academic Medical Center, University of Amsterdam, PO Box 22660, 1100 DD Amsterdam, the Netherlands
E-mail: r.j.dewinter@amc.uva.nl

portion of postmortem studies in young SCD/SUD victims, and the proportion of first-degree relatives of young SCD/SUD victims attending a cardiogenetics department within six months after the event between the intervention regions and the control regions and between the two intervention regions.

An increase in awareness amongst general practitioners, pathologists and cardiologists is important and the study is timely in that respect. The 'intervention' in the two active regions, however, is not well described (bottom-up: information meetings, a letter to GPs and coroners, emergency medical services are instructed to leave an information letter; top-down: central telephone number and website) and importantly, the information campaign aimed at enhanced awareness amongst professionals may 'spill over' to the control regions. The collection of information regarding the annual incidence of SUD in young persons in the Netherlands and the prevalence of inherited cardiac disease in family members seems to be more important than the effect of comparing the effects of an information campaign in active regions versus control regions. Why not simply aim at national implementation of the already available HRUK recommendations concerning genetic testing and counselling, involving GPs, coroners, cardiologists and clinical geneticists. Either way, genetic screening for cardiac diseases that may cause sudden or

unexplained cardiac death for which preventive treatments exist needs to be made available to family members. Genetic counselling may address important issues, including societal and ethical dilemmas incurred by the increase in diagnostic and therapeutic technologies. ■

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