Relatives of people dying suddenly from heart problems have increased risk of cardiovascular disease

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Relatives of young people who have died suddenly from a heart-related problem are at greatly increased risk of developing cardiovascular disease according to a study published online today (Wednesday) in the *European Heart Journal*.

The authors of the study say these findings have two major implications; firstly, they strongly support the fact that autopsies should always be performed in cases of young sudden unexplained death; and secondly, since the involved diseases are all treatable if identified in time, the findings suggest that close relatives of these victims should be screened to detect those who would benefit from preventive treatment.

Researchers identified 470 victims of sudden cardiac death (SCD), aged between 1-35, in Denmark between 2000-2006 and followed their first and second-degree relatives for up to 11 years. They found that relatives who were younger than 35 had a three-fold increased risk of any cardiovascular disease (CVD), a six-fold increased risk of ischaemic heart disease (reduced blood supply to the heart) and a more than 10-fold increased risk of cardiomyopathies (damaged or weakened heart muscle) and ventricular arrhythmias (potentially fatal disturbances in the rhythm of the heartbeat) when compared to the general population.

For young, first-degree relatives of SCD victims, the risks were even higher: a six-fold increase in ischaemic heart disease and a 20-fold

increase in cardiomyopathy and ventricular arrhythmia.

Dr Mattis Flyvholm Ranthe (MD), a PhD student and research fellow at the Department of Epidemiology Research, Statens Serum Institut, Copenhagen, Denmark, who is the first author of the report published today, said: "The most interesting findings were that risk of CVD overall was increased no matter what subgroups of SCD victims and relatives we examined, and that young (under 35 years) first-degree relatives overall had a four-fold increase in risk of any CVD, and nearly 20-fold increases in risk of cardiomyopathy and ventricular arrhythmia. Finding a risk factor associated with a four-fold or greater increase in CVD risk is rare!"

SCD is defined as sudden, unexpected death due to natural unknown or cardiac causes, with an acute change in cardiovascular status within one hour of death or, in unwitnessed cases, in a person last seen functioning normally within 24 hours of being found dead. In young people it is often caused by undiagnosed heart problems that may be hereditary, indicating that there may be genetic mutations involved in the condition.

Dr Ranthe said: "If sudden cardiac death has genetic causes then this would suggest that relatives of young SCD victims are at greater risk of heart disease than the general population and would benefit from screening to identify those at risk so that they could be given appropriate preventive treatment. This could save a significant number of lives. However, as far as we are aware, there have been no population-based findings of this kind before, and current knowledge is limited and based on smaller descriptive studies.

"Our results show SCD, or the underlying heart problems, has a large hereditary component, and that relatives, particularly young, first-degree relatives, are at much greater risk of developing heart conditions compared with the general population. Family members of young SCD

victims should be offered comprehensive and systematic screening, with the focus on the youngest and nearest relatives.

"Most of the cardiovascular diseases leading to sudden cardiac death are treatable, if diagnosed in time, before a fatal event. Our results reinforce the concept of screening as a rational 'tool' to identify such cardiovascular diseases in family members at risk, and thereby possibly prevent future sudden cardiac deaths. However, our findings do not suggest blanket screening of, for example, asymptomatic second-degree relatives of SCD victims, although cascade screening might trigger screening of more distant relatives after a CVD finding in a first-degree relative."

An autopsy was performed in 67% (314) of the SCDs, and the autopsies confirmed a heart-related cause of death in 178 cases, with 136 remaining unexplained. Dr Ranthe said that conducting autopsies in such circumstances was important because having the cause of death correctly identified was vital information for the relatives, and also for guiding screening initiatives.

"Our study, along with findings from previous descriptive studies, suggests that screening in relatives of SCD victims should be driven by the suspected cause of death, based on autopsy findings and description of the circumstances leading up to the SCD. We would like to emphasise the importance of autopsy in guiding such screening initiatives; public awareness of the importance of autopsying all young SCD victims should be increased. Ideally, these autopsies would be carried out by pathologists trained in post-mortem cardiac examination."

The findings on arrhythmia were also new and important, said Dr Ranthe. "Previous studies of familial aspects of arrhythmia have primarily been centred around families with very severe arrhythmic syndromes. Our finding of dramatically increased general risks of

ventricular arrhythmia is therefore novel and shows that the findings from heavily affected families are relevant on a broader scale and possibly just the tip of the iceberg."

Future work by Dr Ranthe and his colleagues at the Statens Serum Institut will focus on examining familial clustering of cardiovascular disease in new large-scale register-based studies. Their co-authors at The Heart Centre, Unit for Inherited Cardiac Diseases, Copenhagen University Hospital (Rigshospitalet) are investigating SCDs in persons older than 35 years. They will be looking at survival and disease courses in the relatives of SCD victims and examining specific subtypes of SCD more closely; those remaining unexplained after autopsy are of particular interest.

More information: "Risk of cardiovascular disease in family members of young sudden cardiac death victims", by Mattis Flyvholm Ranthe et al. European Heart Journal. doi:10.1093/eurheartj/ehs350

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