Sudden cardiac death: Genetic disease ARVC more common than hitherto assumed

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The genetic disease ARVC leads to sudden cardiac death and is more common than it has been hitherto assumed. This is reported by an international team of researchers headed by Prof Dr Hendrik Milting from the Heart and Diabetes Center NRW in the "*European Heart Journal*". The molecular biologist working at the Ruhr-Universität's clinic in Bad Oeynhausen revealed that all families who are known to be affected by the disease share the same genetic origin. There must be other families in Europe who also carry the genetic mutation but who are not yet known.

Mutation initially occurred in Newfoundland

Scientists have thrown light on the genetic mutation that causes a particularly severe genetic disease (ARVC5) on the Canadian island Newfoundland in 2008. At first, they assumed that it was a genetic anomaly limited to this Canadian province. In 2010, Milting's team – and at the same time a team of researchers from Copenhagen – proved that the "Newfoundland mutation" did also occur in Europe. Today, the scientists know about affected families in Germany, Denmark, the USA and Canada. They all share common ancestors, as was demonstrated through genetic analysis. The scientists studied the environment of the TMEM43 gene in which the ARVC5-specific mutation is located. The genetic sequence in the neighbourhood of TMEM43 is typically highly variable; in all affected families, however, it was identical over long stretches. These findings verify a shared genetic origin.

Further families in Europe must also be affected

The affected Danish and German families are not aware of the degree to which they are related; according to calculations, the mutation originated some 1300 to 1500 years ago. Thus, the ARVC5 mutation in the European families is not a novel mutation but an old European heritage. Therefore, there must be other families with that genetic mutation, who constitute the bridge between the patients in Europe and in North America. Two novel families with that mutation have recently been identified in Madrid. "In cases of sudden cardiac death in the family, people should sit up and take notice," says Prof Milting. "The families that are known to us have lost several male family members within a short space of time, even though they were under medical observation. Women frequently suffer from cardiac arrhythmias." Suspected cases must be looked into, warns the molecular biologist, because people carrying that mutation will definitely get the disease. Sudden cardiac death may be prevented if a defibrillator is implanted in good time.

Genetic analyses must be conducted tactfully

Genetic analyses are increasingly gaining in importance in healthcare settings as prevention and diagnostic tools. "Nevertheless, healthcare professionals are called upon to exercise great discretion when deciding which analyses must necessarily be conducted for which patients," stresses Hendrik Milting. "After all, the objective is not to stigmatise the affected families, but to prevent severe heart diseases or even sudden cardiac death." A team of molecular biologists, cardiologists and human geneticists is in charge of this task at the Heart and Diabetes Center NRW.

More information: H. Milting et al. (2014): The TMEM43 Newfoundland mutation p.S358L causing ARVC-5 was imported from

Europe and increases the stiffness of the cell nucleus, *European Heart Journal*, DOI: 10.1093/eurheartj/ehu077