

## ***Brief Report***

# ***Temporal Trends in the Incidence and Characteristics of Sudden Cardiac Death Among Subjects Under 40 Years of Age in Northern Finland During 1998-2017***

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Short Title: Temporal Trends in Sudden Cardiac Death Among Young Subjects

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## Abstract

**Background:** Although the mean age of sudden cardiac death (SCD) victims has increased during recent decades, overall incidence has remained relatively stable. Small but very important proportion of SCDs occur in subjects under 40 years of age and temporal trends in the incidence and characteristics of SCD in this age group are not well known.

**Methods:** The Fingesture study has prospectively gathered data from 5,869 consecutive autopsy verified SCD victims in Northern Finland during 1998-2017. On the basis of Finnish law, all who die unexpectedly undergo autopsy.

**Results:** Out of total 5,869 SCDs, 160 occurred in subjects under 40 years of age (3%) indicating a total incidence of 2.9/100,000/year. Incidence decreased during the study period; 4.0/100,000/year (n=50) in 1998-2002, 3.7/100,000/year (n=45) in 2003-2007, 2.5/100,000/year (n=36) in 2008-2012 and 1.5/100,000/year (n=29) in 2013-2017. Coronary artery disease (CAD) was the cause of death in 46 SCD victims (29%). Among non-ischemic causes, most common were obesity-related hypertrophic myocardial disease (24%), primary myocardial fibrosis (19%) and hypertensive myocardial disease (6%). The incidence of SCD caused by CAD decreased as follows; 1.5/100,000/year in 1998-2002, 1.2/100,000/year in 2003-2007, 0.6/100,000/year in 2008-2012 and 0.2/100,000/year in 2013-2017. Proportion of male gender (81%) and obesity as a comorbidity (body mass index >30 kg/m<sup>2</sup>, 40%) remained relatively stable during the period (p=0.58 and p=0.79, respectively).

**Conclusions:** The incidence of SCD in subjects under 40 years of age has decreased in Northern Finland during 1998-2017. According to autopsy data, most of the deaths are due to non-ischemic myocardial diseases and relative proportion of CAD has decreased.

## Introduction

The mean age of sudden cardiac death (SCD) victims has increased during recent decades, however, the overall incidence has remained relatively stable. [1] Although SCD in young subjects is a rather rare event, it is devastating for both families and communities. Recently, the importance of SCD among young has been acknowledged and public concern is increasing. The etiology of SCD differs slightly in younger individuals from older populations regarding incidence of coronary artery disease or other structural cardiac diseases as cause of death. [2] We aimed to investigate the temporal trends in the incidence and characteristics of SCD in young that have not been well described previously. In the present study, we included those under the age of 40 since coronary artery disease (CAD) becomes the leading cause of SCD beyond that age. [3] Additionally, this age limit has previously been used in epidemiological studies of SCD.

## Materials and Methods

The Fingesture study (The Finnish Genetic Study of Arrhythmic Events; [www.clinicaltrials.gov](http://www.clinicaltrials.gov) NCT02075866) is a large autopsy-based study consisting of consecutive series of victims of autopsy verified SCD in Northern Finland between the years 1998-2017 (n=5,869). In Finland, all unexpected deaths undergo medico-legal autopsy investigations based on the Finnish law. The medico-legal autopsies were performed in the Forensic Medicine Unit of the Finnish Institute for Health and Welfare, Oulu, Finland, and at the Department of Forensic Medicine, University of Oulu, Oulu, Finland. Sudden death was defined as either witnessed death within 6 hours of the onset of symptoms or as an unwitnessed death within 24 hours when the deceased individual was last seen in a stable state of health. Non-cardiac causes (e.g. pulmonary embolism, cerebral hemorrhage, intoxications) were excluded from the study. Determination of the cause of death was based on the combination of autopsy findings, medical records and questionnaires sent to the next of kin. Histological examinations were part of all autopsies and toxicology investigations were performed when necessary. The classifications for the cause of SCD are presented in Table. The reference population in the geographical area of Northern Finland (Statistics Finland, [www.stat.fi](http://www.stat.fi)) for every 5-year period was used for incidence calculations. An average number of inhabitants under 40 years of age was 289,933, with 248,380 in 1998-2002, 242,596 in 2003-2007, 289,218 in 2008-2012 and 379,537 in 2013-2017. The incidence rates were compared between the first and last study period using  $\chi^2$  test.

## Results

Among 5,869 SCDs in the Fingesture population, 160 occurred in subjects under 40 years of age (2.7%) indicating a total incidence of 2.9/100,000/year. The incidence of SCD decreased during the study period; 4.0/100,000/year (n=50) in 1998-2002, 3.7/100,000/year (n=45) in 2003-2007, 2.5/100,000/year (n=36) in 2008-2012 and 1.5/100,000/year (n=29) in 2013-2017 ( $p < 0.001$ ). In autopsies, CAD was the cause of death in 46 (29%) young SCD victims and most occurred among 35–40-year-old individuals (38 victims, 83%). Among non-ischemic causes detected in autopsies, most common were obesity-related hypertrophic myocardial disease (38 victims, 24%), primary myocardial fibrosis (PMF) (30 victims, 19%), hypertensive myocardial disease (10 victims, 6%), myocarditis (8 victims, 5%) and hypertrophic cardiomyopathy (6 victims, 4%). Structurally normal heart was present in 5 subjects (3%). The incidence and proportion of SCD caused by CAD decreased during the study period; 1.5/100,000/year in 1998-2002 (38%), 1.2/100,000/year in 2003-2007 (33%), 0.6/100,000/year in 2008-2012 (22%) and 0.2/100,000/year in 2013-2017 (14%) ( $p < 0.001$ ). Proportion of male gender (81%) and obesity as a comorbidity (body mass index  $>30$  kg/m<sup>2</sup>, 40%) remained relatively stable during the period ( $p=0.58$  and  $p=0.79$ , respectively).

## Discussion/Conclusion

In the present study, we observed a descending trend in the incidence of SCD among young population, strengthening the observations in previous studies. [4] Non-ischemic myocardial diseases comprised the majority of the causes for SCD, the proportion and therefore incidence of CAD as a cause of SCD decreased in subjects under 40 years of age during past two decades as seen in the general population. [1] However, the proportion of obesity as a comorbidity of SCD remained rather stable during the 20-year period. The decrease in the incidence of SCD in the younger subjects may be explained by the decreased proportion of mortality resulting from CAD due to progress in prevention and treatment of CAD, along with the increased mean age of the victims dying due to CAD. Also, the prevalence of asystole and pulseless electrical activity has been shown to be increasing as an initial recorded rhythm in sudden cardiac arrest, possibly due to a decreasing trend of CAD as an underlying cause. [5] Media coverage for sudden deaths in sports and in younger populations has resulted in wide distribution of defibrillators in sporting venues and malls. Therefore, it might be that sudden cardiac arrests are more effectively being treated today. According to Hiltunen et al., [6] the survival rate of patients who experienced out of hospital cardiac arrest has improved in Finland. Despite the progress in primary prevention of CAD and lifestyle changes, the burden of acquired cardiac diseases seems to remain significant. Obesity-related hypertrophic myocardial disease was quite prevalent in the autopsy cohort. Obesity is a global epidemic and is a well-recognized risk factor for cardiac diseases. Obesity-related left ventricular hypertrophy has also

been observed in a previous study among the young. [7] In comparison with more commonly studied inherited causes for SCD among young, obesity-related cardiomyopathy is highly preventable disease. About one fifth of the victims had PMF, which is a common postmortem finding among young individuals with SCD and may be a variable phenotypic or an earlier pathologic expression of cardiomyopathies. [8]

In conclusion, the incidence of SCD in subjects under 40 years of age has decreased in Northern Finland during the years 1998-2017. According to our autopsy data, most of the SCDs in this age group are due to non-ischemic myocardial diseases with a significant proportion of obesity-related cardiomyopathy and PMF. In addition, the incidence of CAD as a cause of SCD in these younger subjects has decreased. In the future, we should focus prevention strategies on non-ischemic heart diseases among the young adults, especially cardiomyopathy related to obesity and hypertension where prevention would be beneficial. However, screening and treating CAD remains also important in the future in order to decrease absolute numbers of SCD among young adults.

## Statement of Ethics

This study complies with the Declaration of Helsinki and has been approved by the Ethics Committee of Northern Ostrobothnia Hospital District and Finland's Ministry of Social Affairs and Health. Finnish Institute for Health and Welfare and the Regional State Administrative Agency of Northern Finland approved the review of autopsy data by the investigators. The Ethics Committee decided to forego the consent from relatives, since medicolegal autopsy does not require consent according to the Finnish law.

## Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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## Author Contributions

**Study design and conception:** Juhani Junttila, Heikki Huikuri, Juha Perkiömäki. **Acquisition, analysis or interpretation of data:** Juha Vähätalo, Lauri Holmström, Lasse Pakanen, Kari Kaikkonen, Juha Perkiömäki, Heikki Huikuri, Juhani Junttila. **Drafting of the manuscript:** Juha Vähätalo, Lauri Holmström, Juhani Junttila. **Statistical analysis:** Juha Vähätalo & Lauri Holmström. **Critical revision of the manuscript for important intellectual content:** Lauri Holmström, Lasse Pakanen, Kari Kaikkonen, Juha Perkiömäki, Heikki Huikuri, Juhani Junttila. **Obtained funding:** Juha Vähätalo & Juhani Junttila. **Supervision:** Juhani Junttila & Heikki Huikuri

## Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## References

1. Junttila MJ, Hookana E, Kaikkonen KS, Kortelainen ML, Myerburg RJ, Huikuri HV. Temporal Trends in the Clinical and Pathological Characteristics of Victims of Sudden Cardiac Death in the Absence of Previously Identified Heart Disease. *Circ Arrhythm Electrophysiol*. 2016;9:e003723. doi: 10.1161/CIRCEP.115.003723.
2. Bagnall RD, Weintraub RG, Ingles J, Duflou J, Yeates L, Lam L, et al. A Prospective Study of Sudden Cardiac Death among Children and Young Adults. *N Engl J Med*. 2016;374:2441-52.
3. Vähätalo J, Holmström L, Pakanen L, Kaikkonen K, Perkiömäki J, Huikuri H, et al. Coronary artery disease as the cause of sudden cardiac death among victims <50 years of age. *Am J Cardiol*. 2021;147:33-8.
4. Lynge TH, Nielsen JL, Blanche P, Gislason G, Torp-Pedersen C, Winkel BG, et al. Decline in incidence of sudden cardiac death in the young: a 10-year nationwide study of 8756 deaths in Denmark. *Europace*. 2019;21:909-17.
5. Kauppila JP, Hantula A, Kortelainen ML, Pakanen L, Perkiömäki J, Martikainen M, Huikuri HV, Junttila MJ. Association of initial recorded rhythm and underlying cardiac disease in sudden cardiac arrest. *Resuscitation*. 2018 Jan;122:76-78. doi: 10.1016/j.resuscitation.2017.11.064.
6. Hiltunen P, Kuisma M, Silfvast T, Rutanen J, Vaahersalo J, Kurola J; Finnresusci Prehospital Study Group. Regional variation and outcome of out-of-hospital cardiac arrest (ohca) in Finland - the Finnresusci study. *Scand J Trauma Resusc Emerg Med*. 2012 Dec 17;20:80. doi: 10.1186/1757-7241-20-80.
7. Finocchiaro G, Papadakis M, Dhutia H, Cole D, Behr ER, Tome M, et al. Obesity and sudden cardiac death in the young: Clinical and pathological insights from a large national registry. *Eur J Prev Cardiol*. 2018;25:395-401.
8. Junttila MJ, Holmström L, Pylkäs K, Mantere T, Kaikkonen K, Porvari K, et al. Primary Myocardial Fibrosis as an Alternative Phenotype Pathway of Inherited Cardiac Structural Disorders. *Circulation*. 2018;137:2716-26.