FINNISH CARDIAC SOCIETY

50th Progress Report Meeting

April 10, 2024, Helsinki

Contents

50th Progress Report Meeting Programme

Honka-sali. Session 1. 50th Progress Report Meeting – YIAC
Chairperson Tuomas Kiviniemi, Finnish Cardiac Society

Meeting is supported by unrestricted educational grant from Boehringer Ingelheim

09.30–09.35	Video by Progress Report Competition supporter Boehringer Ingelheim
09.35–09.40	Opening remarks. Tuomas Kiviniemi, President Elect, Finnish Cardiac Society
09.40–09.50	Lesion-related risk factors after coronary stenting. MD Elina Mäntyniemi, University of Helsinki
09.50–10.00	Age-related trends of ischemic sudden cardiac death in women. MD Ida Hookana, Medical Research Center Oulu
10.00–10.10	Eicosapentaenoic acid rapidly reduces apolipoprotein B and plasma lipids in healthy individuals and thus lowers their risk of atherosclerotic cardiovascular disease. M. Sc. Lauri Äikäs, Wihuri Research Institute
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10.40–10.50	Histopathology and prognosis of new-onset atrio-ventricular block after coronary artery bypass graft surgery. B. Med Anna-Reetta Toiviainen, Turku University Hospital and University of Turku
10.50–11.00	Cardiac structure and function across the continuum of glucose metabolism. BM Tommi Grönlund, University of Oulu
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11.10–11.20	Endomyocardial biopsy in the diagnosis of cardiac sarcoidosis. MD Henriikka Mälkönen, Helsinki University Hospital and University of Helsinki
11.20–11.25	Closing remarks.

Posters are presented on Wednesday April 10 during the coffee breaks. All poster presenters are expected to be available by their posters to discuss the content during the following coffee breaks: 11.15–12.00 and 14.00–14.30 o'clock.

History of the Progress Report Meetings

Progress Report Meeting is organized by Finnish Cardiac Society to present opportunity for young investigators to report results of their studies. An important point is also training in presenting scientific papers to criticism of senior colleagues.

Boehringer Ingelheim has supported organizing the meeting from the beginning, 1975 by helping in practical matters and presenting grants to the best of speakers.

Winners of the Boehringer Ingelheim grants

From year 2007 onwards the competition has had two categories instead of 1st and 2nd prize. However, if less than three eligible abstracts have been received to either category, the organizers reserve the right to combine the categories.

Year	1st Prize	2nd Prize
1975	Erkki Pesonen	–
1976	Heikki Karppanen	Markku S. Nieminen
1977	Matti Halinen	Ulla Korhonen
1978	Ilkka Torstila	Markku S. Nieminen
1979	Olli Meretoja	Aila Rissanen
1980	Jorma Viikari	Jouko Jalonen
1981	Markku Kupari	Irma Koivula
1982	Heikki Huikuri	Markku Kupari
1983	Seppo Hietakorpi	Kari Niemelä
1984	Markku Laakso	Heikki Huikuri
1985	Jukka Räisänen	Kari Niemelä
1986	Pekka Koskinen	Juha Mustonen
1987	Kimmo Mattila	Silja Majahalme
1988	Heikki Tikkanen	Paula Rämö
1989	Hannu Näveri	Keijo Peuhkurinen
1990	Markku Mäkijärvi	Juhani Valkama
1991	Eero Mervaala	Paavo Uusimaa
1992	Eero Mervaala	Anne Remes
1993	Juha Hartikainen	Helena Kovanen
1994	Kai Kiilavuori	Juha Perkiömäki
1995	Sirkku Pikkujämsä	Pasi Tavi
1996	Jorma Kokkonen	Timo Mäkikallio
1997	Pekka Raatikainen	Marja Laitinen
1998	Marja Laitinen	Antti Ylitalo, 3rd Prize Timo Mäkikallio
1999	Mika Laine	Timo Mäkikallio
2000	Saila Vikman	Antti Kivelä
2001	Jari Tapanainen	Pertti Jääskeläinen
2002	Tuomas Rissanen	Markku Pentikäinen
2003	Juhani Junttila	Markus Leskinen
2004	Jere Paavola	Tuomas Rissanen
2005	Mikko Mäyränpää	Satu Helske
2006	Olli Tenhunen	Johan Lassus

Year	Basic Science category	Clinical Research category
2007	Satu Helske	Ville Kytö
2008	Mirella Hietaniemi	Minna Kylmälä
2009	Johanna Lähteenvuo o.s. Markkanen	Annukka Marjamaa
2010	1st Prize Jani Tikkanen 2nd Prize Riina Kandolin	the categories were combined
2011	Markku Lähteenvuo	Aapo Aro
2012	1st Prize Kirsi Kujala 2nd Prize Maija Bry	the categories were combined
2013	Suvi Syväranta	Toni Grönberg
2014	1st Prize Leena Kaikkonen 2nd Prize Heli Tolppanen	the categories were combined
2015	1st Prize Aissa Bah 1st Prize Markus Räsänen	the categories were combined
2016	1st Prize Heli Tolppanen 1st Prize Kaj Ekström	the categories were combined
2017	Tarja Alakoski	Samuli Jaakkola
2018	Maija Ruuth	Tero Penttilä
2019	Annakaisa Tirronen	Anette Haukilahti
2020	1st Prize, Tiia Istolahti Prize, Vilbert Sikorski	1st Prize, Henna Korpela 2nd
2021	1st Prize Aleksi Leikas	2nd Prize Minna Koivunen
2022	1st Prize Markus Ritvos	2nd Prize Kristiina Harju
2023	1st Prize Anne Doedens	2nd Prize Valtteri Muroke

MD Elina Mäntyniemi
University of Helsinki

Lesion-related risk factors after coronary stenting

Elina Mäntyniemi, University of Helsinki; Juha Sinisalo, University of Helsinki; Mitja Lääperi, University of Helsinki

Aims

Despite pharmacotherapy and invasive procedure advances risk for recurring ischemic cardiovascular events remains, partly due to stent failure, partly due to natural progression of atherosclerosis. Late stent restenosis has been studied comprehensively. Less is known about ischemic events occurring as new lesions. We aimed to define which factors predict location of new ischemia-causing stenosis after stenting.

Methods

This observational study used prospectively collected data from the Corogene study registry. 1981 patients assigned to coronary angiogram between June 2006 and March 2008 were included in the study. After the index procedure patients were followed up for ten years or until CABG or death. All subsequent coronary angiograms during the follow-up period were analyzed and compared with previous findings. Baseline characteristics, clinical and laboratory findings, angiographic findings and medication use were obtained. Different outcomes were modeled using logistic regression models. Primary objective was to determine the rate of stent restenosis in relation to the emergence of new coronary lesions, and predictive factors related to disease progression. Secondary outcomes were major adverse cardiovascular events (MACE) defined as cardiovascular death, death from any cause, stroke or repeat revascularization.

Results

During a median of 10.8 years of follow up there were 496 cardiovascular events including 263 cardiovascular deaths in both groups combined. 207 (15.1%) patients in the ACS group and 157 (25.7%) patients in the stable CAD group had repeat revascularization at least once after the index procedure. Site of the repeat revascularization was in 47.5% target lesion site and 52.5 % non-target lesion site. Risk factors associated with target lesion revascularization (TLR) vs non-target lesion revascularization (NTLR) included length of stent(s) and adherence to statin medication. Good adherence to statins significantly lowered probability of TLR compared to NTLR. Combined length of stent(s) correlated with the probability of TLR compared to NTLR. Good adherence to statin medication protected from all end points. During 12 months after PCI antithrombotic medication protected from CV death. (Table 1, Figure 1).

Conclusions

In line with previous studies, we found that longer stents represent a risk for stent restenosis. A new finding is that good adherence to statin medication protected from target lesion revascularization compared to non-target lesion revascularization. This suggests that especially patients with long or multiple stents should be encouraged to adhere to lifetime of lipid-lowering medication.

	OR CV death	P	OR CV event	P	OR TLR vs NTLR	P
Age	1.62 [1.32-1.99]	<0.001	1.18 [1.03-1.35]	0.017	1.09 [0.81-1.47]	0.59
Diabetes	2.22 [1.46-3.36]	<0.001	1.41 [1.02-1.94]	0.036	1.47 [0.74-2.97]	0.28
BMI	1.06 [1.03-1.10]	<0.001	1.03[1.00-1.05]	0.066	0.97 [0.91-1.03]	0.26
Smoking	1.07 [0.66-1.71]	0.79	1.02 [0.75-1.39]	0.90	0.90 [0.45-1.82]	0.78
NTproBNP	1.71 [1.49-1.98]	<0.001	1.17 [1.06-1.29]	0.0016	1.00 [1.00-1.00]	0.24
CystatinC	1.16 [0.83-1.61]	0.37	1.18 [0.91-1.51]	0.21	0.61 [0.31-1.11]	0.12
Stent lenght	1.16 [1.02-1.33]	0.026	1.05 [0.95-1.16]	0.36	1.24 [1.01-1.54]	0.040
Statin adherence>80%	0.48 [0.42-0.74]	<0.001	0.67 [0.49-0.92]	0.014	0.33 [0.16-0.63]	0.0039
Antithr. adherence 1yr>80%	0.63 [0.42-0.95]	0.025	1.02 [0.77-1.36]	0.88	0.97 [0.54-1.77]	0.93

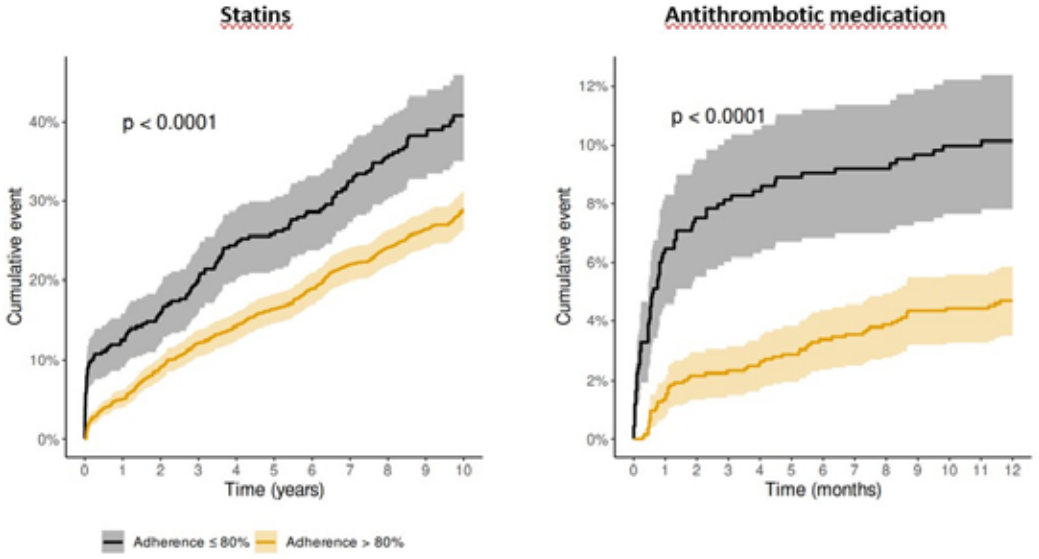


Figure 1. Cumulative incidence of CV-events when adherence to medication is good (>80%) compared to partial or poor (<80%) adherence. Antithrombotic medication use was covered for 12 months after PCI according to current guidelines.

MD Ida Hookana
Medical Research Center Oulu

Age-related trends of ischemic sudden cardiac death in women

Ida Hookana, Medical Research Center Oulu; Anette Eskuri, Medical Research Center Oulu; Lauri Holmström, Medical Research Center Oulu; Juha Vähätalo, Medical Research Center Oulu; Tuomas Kenttä, Medical Research Center Oulu; Jani Tikkanen, Medical Research Center Oulu; Lasse Pakanen, Medical Research Center Oulu; Juha Perkiömäki, Medical Research Center Oulu; Heikki Huikuri, Medical Research Center Oulu; Juhani Junttila, Medical Research Center Oulu

Aim

Sudden cardiac death (SCD) is a significant public health issue, with 70-80% of cases linked to coronary artery disease (CAD). Despite extensive research on general risk factors and mechanisms, there's a recognized need to investigate specific aspects of SCD in women. This study aims to assess age-related trends in ischemic SCD among women.

Methods

The Fingesture cohort consists of 5,869 individuals with SCD (21.1% women) in Northern Finland from 1998 to 2017. Of all SCD cases, 74.8% were due to CAD (ischemic SCD). The cause of death was determined with medico-legal autopsy for each subject.

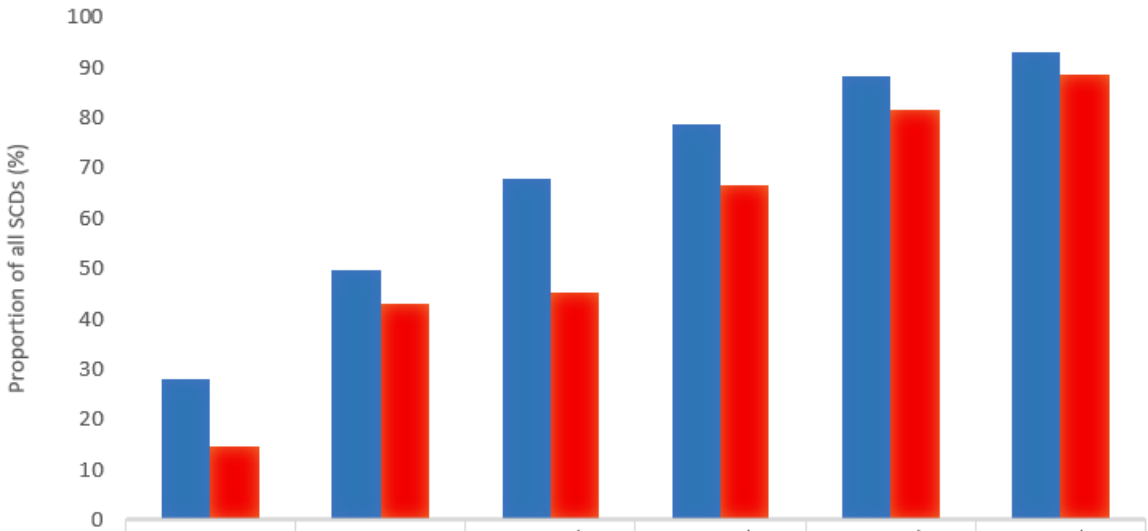
Results

In women, SCD occurred at older ages (73.2±11.3 years vs. 65.6±10.8 years in men, $p<0.001$) and was less often due to CAD compared to men (71.7% vs. 75.7%, respectively, $p=0.005$). Women with ischemic SCD had an average BMI of 27.3±6.3 kg/m^2, decreasing with increasing age (-0.6 kg/m^2 per decade, CI -1.0 to -0.2 kg/m^2, $p=0.002$). The median subcutaneous fat thickness was 3.0 cm (interquartile range 2.0, 3.0) and it also decreased with increasing age (-0.3 cm per decade, CI -0.4 to -0.2 cm, $p<0.001$). The average heart weight of women with ischemic SCD was 404±122 grams, with no significant age-related trend (unadjusted $\beta=4.2$ g, CI -1.6 to 10.0 g, $p=0.159$). Majority of women with ischemic SCD (61.7%) had moderate or substantial myocardial fibrosis and 41.4% had myocardial scars, both prevalences increasing with age: fibrosis by 5.2% (CI 2.2-8.1%, $p<0.001$) and scarring by 5.5% per decade (CI 2.6-8.5%, $p<0.001$).

Conclusion

In women, the profile of CAD-related SCD is age-dependent. Myocardial scars and fibrosis are more common in older subjects, while the prevalence of obesity is higher in younger subjects. These findings suggest that at the population level, the prediction and prevention of ischemic SCD may need a distinct focus for younger and older women.

Figure 1. The proportion of ischemic sudden cardiac death by age and sex



Age (y)	< 40 (p=0.281)	40-49 (p=0.394)	50-59* (p<0.001)	60-69* (p<0.001)	70-79* (p=0.002)	≥ 80* (p<0.050)
Men	28,2	49,6	67,9	78,8	88,2	93,0
Women	14,8	42,9	45,3	66,5	81,7	88,7

Table 1. Demographics and characteristics of women with sudden cardiac death

	Ischemic SCD (N=888)	Nonischemic SCD (N=350)	p-value
Continuous variables			
Age (y)	73.2±11.3	62.2±14.0	<0.001
Heart weight (g)	404.1±95.6	431.4±121.9	<0.001
BMI (kg/m²)	27.3±6.3	29.2±9.4	<0.001
SC fat thickness (cm)	3.0 (2.0, 3.0)	3.0 (2.0, 5.0)	<0.001
Categorical variables			
Myocardial fibrosis (%, N)	61.7, 547	44.0, 154	<0.001
Myocardial scar (%, N)	41.4, 367	11.1, 39	<0.001

M. Sc. Lauri Äikäs
Wihuri Research Institute

Eicosapentaenoic acid rapidly reduces apolipoprotein B and plasma lipids in healthy individuals and thus lowers their risk of atherosclerotic cardiovascular disease

Lauri Äikäs, Wihuri Research Institute; Martin Hermansson, Wihuri Research Institution; Petri Kovanen, Wihuri Research Institute; Katariina Öörni, Wihuri Research Institute

Background and aims

Eicosapentaenoic acid (EPA) supplements have been shown to reduce plasma triglycerides and atherosclerotic cardiovascular disease (ASCVD). However, the mechanistic details underlying the observed reduction in ASCVD events are scarce. Thus, we performed detailed metabolomics, lipidomics, and functional analyses to further investigate the effect of EPA supplementation in humans.

Methods

Healthy normolipidemic volunteers (n=72) received a 4-gram daily dose of EPA for 4 weeks, and fasting blood samples were collected before, during, and after the supplementation (Figure 1). Gas chromatographic and nuclear magnetic resonance methods were used to determine the plasma fatty acid (FA) and lipoprotein subclass profiles, respectively. The binding of plasma lipoproteins to isolated human arterial proteoglycans was determined as a surrogate marker of lipoprotein retention in the arterial wall. Finally, a 10-year ASCVD risk assessment was performed using the Finnish Hertta-test (CERT2-score).

Results

FA analysis revealed that EPA supplementation improved the omega-6/omega-3 ratio from 7.9 to 2.8, and it also reduced saturated FAs (Figure 2A). Increase in plasma EPA concentration correlated inversely with low baseline levels of EPA (Figure 2B). Thus, individuals with low initial EPA concentration had a higher increase in EPA concentration. EPA supplementation reduced the plasma levels of apoB particles in all VLDL and LDL subclasses, and the larger the particles were the stronger was their reduction (Figure 2C, red columns). The reduction in apoB lipoproteins led to a reduction in plasma triglycerides (-15%), non-HDL cholesterol (-4%), and VLDL remnant cholesterol (-5%). Additionally, EPA supplementation improved the HDL subclass profile by increasing the number of XL-HDL particles (Figure 2C, blue columns) and reducing HDL-triglyceride concentration (Figure 2D). The proteoglycan binding of lipoproteins was reduced after EPA supplementation, which could be explained by the significant reductions in cholesterol and phospholipids but not triglycerides present in the apoB–containing particles (Figure 2E). Importantly, EPA supplementation reduced the CERT2-score by -26% (Figure 2F).

Conclusion

EPA supplementation lowered the numbers of atherogenic apoB–containing plasma lipoprotein particles, and so reduced the plasma concentrations of triglycerides and cholesterol. Moreover, the HDL lipoprotein profile was improved. The observed reduction in the binding of the atherogenic apoB-lipoproteins to arterial proteoglycans reveals a novel mechanism by which EPA supplementation in a primary prevention setting could lead to reduced atherogenesis and ensuing ASCVD.

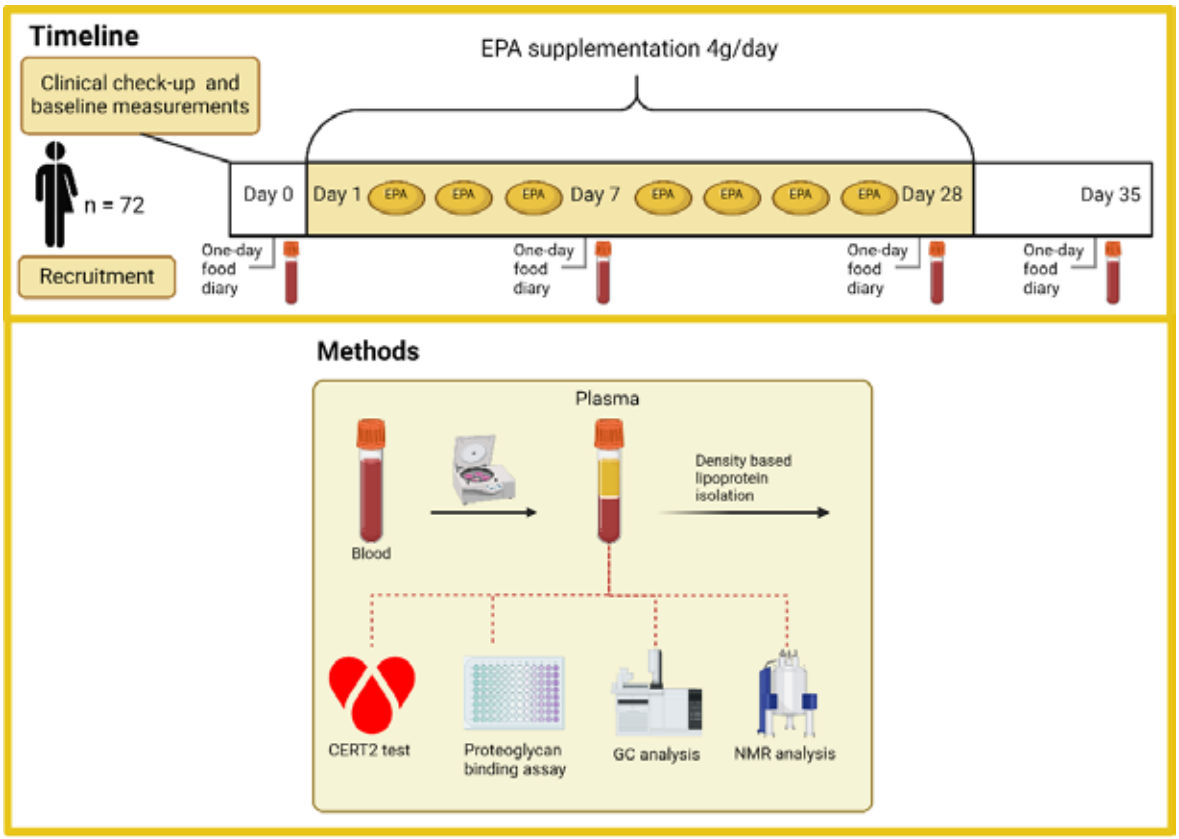


Figure 1. The timeline and methods of the study. *72 participants; 34 male and 38 females were recruited for the study. The participants underwent clinical baseline measurements day prior to starting the EPA suppelementation for 28 days. CERT2 = Coronary event risk test 2, GC = gas chromatography, NMR = nuclear magnetic resonance. Figure created with Biorender.com*

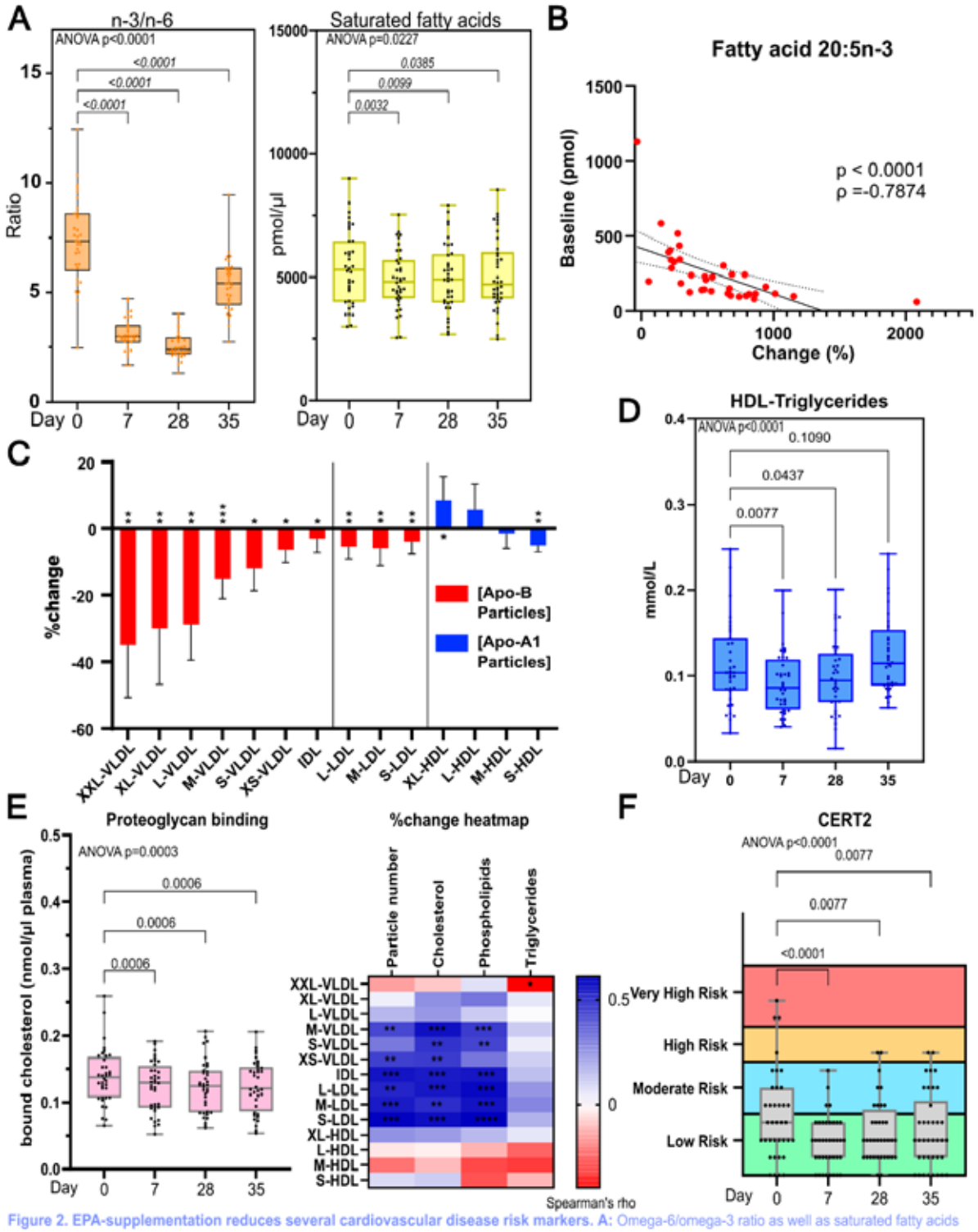


Figure 2. EPA-supplementation reduces several cardiovascular disease risk markers. A: Omega-6/omega-3 ratio as well as saturated fatty acids lowered after EPA-supplementation in plasma. **B:** The increase in the plasma concentration of EPA negatively correlated with low baseline values of EPA. **C:** Lipoprotein subclass particles numbers were determined using nuclear magnetic resonance and are presented by their day 0 vs day 28 percent change. **D:** High-density lipoprotein triglycerides were lowered afer EPA-supplementation. **E:** Shows the lowered arterial proteoglycan binding and the heatmap presents the correlation and their significance of changes occurring in lipoprotein subclass particle number and lipidomes with proteoglycan binding. **F:** Shows the reduction in CERT2-risk score, which is categorised by risk scrore evaluation. The different days mark the four blood sampling points of the EPA-supplementation. All box-plots presents individual values with standard deviation and whiskers represent range. Significance is measure with One-way ANOVA applying multiple test correction using false discovery rate.

MD Antti Lappalainen
Kuopio University Hospital and University of Eastern Finland

Atrial fibrillation, atrial flutter and atrioventricular node catheter ablation trends in a Finnish nationwide cohort study

Antti Lappalainen, Kuopio University Hospital and University of Eastern Finland; Konsta Teppo, Turku University Hospital and University of Turku; Olli Halminen, Aalto University; Rasmus Siponen, University of Eastern Finland; Janne Virrankorpi, University of Helsinki; Aapo Aro, Helsinki University Hospital and University of Helsinki; Annukka Marjamaa, Helsinki University Hospital and University of Helsinki; Birgitta Salmela, Päijät-Häme Central Hospital; Jukka Putaala, Helsinki University Hospital and University of Helsinki; Pirjo Mustonen, Turku University Hospital and University of Turku; Miika Linna, University of Eastern Finland; Jari Haukka, University of Helsinki; Juhani Airaksinen, Turku University Hospital and University of Turku; Juha Hartikainen, Kuopio University Hospital and University of Eastern Finland; Mika Lehto, Jorvi Hospital, Helsinki University Hospital and University of Helsinki

Background

Atrial fibrillation (AF) is the most common cardiac arrhythmia with increasing prevalence. Catheter ablation is a well-established treatment for prevention of AF and atrial flutter (AFL) recurrences and decreasing symptoms. Pacemaker implantation and atrioventricular node (AVN) ablation can be used for rate control in AF or AFL when medical therapy fails.

Aims

We investigated temporal trends of catheter ablation procedures for AF, AFL and AVN in Finland between 2012 and 2018.

Methods

Finnish AntiCoagulation in Atrial Fibrillation (FinACAF) is a registry-based study including all patients with AF or AFL in Finland between 2012 and 2018.

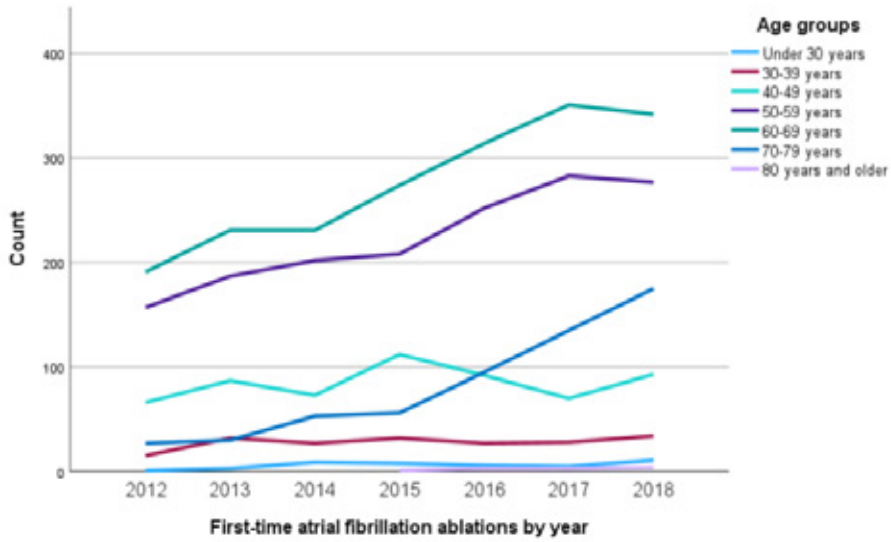
Results

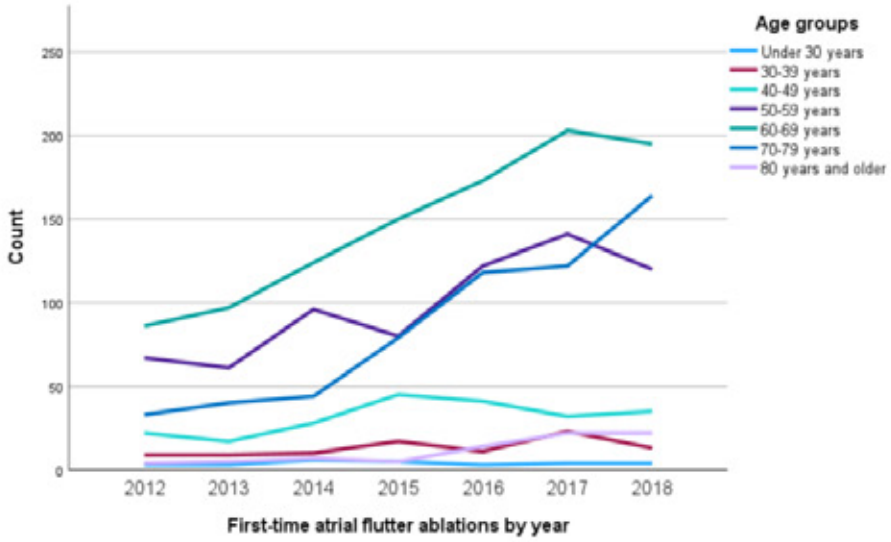
A total of 8961 first-time catheter ablation procedures were identified. Of them, 4913 (54.8 %) were AF ablations, 2734 (30.5 %) AFL ablations and 1314 (14.7 %) AVN ablations. 3427 (69.8 %) of AF ablation patients and 2040 (74.6 %) of AFL patients, and 566 (43.1 %) of AVN patients were men. The use of catheter ablation increased progressively during 2012-2018 for AF (457/year to 936/year), AFL (224/year to 553/year) and AVN (114/year to 238/year). The increase was particularly seen in the age groups of 70-79 years in AF and AFL (Figure) whereas in this age group the use of AVN ablation decreased. The mean age of patients increased in AF ablations (median 60 years, range 15-87 years) from 58.0 to 60.4 years, AFL ablations (median 64 years, range 15-98 years) from 60.2 years to 64.2 years and in AVN ablations (median 74 years, range 26-96 years) from 70.6 to 73.6. The mean CHA2DS2-VASc- score of AF patients increased from 1.6 to 1.8 (p=0.012) and AFL patients from 2.0 to 2.4 (p=0.002). The mean time from AF or AFL diagnosis to catheter ablation increased in AF patients from 4.6 years to 5.4 years, in AFL patients from 3.1 to 4.5 years, and in AVN patients from 4.4 years to 6.3 years.

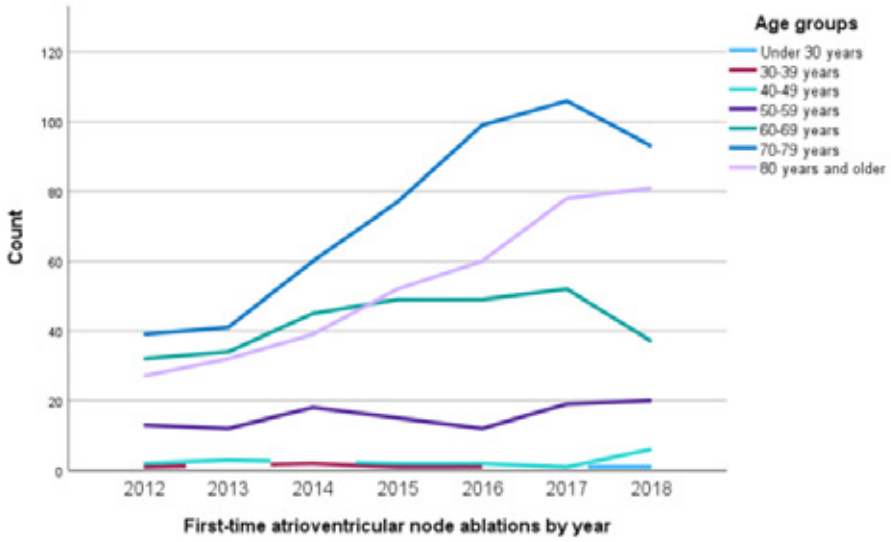
Conclusions

AF and AFL patients undergoing catheter ablation were predominantly men. The use of catheter ablation for AF, AFL and AVN increased during 2012-2018. The age of the patients with first-time AF, AFL and AVN ablation increased. However, the mean delay from AF and AFL diagnosis to catheter ablation increased by time during the observation period.

YIAC 10.10–10.20 MD Antti Lappalainen
Kuopio University Hospital and University of Eastern Finland







MD Marko Taipale
Helsinki University Hospital

Challenging endomyocardial biopsies' gold standard status in rejection screening: a prospective blinded study on cardiovascular magnetic resonance in heart transplant patients

Marko Taipale, Helsinki University Hospital; Markku Pentikäinen, Helsinki University Hospital; Laura Martelius, Helsinki University Hospital; Aino Mutka, Helsinki University Hospital; Soili Kytölä, Helsinki University Hospital; Matti Kankainen, Helsinki University Hospital; Juha Peltonen, Helsinki University Hospital; Arttu Lahtiharju, Helsinki University Hospital; Jyri Lommi, Helsinki University Hospital; Timo Jahnukainen, Helsinki University Hospital; Sari Kivistö, Helsinki University Hospital; Karl Lemström, Helsinki University Hospital; Tiina Ojala, Helsinki University Hospital

Aim

The detection of rejection is crucial for graft survival after heart transplantation. Endomyocardial biopsies (EMBs) serve as the gold standard for rejection surveillance despite its limitations, while cardiac magnetic resonance (CMR), in conjunction with donor-derived cell-free DNA (dd-cfDNA) analysis, holds promise as a non-invasive approach. In this prospective blinded study (Trial NCT04311346), our aim was to evaluate feasibility of CMR for rejection screening, validating it against EMB and dd-cfDNA.

Methods

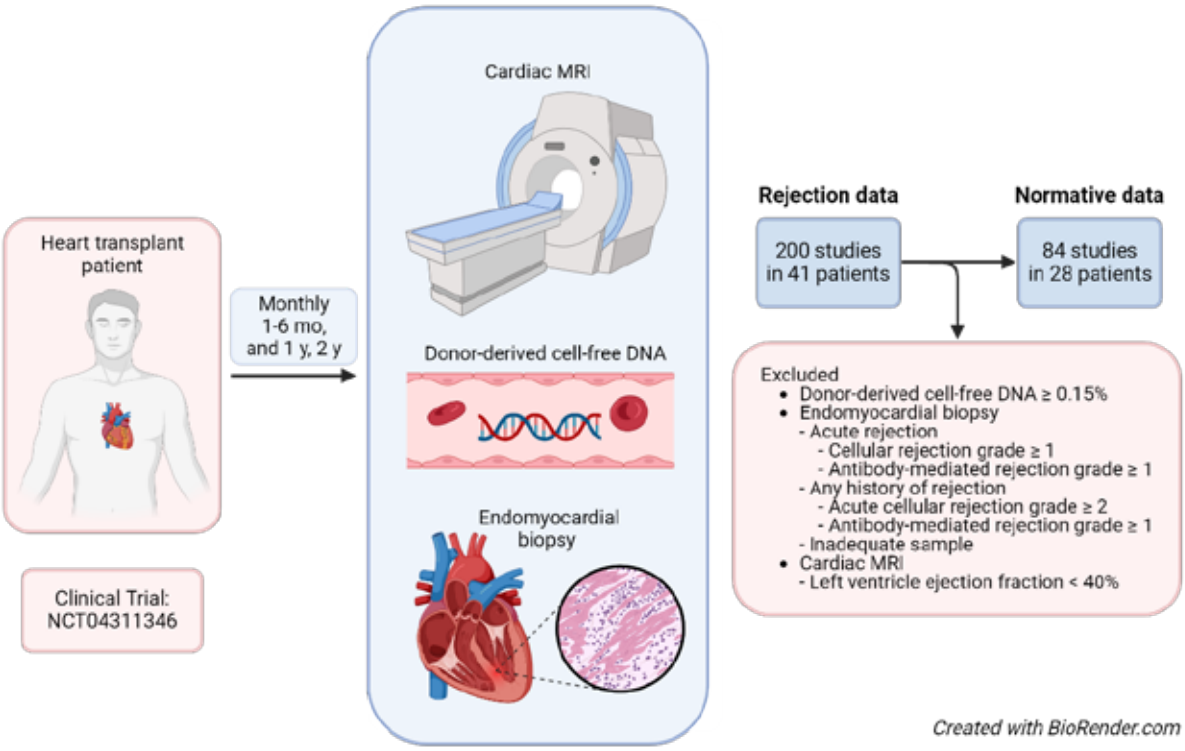
We blindly analyzed 200 comparisons involving CMR, EMB, and dd-cfDNA in 41 heart transplant recipients within 1 to 24 months post-transplant. In CMR T1- and T2-mapping analyses, we categorized 16 myocardial segments based on their coronary supply and anatomical location. Further, the graft's systolic function was assessed through strain analyses and volumetric ejection fractions. EMB results were graded according to the ISHLT criteria (2005 and 2013). The cutoff for abnormal dd-cfDNA was set at 0.2%. We established rejection-free CMR reference values and explored the capability of CMR in detecting acute rejection.

Results

In normative data over the 24 months post-transplant, global T1 time remained stable, while T2 time biphasically decreased. We also observed variability in mapping values, specifically according to the coronary territories and anatomical location of the segments. In rejection data, among the 13 EMB verified acute rejections (nine acute cellular rejection grade ≥ 2 and three antibody-mediated rejection grade ≥ 1), CMR indicated rejection in eight. Further, both CMR and dd-cfDNA were normal in four instances. Additionally, in three comparisons, both CMR and dd-cfDNA suggested rejection, but EMB showed no rejection. These results suggest that EMB may both over- and underdiagnose acute heart transplant rejection.

Conclusions

EMB presents challenges in both under- and overdiagnosing rejection in heart transplant surveillance. A strategy based on CMR, combined with dd-cfDNA analyses, shows promise as a new gold standard for rejection screening.


Heart transplant patient
Clinical Trial: NCT04311346
Monthly 1-6 mo, and 1 y, 2 y
Cardiac MRI
Donor-derived cell-free DNA
Endomyocardial biopsy
Rejection data
200 studies in 41 patients
Normative data
84 studies in 28 patients
Excluded
• Donor-derived cell-free DNA ≥ 0.15%
• Endomyocardial biopsy
- Acute rejection
- Cellular rejection grade ≥ 1
- Antibody-mediated rejection grade ≥ 1
- Any history of rejection
- Acute cellular rejection grade ≥ 2
- Antibody-mediated rejection grade ≥ 1
- Inadequate sample
• Cardiac MRI
- Left ventricle ejection fraction < 40%
Created with BioRender.com

Characteristics of sudden cardiac death according to body mass index group: The FinGesture study

Lassi Mäntyniemi, University of Oulu; Lasse Pakanen, Finnish Institute for Health and Welfare; Lauri Holmström, University of Oulu; Jani Tikkanen, University of Oulu; Juha Vähätalo, Oulun Yliopisto; Anette Eskuri, University of Oulu; Juha Perkiömäki, University of Oulu; Heikki Huikuri, University of Oulu; Juhani Junttila, University of Oulu

Aims

We aimed to investigate the characteristics of SCD according to the BMI group. The prevalence of obesity has increased significantly in Western Societies. Obesity increases the risk of sudden cardiac death (SCD), but the etiology and mechanisms of obesity-related SCD are unclear.

Methods

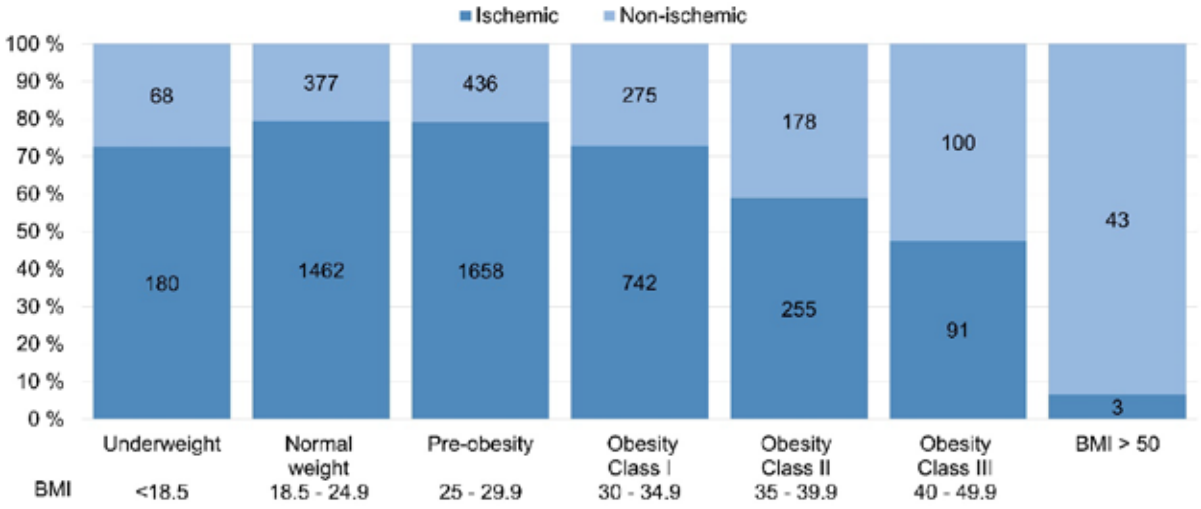
This study is derived from the FinGesture study, which has prospectively collected all out-of-hospital SCD cases from Northern Finland since 1998 (population ~700,000). As required by Finnish law, all sudden deaths undergo medicolegal autopsy, and the Fingesture study has included all sudden deaths from Northern Finland with autopsy-verified cardiac etiology (i.e., SCD). The determination of the cause of death was based on a combination of autopsy findings, medical records, and police and emergency medical service reports.

Results

The study population consisted of a total of 5,869 autopsy-verified SCD victims. Mean age was 64.9±12.4 and 78.9 % were male. The mean age decreased along with increasing BMI class (Table) ($p < 0.001$). The proportion of non-ischemic cardiac disease ($p < 0.001$, Figure) and the mean heart weight at autopsy ($p < 0,001$, Table) increased along with increasing BMI.

Conclusions

Obesity-related SCD is associated with younger age and a higher proportion of non-ischemic cardiac disease with hypertrophy. These results suggest that early development of non-ischemic cardiac disease may contribute to obesity-related SCD.



	Under weight	Normal weight	Pre-Obesity	Obesity Class I	Obesity Class II	Obesity Class III	BMI > 50	P-value
N	248	1869	2097	1017	433	191	46	
BMI	<18.5	18.5-24.9	25-29.9	30-34.9	35-34.9	40-40.9	>50	
Age	65.3 (±15.8)	66.1 (±12.8)	65.2 (±11.8)	64.1 (±11.7)	62.8 (±11.9)	60.1 (±11.4)	51.7 (±11.8)	<0.001
Male sex (%)	70.2	79.4	82.3	78.9	72.7	65.4	67.4	<0.001
Heart weight (g)	324 (±88)	423 (±100)	488 (±104)	537 (±120)	584 (±142)	618 (±146)	675 (±132)	<0.001
Abdominal fat (cm)	1.1 (±0.75)	2.0 (±0.74)	2.8 (±0.88)	3.5 (±1.1)	4.2 (±1.7)	6.1 (±2.2)	8.7 (±3.5)	<0.001

B. Med Anna-Reetta Toiviainen
Turku University Hospital and University of Turku

Histopathology and prognosis of new-onset atrio-ventricular block after coronary artery bypass graft surgery

Anna-Reetta Toiviainen, Turku University Hospital and University of Turku; Arto Relander, Turku University Hospital and University of Turku; Veikko Lahtinen, Turku University Hospital and University of Turku; Ilkka Ruohonen, Turku University Hospital and University of Turku; Joonas Lehto, Turku University Hospital and University of Turku; Tuija Vasankari, Turku University Hospital and University of Turku; Jarmo Gunn, Turku University Hospital and University of Turku; Maija Hollmen, University of Turku; Tuomas Kiviniemi, Turku University Hospital and University of Turku

Aim

Atrio-ventricular block (AVB) can often be seen in patients undergoing cardiac procedures. Nevertheless, little is known about the histopathological features of new-onset postoperative AVB prior to the clinical manifestation and its prognostic impact.

Methods

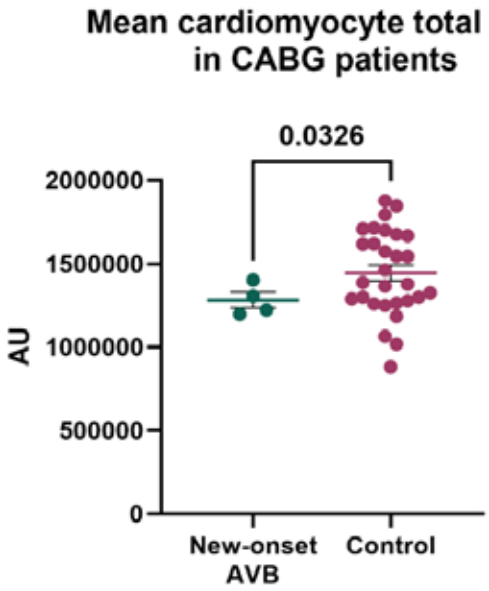
CAREBANK is a prospective study with atrial biopsies obtained at the time of open-heart cardiac surgery and long-term follow-up focusing on the adverse events. We analyzed preoperative as well as postoperative ECGs derived after index hospitalization (1-18mo) in patients undergoing CABG. We assessed the association of preoperative and new-onset post-operative first-degree AVBs with mortality. Histopathological analysis was used to assess the amount of fibrosis, cardiomyocytes, nuclear area and macrophages.

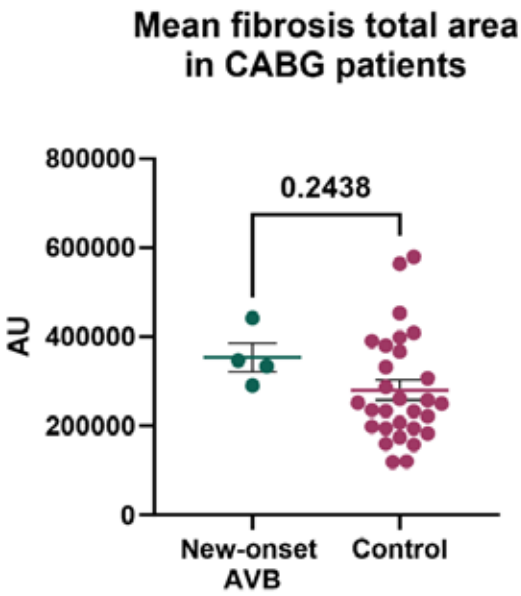
Results

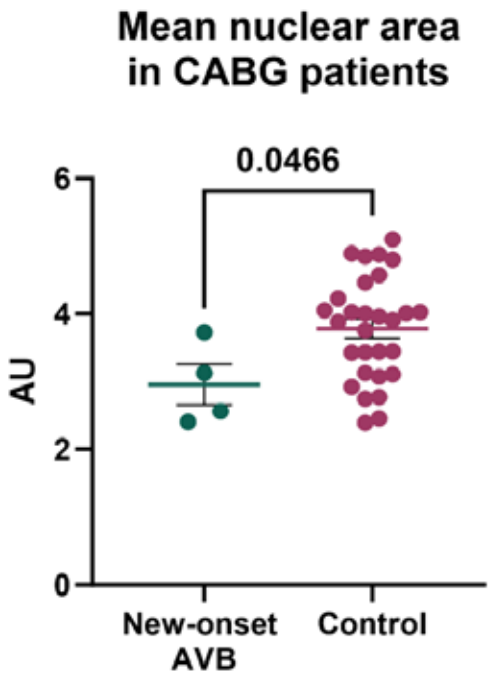
Median follow up time was 4.0 (IQR 2.7–5.0) years. First degree AVB was found in 84/373 (22.5%) preoperative ECGs. Altogether 25/289 (8.7%) cases where ECG was available (after excluding preop AVB) developed first-degree AVB after index hospitalization. New-onset first-degree AVB was associated with increased mortality (aHR 4.033 (95-CI% 1.019–15.965, p=0.047). In atrial histopathological analysis, the total area covered by cardiomyocytes (p=0.033) as well as the nuclear area (p=0.047) were smaller in those with new-onset AVB after surgery, but not in those with preoperative first-degree AVB (p=0.692 and p=0.384) as compared with controls, respectively. Similarly, the total area of fibrosis was greater in those with preoperative first-degree AVB (p<0.001), but not in those with postoperative new-onset AVB (p=0.244). When compared with controls, share of CD68 positive macrophages was similar (p=0.073), but anti-inflammatory CD206 positive M2 macrophages were absent in patients with new-onset AVB (p=0.042).

Conclusions

Patients with new-onset AVB after CABG have increased mortality in the long-term compared to those without. Histopathology identifies marked differences in macrophage populations between those with and without new-onset AVB.


Mean cardiomyocyte total area in CABG patients
0.0326
2000000
1500000
1000000
500000
0
AU
New-onset AVB
Control


Mean fibrosis total area in CABG patients
0.2438
800000
600000
400000
200000
0
AU
New-onset AVB
Control


Mean nuclear area in CABG patients
0.0466
6
4
2
0
AU
New-onset AVB
Control

Cardiac structure and function across the continuum of glucose metabolism

Tommi Grönlund, University of Oulu; Kari Kaikkonen, University of Oulu; Juhani Junttila, University of Oulu; Olavi Ukkola, University of Oulu; Heikki Huikuri, University of Oulu; Mikko Tulppo, University of Oulu

Aim

Glycated hemoglobin (HbA1c) is an important biomarker of long-term glucose metabolism. Heart failure is a common co-morbidity among subjects with diabetes or prediabetes, but the relationship between HbA1c and modern sophisticated measures of cardiac function such as Global longitudinal strain (GLS) and diastolic function (E/e') are not well known in the middle-aged general population. This study aimed to investigate the relationship between glucose metabolism and cardiac structure and function in nondiabetic subjects within a wide range of HbA1c levels.

Methods

A subpopulation of the Northern Finland Birth Cohort 1966 took part in follow-up, including extensive medical examination and echocardiography (n = 1155) at the age of 46. Participants with a suboptimal quality of echocardiography (n=87), heart rate during echocardiography ≥ 85 bpm (n=105), or any significant echocardiographic abnormalities (n=21), cardiac disease (n=24), type 2 diabetes (n=27) or respiratory disease (n=61) were excluded. The final study population included 664 subjects, 290 men (44%) and 374 women. Normal HbA1c levels were divided into sex-specific tertiles and prediabetes which were later pooled together. Univariate analysis after adjusted with covariates (Framingham risk factors, body mass index, and alcohol consumption) was used to compare cardiac function in Hba1c groups. Multivariate linear regression (enter method) was used to estimate the relationship between echocardiographic measures, HbA1c and covariates.

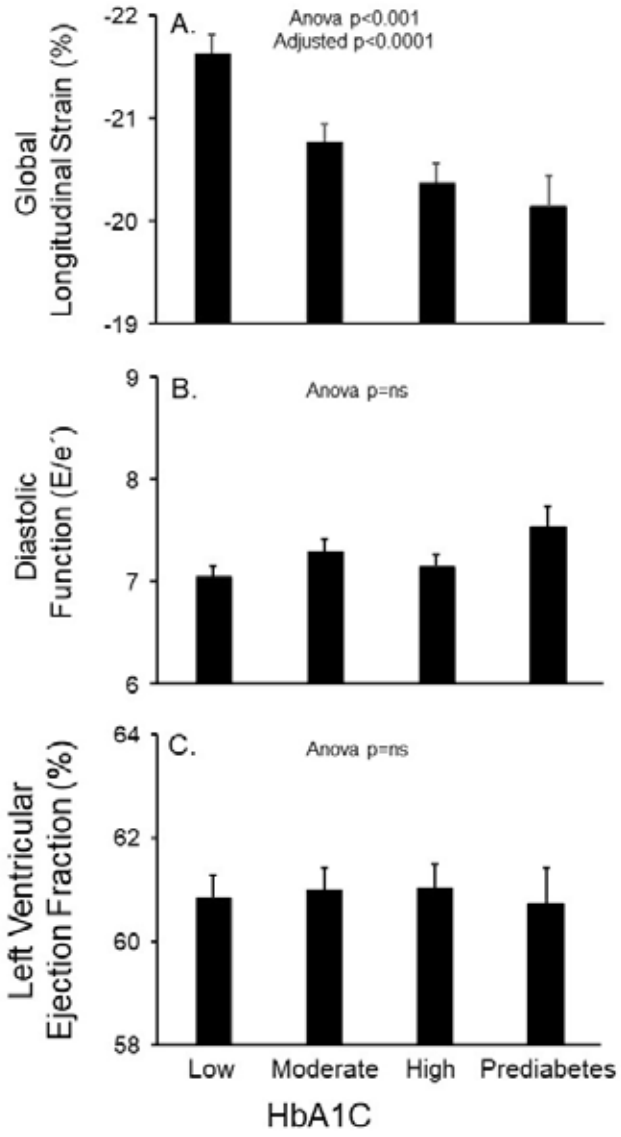
Results

HbA1c groups were defined as low (30.9±1.7 mmol/mol, n=190), medium (34.6±1.0 mmol/mol, n=189), high (37.4±1.0 mmol/mol, n=190) and prediabetes (41.0±1.3 mmol/mol, n=67) values groups. The corresponding GLS were -21.6±2.5, -20.8±2.4, 20.4±2.7 and 20.1±2.4 (adjusted main effect $p<0.0001$). The number of subjects with abnormal absolute GLS (<18) were 7.4%, 12.7%, 21.1% and 17.9% (main effect $p<0.01$) in low, medium, high HbA1c and prediabetes groups, respectively. In multivariate linear regression analysis, the most powerful and independent determinants of GLS were sex (partial correlation r=-0.30, ß=-0.31, $p<0.001$), HbA1c (partial correlation r=0.19, ß=0.16, $p<0.001$), BMI (partial correlation r=0.17, ß=0.16, $p<0.001$), systolic blood pressure (partial correlation r=0.15, ß=0.14, $p<0.001$) and alcohol consumption (partial correlation r=0.08, ß=0.07, $p<0.05$). HbA1c was not associated with diastolic function (E/e') or any cardiac structure variables.

Conclusions

In a healthy middle-aged population, high normal HbA1c levels and prediabetes are associated with impaired cardiac systolic function as indicated by GLS.

Figure 1.


A.
Anova p<0.001
Adjusted p<0.0001
Global Longitudinal Strain (%)
-22
-21
-20
-19
B.
Anova p=ns
Diastolic Function (E/e´)
9
8
7
6
C.
Anova p=ns
Left Ventricular Ejection Fraction (%)
64
62
60
58
Low
Moderate
High
Prediabetes
HbA1C

MD Lauri Mansikkaniemi
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Evaluation of long coronary artery stents with third-generation dual source computed tomography angiography

Lauri Mansikkaniemi, University of Helsinki and Helsinki University Central Hospital; Juhani Stewart, University of Helsinki and Helsinki University Central Hospital; Juha Sinisalo, University of Helsinki and Helsinki University Central Hospital; Petri Laine, University of Helsinki and Helsinki University Central Hospital; Miia Holmström, University of Helsinki and Helsinki University Central Hospital

Aim

Modern coronary computed tomography angiography (CCTA) techniques have increased resolution and can visualize even coronary stents. We investigated third-generation CCTA visualization of long coronary artery stentings.

Methods

This prospective study included patients who had received treatment for coronary artery chronic total occlusion (CTO) with a long stenting between 2014 and 2019 in Helsinki University Central Hospital. Long stenting was defined as ≥ 38 mm in left anterior descending (LAD) and right coronary artery (RCA) and ≥ 30 mm in left circumflex artery (LCX). Segments 5mm proximal and distal to the stent were considered as stent affected and were included in CCTA performance analyses. All patients underwent third-generation CCTA. Patients with in-stent restenosis (ISR) or an inconclusive result were defined as CCTA positive. Confirmation imaging was conducted with invasive coronary angiography (ICA) in patients with a positive CCTA in the long stenting or in a non-CTO stent, or ≥ 50% stenosis or an inconclusive finding in any native coronary artery combined with anginal symptoms. CCTA sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) were assessed. Effect of patient and stenting related factors on CCTA result were analyzed with Fishers's exact test, Pearson's chi squared test and Mann-Whitney U test.

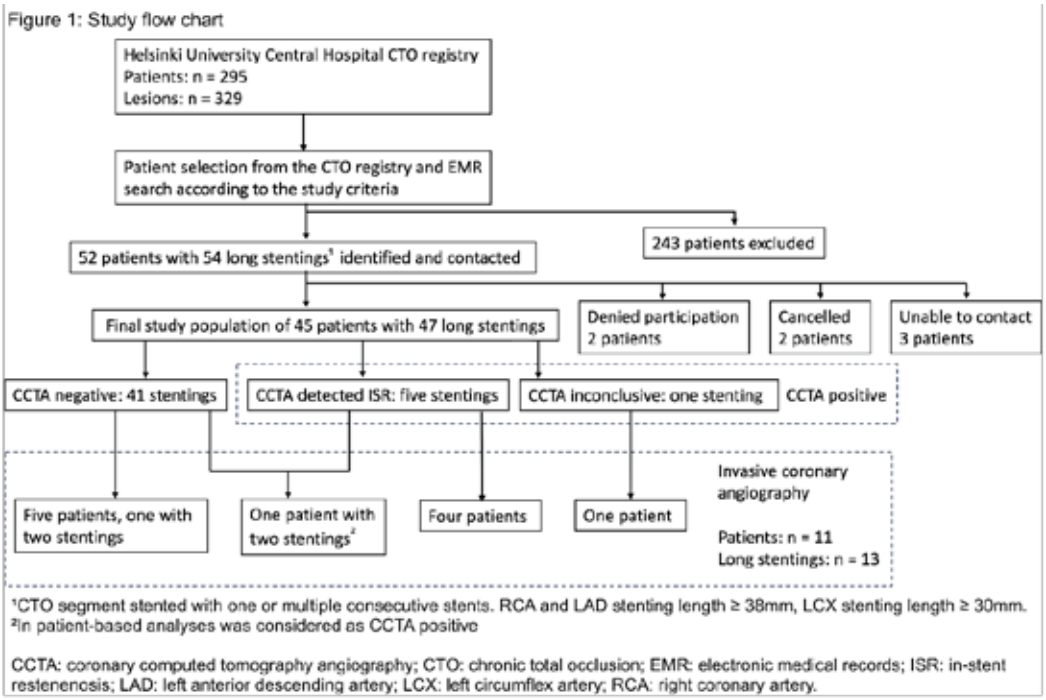
Results

The study included 45 patients (median age 61 years, (IQR, 56-67), 39 males). After CCTA ISR was ruled out in 39 patients (87%) and six patients (13%) had a positive result, of which one inconclusive and five suggested ISR. Median CCTA dose length product (DLP) was 116 (IQR, 66-216) mGy*cm. ICA was conducted for 11 patients and all six CCTA positive had ISR. In two patients CCTA suggested stenosis in a native coronary artery in 5mm segment near the stent edge, but in ICA ISR was diagnosed. CCTA sensitivity, specificity, NPV and PPV were all 1.0. Patients with a positive CCTA more commonly had diabetes (18% vs. 67%, p= 0.025), insulin required diabetes (5.1% vs. 50%, p= 0.013) and peripheral artery disease (0% vs. 33%, p= 0.015). No significant differences were observed in stenting characteristics between the groups.

Conclusion

Patency of long stents can be reliably assessed with modern CCTA with sparing use of radiation. CCTA can dependably outrule ISR, but accuracy is limited in detailed quantification such as exact location or degree of the stenosis. Diabetes and peripheral artery disease are factors related to ISR. CCTA provides a new non-invasive, lower risk method for long-term revascularisation follow-up.

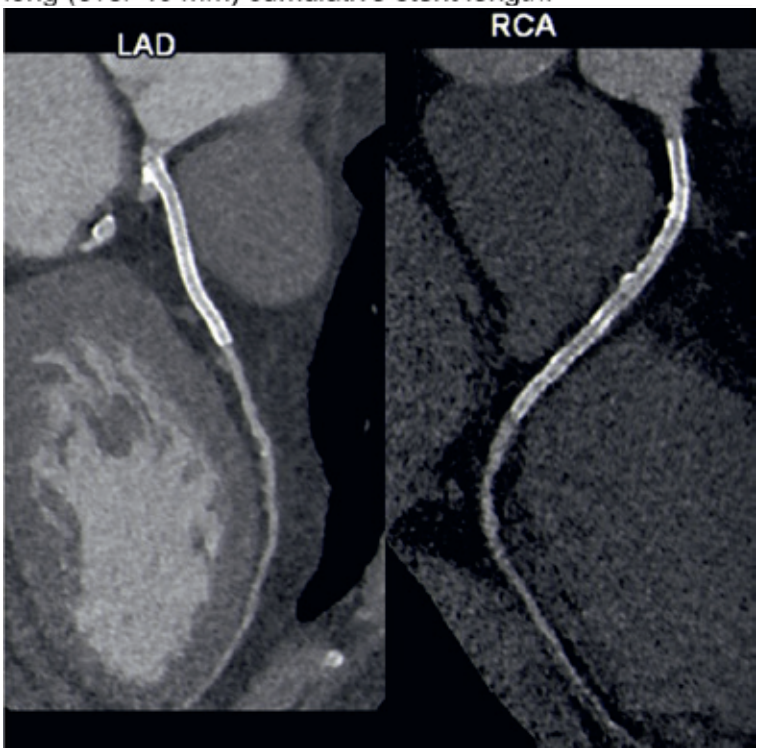
Figure 1: Study flow chart



[1]CTO segment stented with one or multiple consecutive stents. RCA and LAD stenting length ≥ 38mm, LCX stenting length ≥ 30mm.
[2]In patient-based analyses was considered as CCTA positive

CCTA: coronary computed tomography angiography; CTO: chronic total occlusion; EMR: electronic medical records; ISR: in-stent restenencsis; LAD: left anterior descending artery; LCX: left circumflex artery; RCA: right coronary artery.

Figure 2: CCTA images from two CTO PCI patients with long (over 40 mm) cumulative stent length.



CCTA: coronary computed tomography angiography; CTO: chronic total occlusion; PCI: percutaneous coronary intervention

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Endomyocardial biopsy in the diagnosis of cardiac sarcoidosis

Henriikka Mälkönen, Helsinki University Hospital and University of Helsinki; Jukka Lehtonen, Helsinki University Hospital and University of Helsinki; Pauli Pöyhönen, Helsinki University Hospital and University of Helsinki; Valtteri Uusitalo, Helsinki University Hospital and University of Helsinki; Mikko Mäyränpää, Helsinki University Hospital and University of Helsinki; Markku Kupari, Helsinki University Hospital and University of Helsinki

Aim

Definite diagnosis of cardiac sarcoidosis (CS) requires proof of sarcoid granulomas in the heart. Endomyocardial biopsy (EMB) is widely considered a risky procedure with poor sensitivity (<25%) in CS. This view being based on small reports from the turn of the millennium, we investigated EMB's diagnostic performance in a large and more contemporaneous cohort of CS.

Methods

We analyzed the data of 260 consecutive patients diagnosed with CS in 1988-2022 at our institution. All met the diagnostic criteria of the Heart Rhythm Society. The use, findings, and complications of EMB were retrospectively noted in addition to patients' demographics, presenting phenotype, diagnostic examinations, and future serious cardiac events. The data were retrieved from hospital records and an ongoing CS registry. Cardiac studies with advanced imaging (magnetic resonance, positron emission tomography) were re-analyzed and the follow-up information was updated until June 2023. EMB's performance was assessed also in 30 cardiac transplant recipients having CS at the histopathologic study of the explanted heart.

Results

Of the 260 patients with CS (mean age 49, 60% females), 216 (83%) underwent diagnostic EMB, 48 with repeat procedures. The sensitivity of EMB was 38%, rising to 49% after repeats. The predictors of positive EMB (Table 1) included the presenting phenotype and several indexes of the activity, extent, and location of myocardial involvement. Presentation with ventricular tachyarrhythmia, left ventricular ejection fraction ≤45%, elevation of cardiac troponins, and presence of middle or apical interventricular septal late gadolinium enhancement on magnetic resonance imaging constituted the independent predictors ($p<0.05$) of positive biopsy. The sensitivity of EMB was 16% in the 37 patients with none of the aforementioned predictors vs 40%, 60%, 79%, and 88% in those with 1 (n=76), 2 (n=62), 3 (n=33), and 4 (n=8) predictors, respectively. The rate of complications (Table 2) was 9.7% overall and 0.7% for major events. In the 30 patients with CS in explanted hearts, the sensitivity of pre-transplantation EMB, including repeats, was 60%. Inferior survival was observed in patients with positive EMB, but it did not predict long-term prognosis independent of the severity of cardiac involvement.

Conclusions

The sensitivity of EMB in CS is better than usually presented and the higher the more extensive myocardial involvement is. Risk of serious complications is <1%. In patients with suspect CS, the pre-test likelihood and value of positive EMB should be weighed against the procedural risks in shared decision-making when choosing the diagnostic pathway.

Table 1. Results of Logistic Regression Analyses for Factors Predictive of Positive Endomyocardial Biopsy in Patients with Cardiac Sarcoidosis

Potential Predictive Factor		Univariable Analysis			Multivariable Model (n/N = 49/126)		
	n/N	Odds Ratio	95% CI	P-value	Odds Ratio	95 % CI	P-value
Age, per +10 years	83/216	1.40	1.06 – 1.86	0.018	1.49	0.90 – 2.46	0.121
Female sex	83/216	0.81	0.47 – 1.42	0.464			
Presentation with VT/VF vs any other manifestation	83/216	2.17	1.10 – 4.26	0.025	4.47	1.38 – 14.53	0.013
LV ejection fraction on echocardiography							
per -10 %	83/216	1.58	1.28 – 1.95	<0.001			
≤45 %	83/216	3.84	2.15 – 6.86	<0.001	4.62	1.85 – 11.57	0.001
Elevated cardiac troponins*	79/204	3.55	1.96 – 6.41	<0.001	2.69	1.12 – 6.48	0.027
Elevated natriuretic peptides†	68/184	2.10	1.13 – 3.90	0.019			
LV LGE mass on CMRI, per +5 %	50/129	1.68	1.35 – 2.11	<0.001			
LGE present in middle/apical septum on CMRI‡	50/129	8.25	2.71 – 25.17	<0.001	4.09	1.19 – 14.06	0.025
Number of LV segments with FDG uptake on PET, per +1	12/47	2.03	1.27 – 3.23	0.003			
RV FDG activity on PET	12/50	1.37	0.36 – 5.19	0.640			
Number of histological samples, per +1	82/214	1.04	0.95 – 1.15	0.403			
Experience of the operator ≥5 years	78/207	1.00	0.54 – 1.85	0.996			

*hs-troponin I ≥50 ng; or troponin T by Elcsys® immunoassay (Roche Diagnostics, Germany) ≥ 0.03 ug/L by the 4th generation assay or ≥15 ng/L by the 5th generation assay).
†brain natriuretic peptide >100 ng/L or N-terminal brain natriuretic propeptide >400 ng/L at presentation
‡late gadolinium enhancement (LGE) detected in segments 8, 9, or 14 by American Heart Association's 17-segment left ventricular (LV) model
CI indicates confidence interval; CMRI, cardiac magnetic resonance imaging; ; FDG-PET, fluorodeoxyglucose positron emission tomography; n/N, patients with positive biopsy/patients with analyzable data; RV, right ventricular.

Table 2. Complications in 278* Endomyocardial Biopsies in 216 Patients with Cardiac Sarcoidosis

Complication	Number	%
Any	27	9.7
Major	2	0.7
Pericardial effusion needing pericardiocentesis	1	0.4
Need of intensive care support†	1	0.4
Minor	25	9.0
Ventricular tachycardia	10	3.6
Minor pericardial effusion without need of drainage	6	2.2
Transient hypotension or vasovagal reaction	3	1.1
Tricuspid valve damage with mild regurgitation	2	0.7
Significant vascular access site hematoma	2	0.7
Atrial flutter	1	0.4
Transient total atrioventricular block	1	0.4

*biventricular biopsies (n=6) were considered separate procedures for complications.
†the patient needed surveillance and hemodynamic support in the intensive care unit for prolonged postoperative hypotension. The cause of hemodynamic compromise remained unknown; pericardial tamponade, myocardial infarction, pulmonary embolism, and internal hemorrhage were all excluded, and no signs of a central cause was observed. The patient recovered completely in 12 hours.

Prevalence of myocardial adipose tissue in non-ischemic and ischemic victims of sudden cardiac death

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Aim

Recent imaging studies have shown that patients with myocardial infarction scar who have ventricular arrhythmias show more adipose tissue around the scar. Similar changes are seen in ARVC. It has been suggested that myocardial adipose tissue plays an important role in arrhythmogenesis. The aim of this study was to determine the prevalence of myocardial adipose tissue that co-localize with fibrosis in non-ischemic and ischemic sudden cardiac death (SCD) victims.

Methods

The ischemic and non-ischemic subjects were derived from the FinGesture cohort, consisting of autopsy verified consecutive victims of SCD in Northern Finland between years 1998-2017 (n=5,869). Total of 48 non-ischemic, 47 ischemic and 37 accidental/intoxication related death subjects were included in the study. Hematoxylin-eosin-stained slides were digitized and fibrofatty deposits was determined using virtual microscopy software.

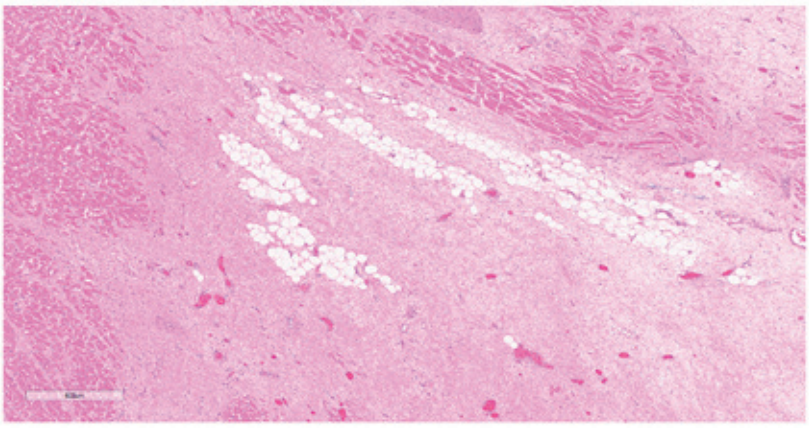
Results

Myocardial adipose tissue was present in 51% of ischemic cases, 29% of non-ischemic cases and 14% of controls ($p< 0.001$). In ischemic cases, BMI seems to be associated with the presence of myocardial adipose tissue. Mean BMI was higher in subjects with myocardial adipose tissue versus subjects without (29.2 vs 24.9. $p=0.022$).

Conclusions

The findings suggest that adipose tissue might have an influence in creation of fatal arrhythmias in SCD as it does in scar related ventricular arrhythmias. In addition, it seems that obesity is associated with ischemic scar related adipose tissue metaplasia.

Figure 1. *Myocardial adipose tissue deposit within fibrosis (600µm)*



Sudden cardiac death in the setting of acute coronary syndrome with and without prior diagnosis of coronary artery disease

Samuli Juntunen, University of Oulu; Lauri Holmström, University of Oulu; Jani Tikkanen, University of Oulu; Lasse Pakanen, University of Oulu; Kari Kaikkonen, University of Oulu; Juha Perkiömäki, University of Oulu; Heikki Huikuri, University of Oulu; Juhani Junttila, University of Oulu

Aim

Coronary artery disease is the leading cause of death worldwide. It's a common statement in the literature that the SCD is often the first and only manifestation of CAD. However, the incidence of SCD in CAD as the first manifestation is unclear and assumed incidence rates vary from one third to a half of the SCDs. ACS is considered to explain roughly 20-25% of SCDs. Strong evidence endorsing the proportion of the first events or ACS in SCD is lacking. The aim of the present study was to investigate these incidences, which would hopefully help understanding their significance in SCD prevention.

Methods

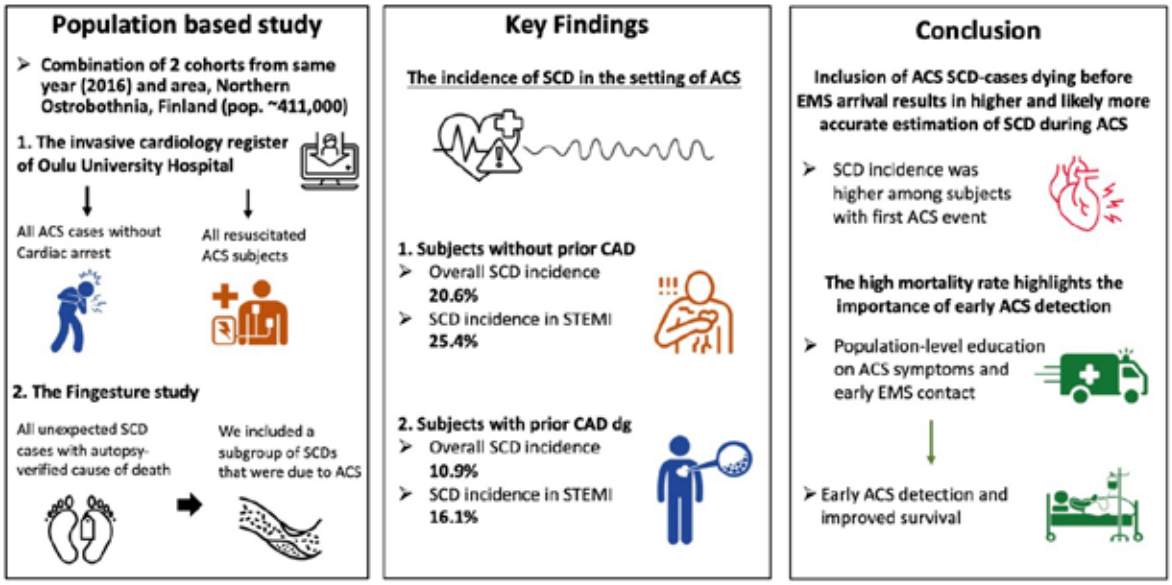
We gathered all ACS patients (n=472) going through invasive coronary angiography in Oulu University Hospital with temporal and areal restriction limiting the subjects to those being treated in 2016 and living in Northern Ostrobothnia, Finland (population ~411000). Then we combined this hospital registry data to the autopsy data of SCD victims due to CAD from the same year with the same areal restriction. Subjects > 80 years were excluded. Altogether we got study population of 634 ACS patients. We analyzed SCA/SCD incidence separately in STEMI and in NSTE-ACS patients with or without prior CAD diagnoses.

Results

The SCA/SCD incidence was 20.6 % in the subjects with the first ACS event and 25.4 % in the subjects with the first STEMI. In those subjects with previously established CAD diagnosis the SCA/SCD incidence was 10,9% in ACS and 16,1% in STEMI. There was a statistically significant difference between the incidence rate ratio of the SCA/SCD victims with prior CAD diagnoses and those without (CI 95%, 0.3013-0.8801, P = 0.0088).

Conclusions

SCA/SCD in the setting of ACS is more common among those individuals without prior CAD compared to those with established CAD diagnoses. SCA/SCD rate in the setting of ACS is also higher than previously reported. To decrease the burden of SCDs in the setting of ACS, we need population-level education and better remote detection of immediate risk of SCA. Also, earlier diagnoses of CAD and preventive actions may be beneficial. More research is needed to distinguish patients at high SCD risk in CAD from those without elevated risk.



Graphical abstract/Central illustration: Study population, key findings, and clinical implications

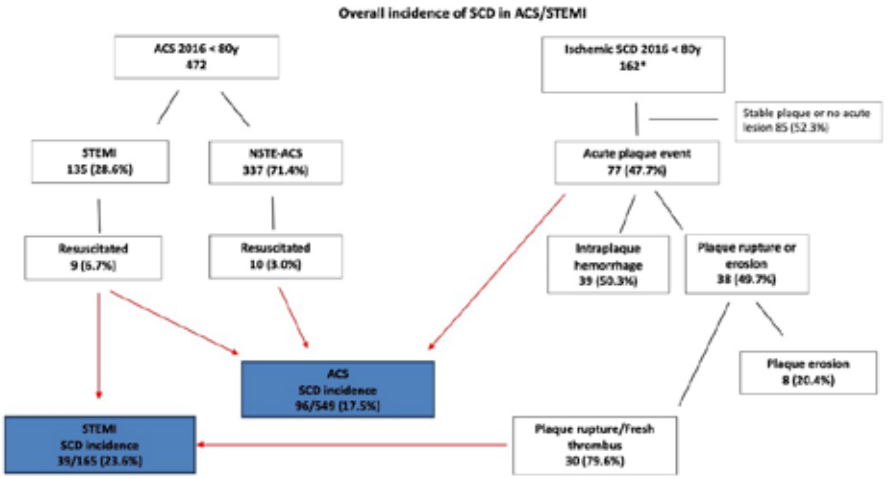


Figure 1. Overall incidence of SCD in the setting of ACS. *Number of SCD victims in 2016 extrapolated with the SCD autopsy-rate of 73.9%

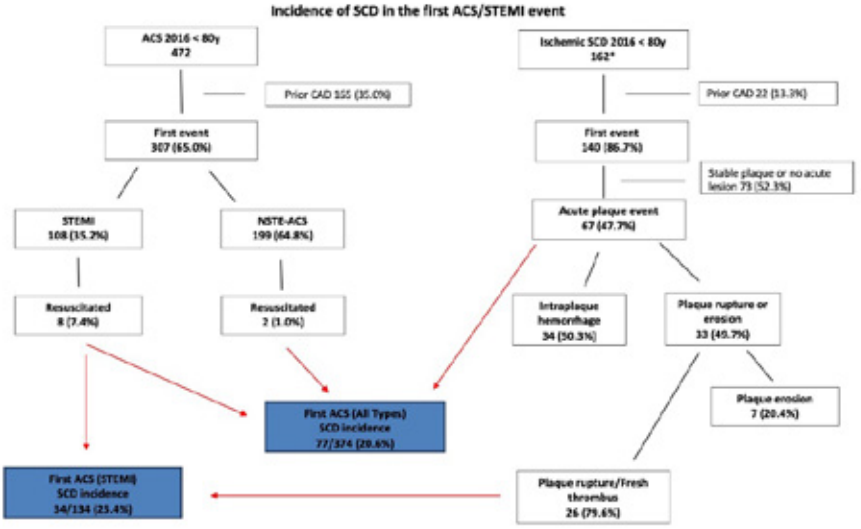


Figure 2. Incidence of SCD among ACS subjects without prior CAD diagnosis. *Number of SCD victims in 2016 extrapolated with the SCD autopsy-rate of 73.9%

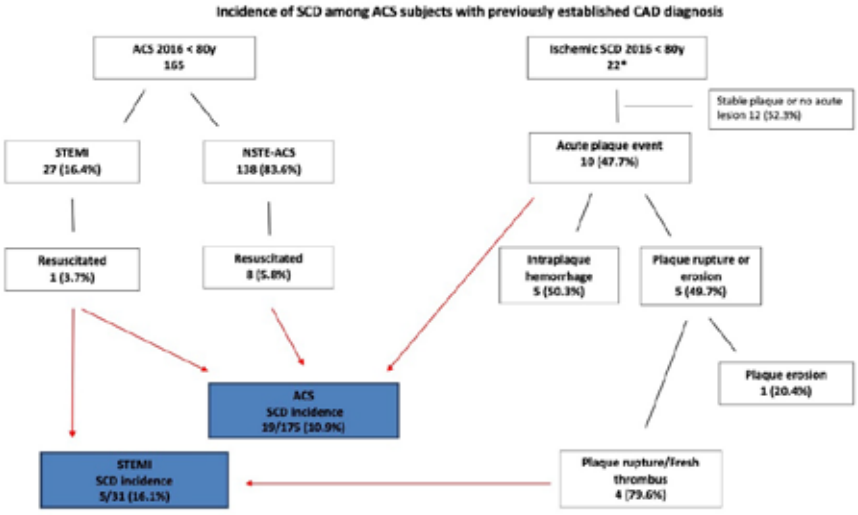


Figure 3. Incidence of SCD among ACS subjects with previously established CAD diagnosis. *Number of SCD victims in 2016 extrapolated with the SCD autopsy-rate of 73.9%

Ventricular arrhythmias and hemodynamic collapse during acute coronary syndrome – increased risk for sudden cardiac death?

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Aim

In acute phase of acute coronary syndrome (ACS), ventricular tachycardia (VT) and/or ventricular fibrillation (VF) leading to resuscitation are not considered to be associated with increased long-term sudden cardiac death (SCD) because the cause – acute ischemia – is believed to be reversible. Aim of this study was to investigate whether ventricular arrhythmias leading to sudden cardiac arrest during ACS associate with the risk of incident SCD in patients with normal or mildly impaired left ventricular ejection fraction (LVEF).

Methods

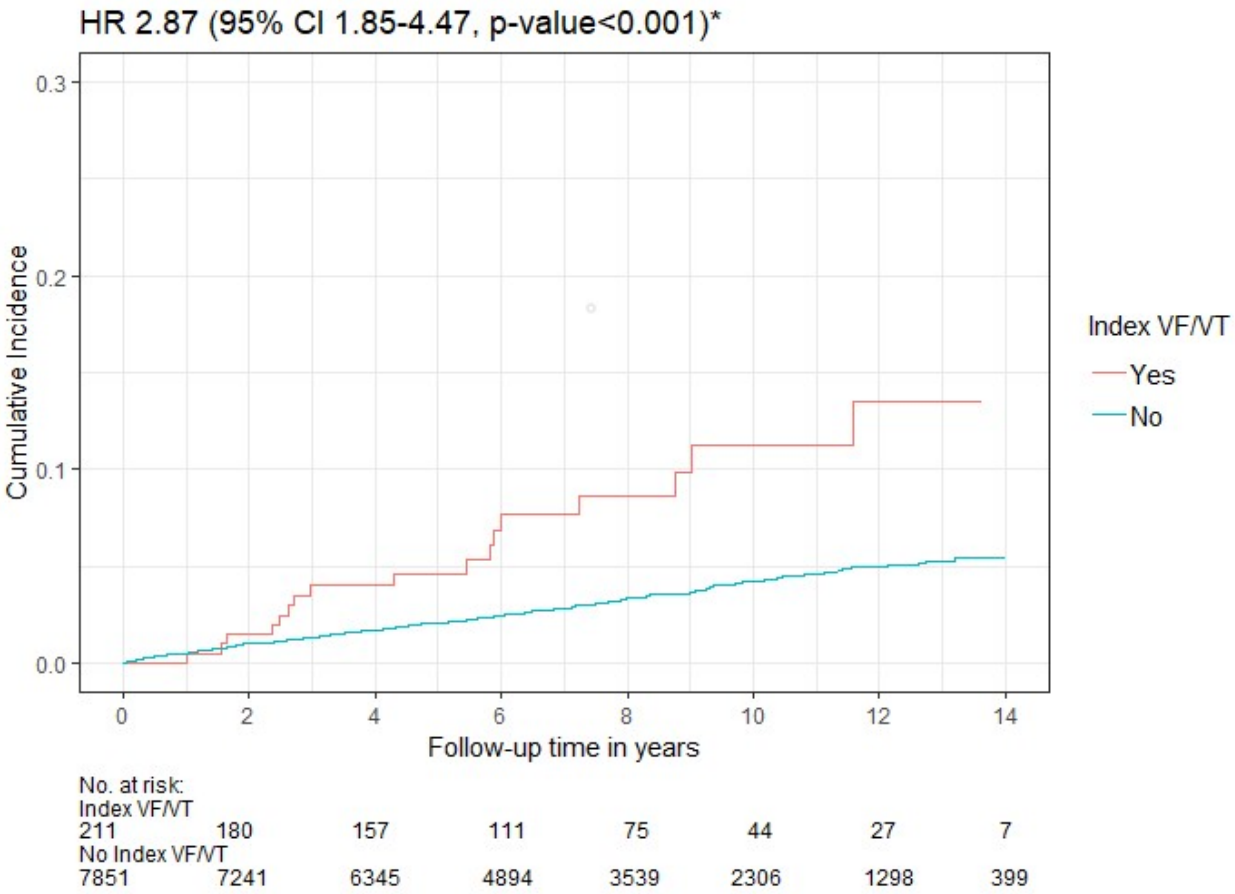
This study is based on a retrospective analysis of all 8,062 consecutive ACS patients undergoing coronary angiography with baseline LVEF ≥40% between 2007-2018 (follow-up until December 31st, 2021). The primary outcome was SCD equivalent life-threatening ventricular arrhythmias (LTVA) composing of true SCDs, aborted SCDs by successful resuscitation or appropriate ICD therapy. The risk of sudden LTVA was estimated with multivariate subdistribution hazard model using other deaths as competing events.

Results

Two-hundred and thirteen (n=211, 2.6%) patients suffered acute phase VF/VT leading to resuscitation and survived to discharge and most happened before angiography (80.6%, N=170) and were VF (92.9%, N=196). During a median follow-up of 7.6 years, 3.9% (N=316) of all the patients had LTVA (10.0% in VF/VT group vs 3.8% in other patients). VF/VTs during ACS associated with an increased risk for future SCD (HR 3.07; 95% CI 1.94-4.85, p<0.001). Most LTVAs occurred in patients without ICDs.

Conclusions

VF/VT in ACS associates with remarkably high long-term risk for SCD in patients with LVEF ≥40%.


HR 2.87 (95% CI 1.85-4.47, p-value<0.001)*
Cumulative Incidence
0.0
0.1
0.2
0.3
0
2
4
6
8
10
12
14
Follow-up time in years
Index VF/VT
Yes
No
No. at risk:
Index VF/VT
211 180 157 111 75 44 27 7
No Index VF/VT
7851 7241 6345 4894 3539 2306 1298 399

Abnormal smooth muscle cell phenotype impairs aortic wall stability in thoracic aortic aneurysm

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Aim

In thoracic aortic aneurysm (TAA) of the ascending aorta (AA), AA dilates progressively, and can lead to aortic rupture without any prior symptoms. Media degeneration including a decrease in smooth muscle cell (SMC) amount has been associated with TAA. Besides the amount, the change in SMC phenotype can weaken aortic wall structure. Relevance of this phenotypic switching is however unknown in human TAA. Here, we investigated pathological changes of the aortic wall and tissue strength in relation to SMC phenotype.

Methods

TAA patients (n=21) with tricuspid aortic valve were included in the study. Broad array of histological, cell biological, biomechanical, and sequencing methods were used to analyze histopathology, tissue strength, cell composition, and SMC phenotypes separately from inner and outer curve segments of the resected AA, and compared to controls with no cardiovascular diseases.

Results

Outer curves of the AA had lower quantity of elastin ($p=0.012$), tolerated lower strain ($p<0.0001$) and were less elastic ($p=0.017$) compared to the inner curves of TAA patients. No differences were detected in total SMC amount between the different areas of the AA in TAA patients. However, SMCs expressing MYH10 (myosin heavy chain 10) was increased in the outer curves ($p=0.047$) indicating the presence of abnormal SMC type in the outer curves. Tissue strength, measured with an extension test, correlated with MYH10+ SMC density ($r=-0.447$, $p=0.017$) demonstrating more abnormal SMCs in the areas with a weaker aortic wall structure. Sequencing techniques were used for deeper mechanistical understanding of this SMC phenotype in TAA and its relevance in disease progression.

Conclusions

Abnormal, MYH10+ SMC phenotype is present in the outer curves of AA in TAA patients, an area known to be prone to rupture. Our results suggest that MYH10+ SMC phenotype has a significant role in aortic wall stability and strength in TAA.

MRI markers of liver fibrosis in Fontan survivors: Insights from a Finnish pediatric cohort

Alma Kormi, Helsinki University Hospital; Tiina Ojala, Helsinki University Hospital; Sabina Selenius, Helsinki University Hospital; Anna Yanovskiy, Helsinki University Hospital; Juha Peltonen, Helsinki University Hospital; Reetta Kivisaari, Helsinki University Hospital; Laura Martelius, Helsinki University Hospital

Introduction

Liver fibrosis is a serious complication of single ventricle Fontan survivors, and the exploration of its causes is of great interest. Our aim was to study the associations between MRI markers indicating liver fibrosis and hemodynamic cardiac magnetic resonance (CMR) in a national four- year cohort of pediatric Fontan patients.

Materials and Methods

This study cohort included all pediatric patients (N=111) with Fontan circulation undergoing post-Fontan hemodynamical CMR examination between 2019 and 2023 in Finland. MRI markers indicating liver fibrosis included liver MRI score and T1-mapping. The CMR study included Fontan hemodynamics, peripheral venous pressure, and evaluation of the lymphatics system (Figure).

Results

In these patients, MRI markers indicating liver fibrosis were associated with time under Fontan circulation, functional cardiac index, type of systemic ventricle (RV morphology being a risk factor), systemic ventricle size (end diastolic and systolic volumes) and function (ejection fraction), burden of aortopulmonary collaterals (all $p < 0.001$), and abdominal lymphatic abnormalities ($p=0.03$). No associations were found between MRI markers indicating liver fibrosis and peripheral venous pressure, or lymphatic abnormalities in thorax or neck.

Conclusions

Liver fibrosis stands out as a crucial endpoint in Fontan patients. Our study demonstrated a broad association with various CMR hemodynamic parameters and MRI markers indicating liver fibrosis. This emphasizes the need to routinely check the liver as part of Fontan CMR follow-ups for a more comprehensive patient evaluation.

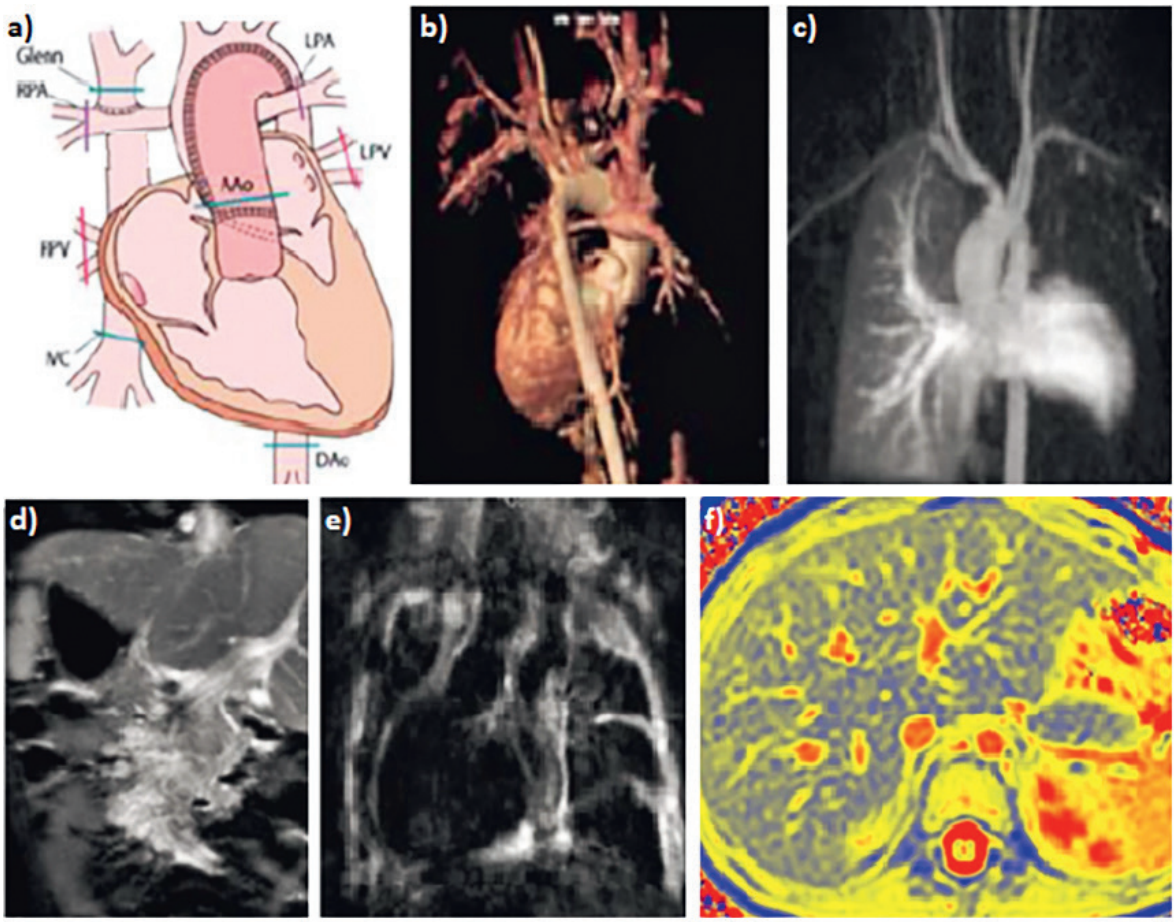


Figure. Example of a CMR study comprising evaluation of Fontan hemodynamics, lymphatics system, and liver. a) Illustration of sites of the through- plane flows used for complete hemodynamics assessment of patients with Fontan circulation, b) three-dimensional reconstruction of a patient with Fontan anatomy c) contrast enhanced MR angiography. T2 weighted images demonstrating d) enhanced abdominal lymphatics e) thoracic gr 4 lymphatic networks f) Native T1 map of the liver.

Distinct circulating cytokine levels in patients with angiography-proven coronary artery disease compared to disease-free controls

Eveliina Maaniitty, Turku University Hospital; Sami Sinisilta, Turku University Hospital; Juho Jalkanen, Turku University Hospital; Tuija Vasankari, Turku University Hospital; Fausto Biancari, South Karelia Central Hospital, University of Helsinki; Jarmo Gunn, Turku University Hospital; Sirpa Jalkanen, University of Turku; Juhani Airaksinen, Turku University Hospital; Maija Hollmén, University of Turku; Tuomas Kiviniemi, Turku University Hospital

Aim

Systemic inflammation has a critical role in the development of symptomatic coronary artery disease (CAD). Identification of inflammatory pathways may provide a platform for novel therapeutic approaches. We sought to determine whether there are differences in circulating cytokine profiles between patients with CAD and disease-free controls or depending on the severity of the disease.

Methods

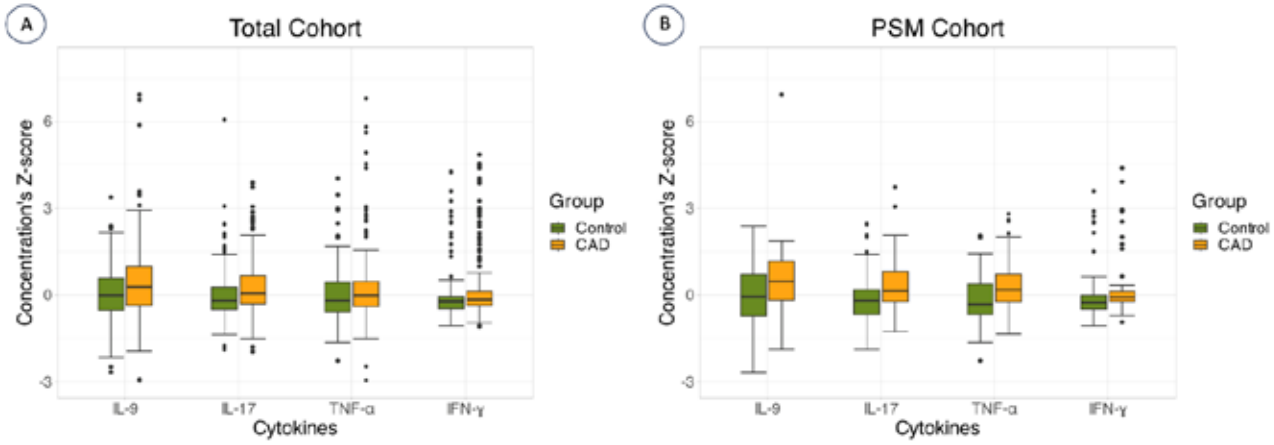
The study population consisted of 452 patients who underwent diagnostic invasive coronary angiography due to clinical indications. We measured the serum concentrations of 48 circulating cytokines. Z-score was used to diminish the potential differences due to batch-induced variability in cytokine analyses. Propensity score matching (PSM) was used to reduce the effect of differences in baseline characteristics. This yielded 61 pairs with similar baseline characteristics, as expected, with the exception of diabetes and antiplatelet drugs. Extent of CAD was assessed using the SYNTAX Score. SYNTAX Score was calculated for 116 patients.

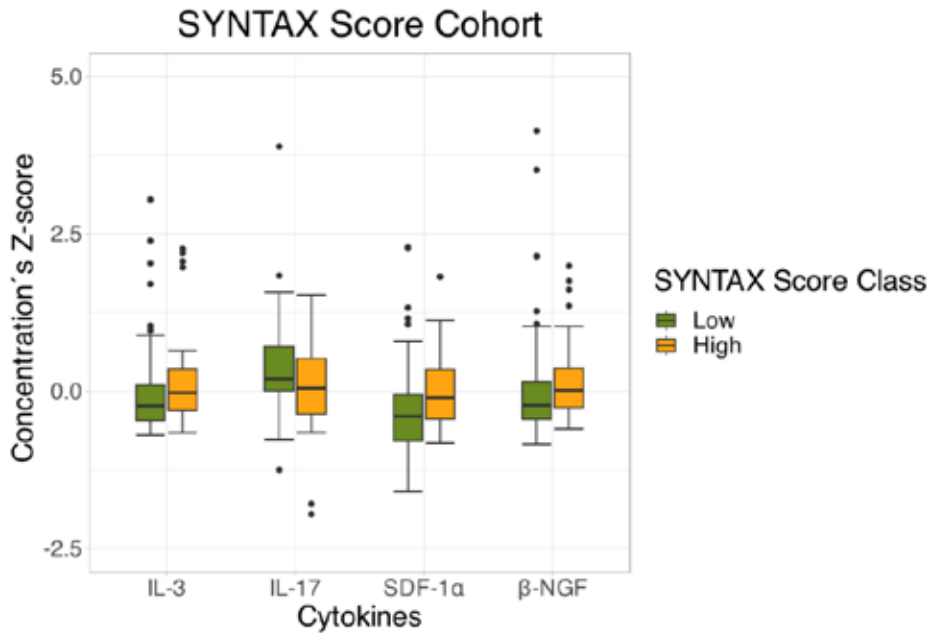
Results

Overall, 310 patients had angiographically verified CAD whereas 142 had no angiographically-detected coronary atherosclerosis. In multivariable logistic regression models adjusted for age, sex, hypertension, atrial fibrillation, history of smoking and treatment for diabetes and hyperlipidemia, increased levels of interleukin 9 (OR 1.359, 95%CI 1.046-1.766, p=0.022), IL-17 (1.491, 95%CI 1.115-1.994, p=0.007) and tumor necrosis factor alpha (TNF-α) (OR 1.440, 95%CI 1.089-1.904, p=0.011) were independently associated with CAD (Fig. 1A). In PSM cohort, IL-9, IL-17, IFN-ɣ and TNF-α were still significantly higher among CAD patients (Fig. 1B). In logistic regression models adjusted for treatment of diabetes conducted in the PSM cohort, IL-9 (OR 1.654, 95%CI 1.129-2.422, p=0.010), IL-17 (OR 1.948, 95%CI 1.259-3.012, p=0.003) and TNF-α (OR 1 2.051, 95%CI 1.286-3.272, p=0.003) were independently associated with CAD. Patients with high SYNTAX Score (SYNTAX Score >22, n=86) had increased levels of stromal cell-derived factor 1 alfa (SDF-1α), beta-nerve growth factor (β-NGF), IL-3 and decreased level of IL-17 compared to those with low SYNTAX score (SYNTAX Score ≤22, n=30) when adjusted for smoking and use of beta-blockers (Fig 2).

Conclusions

Patients with CAD have distinct circulating cytokine profiles compared to disease-free controls. Distinct cytokines may have pivotal roles at different stages of coronary atherosclerosis and to severity of the disease.


A
Total Cohort
Concentration's Z-score
6
3
0
-3
IL-9
IL-17
TNF-α
IFN-γ
Cytokines
Group
Control
CAD
B
PSM Cohort
Concentration's Z-score
6
3
0
-3
IL-9
IL-17
TNF-α
IFN-γ
Cytokines
Group
Control
CAD


SYNTAX Score Cohort
Concentration´s Z-score
5.0
2.5
0.0
-2.5
IL-3
IL-17
SDF-1α
β-NGF
Cytokines
SYNTAX Score Class
Low
High

Association of retinal abnormalities and adverse cardiac events in patients with coronary artery disease

Henna Qian, Oulu University Hospital; Annika Konttinen, Oulu University Hospital; Lauri Holmström, Oulu University Hospital; Joonas Wirkkala, Oulu University Hospital; Samuli Lepojärvi, Oulu University Hospital; Mikko Tulppo, University of Oulu; Juha Perkiömäki, Oulu University Hospital; Heikki Huikuri, Oulu University Hospital; Anna-Maria Kubin, Oulu University Hospital; Nina Hautala, Oulu University Hospital; Juhani Junttila, Oulu University Hospital

Aim

Diabetes mellitus (DM) causes retinopathy. Direct association of microvascular abnormalities such as diabetic retinopathy (DR) with cardiovascular events among coronary artery disease (CAD) patients has not been comprehensively studied. The aim of this study was to evaluate the association of retinal abnormalities and cardiac mortality in patients with CAD and type 2 DM.

Methods

ARTEMIS study is a prospective cohort study of 1946 patients (68 % male; mean age 66.9 ± 8.6 years) diagnosed with CAD in Oulu University Hospital between years 2007 - 2014. Type 2 DM was diagnosed with 834 patients (43 %) of ARTEMIS population and 525 patients (27 %) had retinal images available. The retinal images at the time of ± 2 years of enrollment to the study were comprehensively analyzed.

Results

During the mean follow up of 8.7 ± 2.2 years 156 cardiac deaths occurred. From all analyzed retinal abnormalities DR was the only one associated with the outcomes. DR was independently associated with increased risk of cardiac death (hazard ratio [HR] 2.4, 95 % CI: 1.3 - 4.5, $p = 0.008$) when adjusted with confounding factors. DR was associated with sudden cardiac death (SCD) (HR 2.9, 95 % CI: 1.2 - 7.3, $p = 0.02$) but not with non-sudden cardiac death (HR 2.1, 95 % CI: 0.9 - 5.1, $p = 0.1$). Interestingly, increased hs-TnT, measured in stable phase of CAD, was also associated with DR ($p < 0.001$).

Conclusions

DR is associated with cardiac death and more specifically with SCD in patients with CAD and type 2 DM. DR might be a novel marker of microvascular cardiac disease resulting in on-going myocardial injury and SCD.

Cardiac magnetic resonance imaging: assessing risk factors for myocardial fibrosis in individuals with a univentricular heart

Sabina Selenius, University of Helsinki, Helsinki University Hospital; Marko Taipale, Helsinki University Hospital; Emmi Helle, Helsinki University Hospital; Ilkka Mattila, Helsinki University Hospital; Tommi Pätilä, Helsinki University Hospital; Juha Peltonen, Helsinki University Hospital; Teemu Vepsäläinen, Helsinki University Hospital; Laura Martelius, Helsinki University Hospital; Tiina Ojala, Helsinki University Hospital

Aim

Ventricular function plays a crucial role as a prognostic factor in the long-term outcomes of Fontan patients. However, the factors contributing to the decline in ventricular function are not fully understood. Our objective was to elucidate these factors, with a particular emphasis on the development of myocardial fibrosis by integrating cardiac magnetic resonance imaging (CMR) data with clinical parameters.

Methods

This national retrospective observational cohort study included all patients with Fontan circulation undergoing post-Fontan CMR examination between 2017 and 2023 (N=148) in Finland. Clinical and CMR parameters were analyzed using univariate and multivariate analysis. Primary endpoint focused on assessment of cardiac fibrosis measured by T1-mapping.

Results

Median time between the Fontan procedure and CMR-examination was 10.8 years (6.9 – 13.4 years). Median myocardial T1-values were higher in patients with prior right ventricular-pulmonary artery (RV-PA)-shunt (1050 ms, IQR 33.8) than in patients with prior Blalock-Taussig-shunt (1027.5 ms, IQR 31.9) or pulmonary artery-banding (1022.5 ms, IQR 35) ($p = 0.009$). Specifically, higher T1 values were observed in the lateral wall (1065 ms, IQR 50, 1020 ms, IQR 67.5 and 1010 ms, IQR 57.5 respectively, $p<0.001$) and in the anterior wall (1050 ms, IQR 70, 1025 ms IQR 47.5, 1025 ms, IQR 50 respectively, $p=0.075$). There was no statistically significant difference in T1 values in the inferior ($p=0.94$) and septal ($p=0.19$) walls between the shunt types. In the univariate analysis, increased myocardial T1-values were associated with decreased ejection fraction ($p=0.02$), decreased stroke volume ($p=0.005$), type of cardiac defect (hypoplastic left heart syndrome) ($p=0.003$) and increased heart rate ($p<0.001$). In the multivariate analysis, shunt type (RV-PA) ($p=0.008$) and increased heart rate ($p=0.007$) were associated with increased myocardial T1-value.

Conclusions

IDuring later follow-up, individuals with prior RV-PA-shunts faced a heightened risk of developing myocardial fibrosis compared to those exposed to other types of blood supply during early infancy. The elevated T1-values in the myocardium, serving as marker for fibrosis, were particularly pronounced in the lateral region, corresponding to the anatomical location of the RV-PA shunt. CMR proves to be a valuable tool for detecting early signs of ventricular dysfunction in single ventricle patients, facilitating timely intervention strategies, and improving prognosis.

Left ventricle ejection fraction and myocardial fibrosis in sudden cardiac death: a population based study

Harri Silvola, Research Unit of Biomedicine and Internal Medicine, Medical Research Center Oulu; Holmström Lauri, Research Unit of Biomedicine and Internal Medicine, Medical Research Center Oulu; Lasse Pakanen, Department of Forensic Medicine, Research Unit of Biomedicine and Internal Medic; Ida Hookana, Research Unit of Biomedicine and Internal Medicine, Medical Research Center Oulu; Anette Eskuri, Research Unit of Biomedicine and Internal Medicine, Medical Research Center Oulu; Jani Tikkanen, Research Unit of Biomedicine and Internal Medicine, Medical Research Center Oulu; Juha Perkiömäki, Research Unit of Biomedicine and Internal Medicine, Medical Research Center Oulu; Heikki Huikuri, Research Unit of Biomedicine and Internal Medicine, Medical Research Center Oulu; Juhani Junttila, Research Unit of Biomedicine and Internal Medicine, Medical Research Center Oulu

Aim

We evaluated the spectrum and temporal trends of left ventricle ejection fraction (LVEF) among SCD victims with ischemic and nonischemic etiologies as well as the correlation between myocardial fibrosis at autopsy and LVEF.

Methods

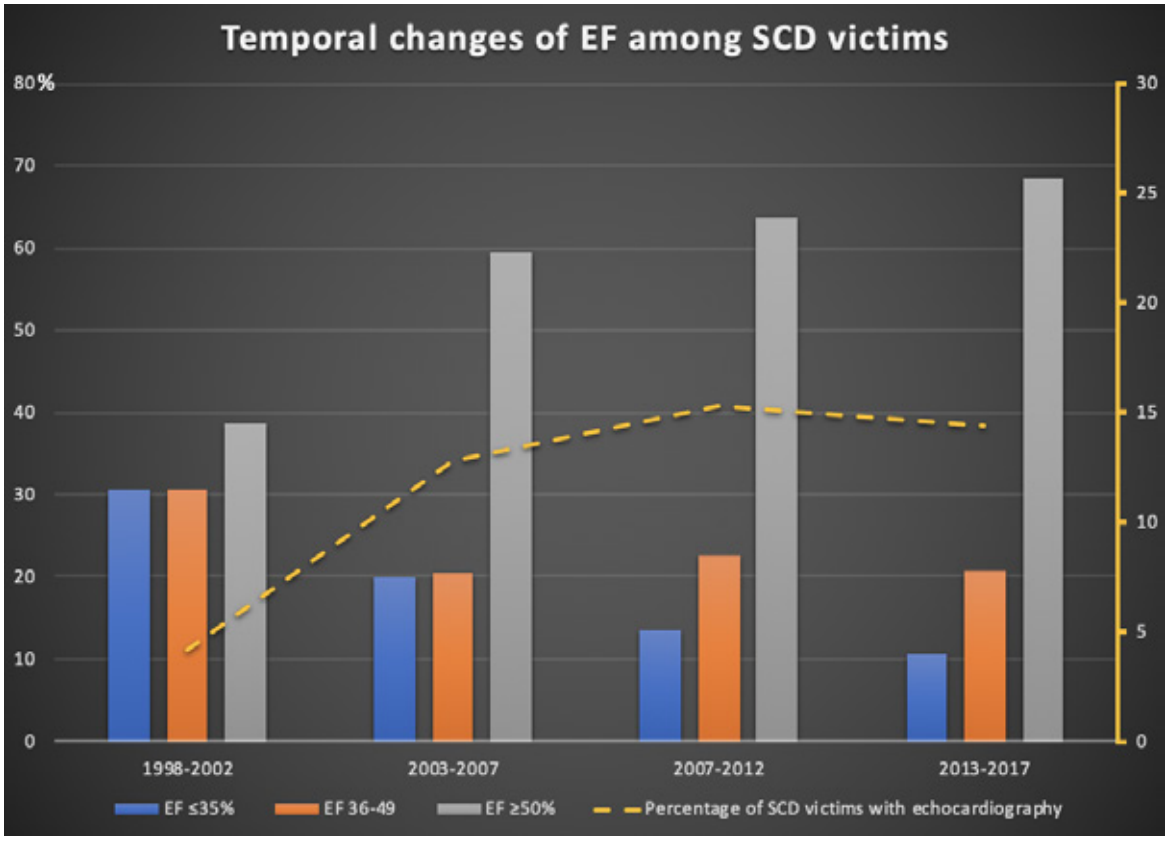
The Fingesture study is a population-based study which has prospectively collected autopsy and clinical data from consecutive SCD victims from Northern Finland between 1998 and 2017 (n=5,869). Echocardiography data was acquired from electronic health records. LVEF was categorized by quantitative assessment as normal (≥ 50%) and severely reduced (≤ 35%). The extent of myocardial fibrosis was categorized into two classes (mild-to-none and moderate-to-substantial) following forensic pathologists macroscopic and histological evaluation.

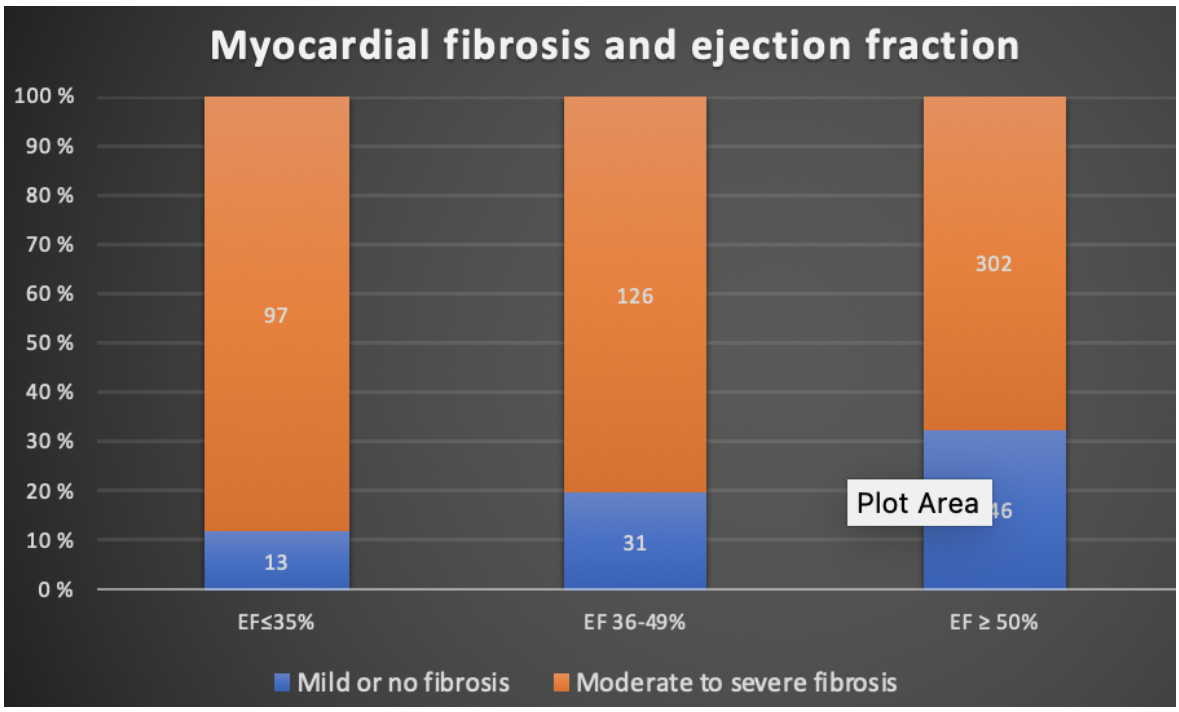
Results

Pre-SCD echocardiography was available in 717 SCD victims. The majority of subjects (n=449, 62,7%) had normal LVEF prior to SCD. The prevalence of severely reduced LVEF was 110 subjects (15,4%) and was similar between ischemic SCD and nonischemic SCD (15,1% vs. 16,3%, respectively; p=0,72). LVEF was severely reduced more commonly in men compared to women (17,4% vs 10,9% respectively; p<0.001). Severely reduced LVEF was found in 30.6% of SCD victims during the first quartile (1997-2002) and gradually became less common over the following quartiles (20.0% during 2003-2007, 13.5% during 2008-2012, and 10.6% during 2013-2017; p<0.001, unadjusted β=-5.6% per 5 years, 95% CI -0,083 to -0,029). Those with LVEF≤35% had more often moderate or substantial fibrosis (88.2%), in comparison to those with normal left ventricular function (67.4%; p<0.001). Yet more than half (57.5%) of SCD victims with moderate or substantial myocardial fibrosis had normal LV function and only 18.5% of those with moderate to severe fibrosis had LVEF≤35%.

Conclusions

The proportion of SCD cases who fulfill the current criteria (LVEF≤35%) for primary prevention ICD at the population level is low and has declined in recent decades. The association between reduced LVEF and myocardial fibrosis was modest. Novel approaches to identify fibrotic accumulation and to individualize SCD risk stratification among subjects with LVEF>35% are warranted, especially among women.


Temporal changes of EF among SCD victims
80%
70
60
50
40
30
20
10
0
30
25
20
15
10
5
0
1998-2002
2003-2007
2007-2012
2013-2017
EF ≤35%
EF 36-49
EF ≥50%
Percentage of SCD victims with echocardiography


Myocardial fibrosis and ejection fraction
100 %
90 %
80 %
70 %
60 %
50 %
40 %
30 %
20 %
10 %
0 %
97
13
126
31
302
46
Plot Area
EF≤35%
EF 36-49%
EF ≥ 50%
Mild or no fibrosis
Moderate to severe fibrosis

The surveillance imaging of ascending aortic aneurysm may be optimized by determining an individual aneurysm growth rate

Iida-Mari Viitala, Kuopio University Hospital; Tuomas Selander, Kuopio University Hospital; Marja Hedman, Kuopio University Hospital; Johanna Turtiainen, Central Hospital of North Karelia

Aim

Current guidelines recommend that surveillance imaging should be performed at least for every third year of patients with ascending thoracic aortic aneurysm (ATAA) even though most of the aneurysms' growth rate is minimal. The purpose of this study was to clarify the mode of the growth of ATAAs' in a real-life patient population to adjust the optimal timing of aortic surveillance for each patient and to be able to target the limited imaging resources to high risk patients in the future.

Methods

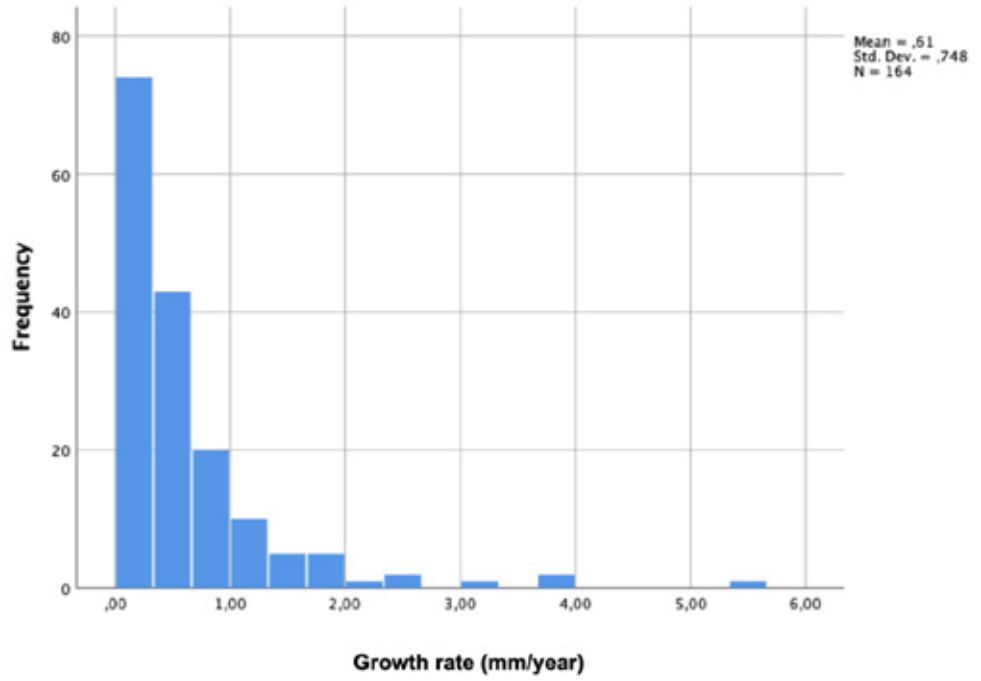
This study includes patients who had been followed due to ATAA in the central hospital of North Karelia in Eastern Finland between years 2007 and 2023 (n=209). The mean surveillance time was 5.0±3.5 years. Aortic imaging had been performed either with computed tomography (CT) or transthoracic echocardiography (TTE). In CT images, the aortic dimensions were measured according to guidelines in four levels of ascending aorta. TTE measurements were collected from medical records as well as demographic variables and cardiovascular risk factors.

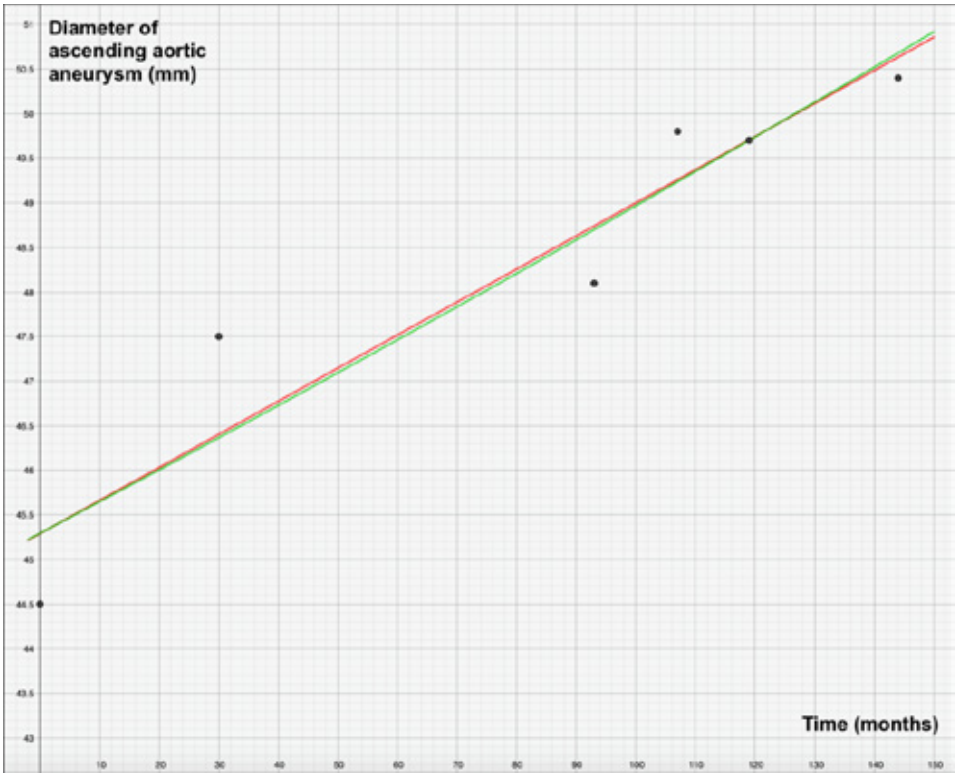
Results

The median growth rate of ATAA was 0.38 mm/year (mean 0.61±0.75 mm/yr). One fifth (21.5%) of the aneurysms showed no expansion during the follow-up. Most of the patients had very low growth rate of ATAA (histogram 1). In patients with at least four repeated imaging (n=51) graphs were drawn to illustrate the growth rate of ATAAs. The graphs demonstrated the growth of ATAAs to be linear rather than exponential regardless of duration of the surveillance time (figure 1). Eighteen of the patients ended up to surgery during the follow up.

Conclusions

Majority of the patients had a very low growth rate of ATAA. Based on this study, ATAA's growth is linear and this information may be used to predict the growth of an aneurysm. Determining individual aneurysm's growth rate by multiple aortic images and combining it to aortic diameter, the timing of repeated surveillance imaging can be optimized to be more cost-effective.


Mean = ,61
Std. Dev. = ,748
N = 164
Frequency
80
60
40
20
0
,00
1,00
2,00
3,00
4,00
5,00
6,00
Growth rate (mm/year)


Diameter of ascending aortic aneurysm (mm)
Time (months)