Suomen Kardiologinen Seura

Finnish Cardiac Society

47th Progress Report Meeting

April 14, 2021

eKevätkokous

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47th Progress Report Meeting Programme

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Meeting is supported by unrestricted educational grant from Boehringer Ingelheim

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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 1st Prize, Henna Korpela	2nd Prize, Vilbert Sikorski

24-hour wrist band photoplethysmogram monitoring in the detection of atrial fibrillation

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Aim

Asymptomatic and undiagnosed atrial fibrillation (AF) is estimated to cause 10% of ischaemic strokes. Most of the available consumer-grade automated arrhythmia detection technologies provide only intermittent or semi-continuous rhythm monitoring. We evaluated a continuous wrist band photoplethysmogram (PPG) with automated algorithms for signal quality, AF detection and accuracy of simulated alarms. AF alarms could possibly be used in the future to trigger timely ECG registration for rhythm confirmation and diagnosis of clinical AF in daily wrist band use.

Methods

A 24-hour PPG was recorded with a wrist band simultaneously with a 3-lead Holter ECG. PPGs were analyzed in 10-, 20-, 30- and 60-minute windows with an automated AF detection algorithm developed in our previous study and a simulated AF alarms were generated. Sensitivities and positive predictive values (PPV) for these alarms were evaluated for each hour.

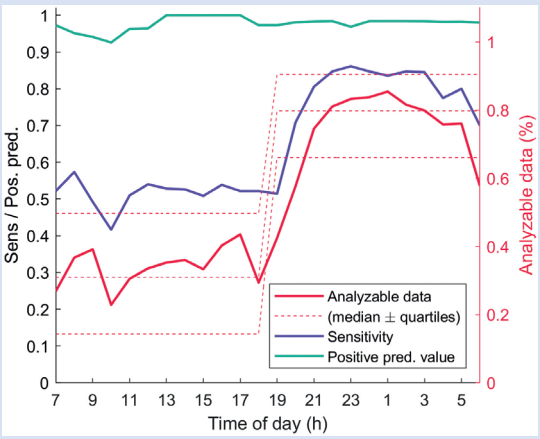

Figure 1. PPG quality and 30-minute detector window AF detection.

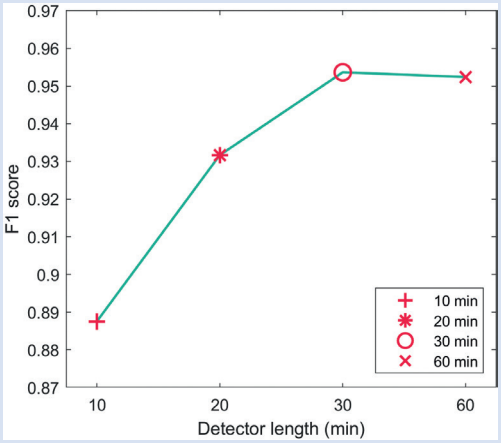

Figure 2. 24-hour performance of AF detector windows.

Results

The study population consisted of 173 patients (76 AF, 97 sinus rhythm). A higher proportion of the PPG signal was of sufficient quality for analysis between 19:00-7:00 compared to 7:00-19:00 (67.3%±22.4%, mean±SD, vs. 30.5%±19.4%, $p<0.001$; Figure 1). The 30-minute AF detector window yielded highest F1 score of 0.9536 (Figure 2). During 24 hours, 72/76 AF patients were correctly identified by this detector (sensitivity 94.7%) and only 3/97 sinus rhythm patients received a false positive result (specificity 96.9%) due to excessive extrasystoles. Sensitivities/PPVs for hourly simulated AF alarms between 19:00-7:00 were 78.3%/98.1% and 51.7%/97.4% between 7:00-19:00 (Figure 1).

Conclusions:

The results demonstrate that the quality of PPG is lower during daytime, mostly because of hand movements, but reasonably reliable AF detection can be made during long-term monitoring with automated algorithms. Unlike event-ECGs, wearable PPG devices such as wrist bands could provide a continuous monitoring and alarming system in the search of an asymptomatic AF followed by a timely ECG for diagnostic confirmation, and even longer monitoring periods compared to Holter-ECGs due to convenience of use.

Pharmacoepigenetics of hypertension: genome-wide methylation analysis of responsiveness to four classes of antihypertensive drugs using a double-blind crossover study design

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Aim

Essential hypertension remains the leading risk factor of global disease burden, but its treatment goals are not often met.

The aim of this study was to investigate whether DNA methylation, a central epigenetic mechanism of gene regulation, is associated with antihypertensive responses to four different drug classes (a diuretic, a beta-blocker, a calcium channel blocker, an angiotensin receptor antagonist). In addition, since we previously identified an SNP at the transcription start site (TSS) of the catecholamine biosynthesis-related ACY3 gene (coding for aminoacylase 3) to associate with blood pressure (BP) response to beta-blockers, we specifically analyzed the association of methylation sites close to the ACY3 TSS with BP responses to beta-blockers.

Methods

We conducted an epigenome-wide association study (EWAS) between peripheral leukocyte DNA methylation variation and BP responses to antihypertensive monotherapies in hypertensive Finnish individuals from the GENRES study and the LIFE study.

GENRES is a double-blind, placebo-controlled, crossover study with four different 4-week antihypertensive monotherapies (amlodipine 5mg, bisoprolol 5mg, hydrochlorothiazide 25mg and losartan 50mg daily) separated by 4-week placebo periods. We used BP data from 198 individuals for amlodipine, 204 for bisoprolol, 200 for hydrochlorothiazide and 197 for losartan.

LIFE is a randomized, double-blind study evaluating long-term effects of losartan compared with atenolol in patients with signs of left ventricular hypertrophy. We used data from 200 individuals on atenolol (50mg daily) and 197 individuals on losartan (50mg daily) monotherapy at two months of the study for replication analyses.

Results

We identified 64 methylation sites suggestively associated ($P<10^{-5}$) with either systolic (SBP) or diastolic blood pressure (DBP) responses by the study drugs in GENRES. Five associations reached a significance level of $P<10^{-6}$ (two for DBP change by bisoprolol, and three for SBP change by losartan). These associations did not replicate in the LIFE study.

Three methylation sites close to the ACY3 TSS were associated with SBP responses to bisoprolol in GENRES, thus linking the genetic and epigenetic sites associated with beta-blocker responses closely to each other.

Conclusions

No robust associations between DNA methylation sites and BP responses to four antihypertensive drugs were identified. However, the findings on the methylation sites close to the ACY3 TSS seem to support the role of ACY3 genetic and epigenetic variation in BP response to bisoprolol. This is further substantiated by our previous findings showing that response to bisoprolol was correlated to plasma levels of N-acetylphenylalanine and phenylalanine (ACY3 substrate and end product).

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Flow displacement and wall shear stress predict the growth rate of the ascending aortic dilatation

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Aim

The aim was to investigate whether four-dimensional (4D) flow MRI parameters predict the growth rate of ascending aortic (AA) dilatation.

Methods

This prospective study included 30 patients (aged 65.6±8.3 years, 80% were males) followed in Kuopio University Hospital due to AA dilatation (max. diameter > 40 mm). Aortic MRI (anatomic, and 4D flow) was performed with 1.5T scanner at the baseline and after one-year follow-up between 8/2017 and 7/2020. Flow parameters were analyzed in 10 planes and wall shear stress (WSS) in 5 planes (Fig.). Flow displacement (FD) was transformed to a class-scaled parameter by considering FD±5% as a threshold. Association between dichotomized FD and the growth rate of the AA dilatation was tested with Chi-Square test. Standard error of measurement (SEM) method was used to assess statistically significant growth rate of AA dilatation.

Results

Statistically significant growth in AA dilatation (2.1mm [1.5-2.2mm]) was found in 6 patients (20 %) while AA diameter remained unchanged (0.2mm [-0.3-0.9mm]) in 24 patients (80 %); (p= 0.003). All 6

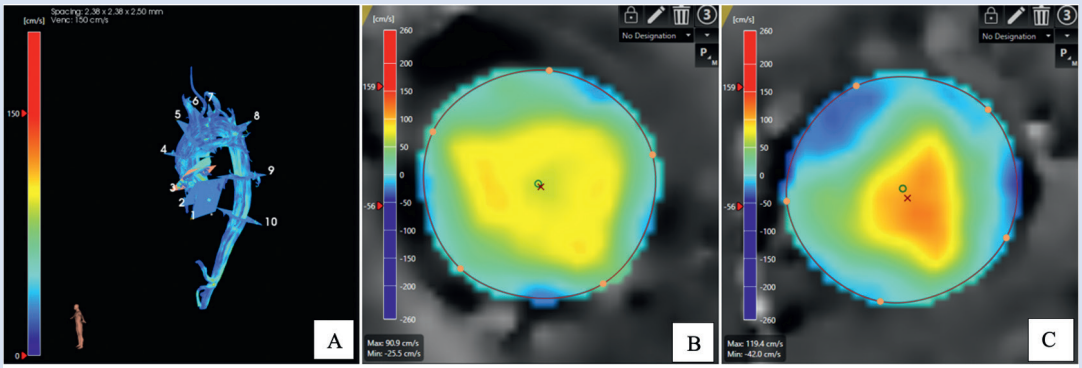

Figure.

A) Flow parameters were determined in planes 1-10 and wall shear stress in planes 1-5.

Planes; 1) sinus Valsalva, 2) sinotubular junction, 3) proximal ascending aorta, 4) mid-ascending aorta, 5) proximal aortic arch, 6) after brachiocephalic trunk, 7) mid-aortic arch, 8) distal aortic arch, 9) proximal descending aorta, 10) mid-descending aorta

B) Illustrative image of 2% flow displacement in plane 3.

C) Illustrative image of 6% flow displacement in plane 3.

patients with AA growth were males and they had normal tricuspid aortic valve. FD at the baseline associated with AA dilatation growth in one-year follow-up in the proximal part of AA (Fig.).

The growth rate of increased AA dilatation (n=6) associated with decreased total WSS compared to unchanged AA patients (n=24): in the inner curve of sinotubular junction (528.5 mPa [448.5–663.6 mPa] vs. 774.8 mPa [609.1–944.4 mPa], p=0.03) and in the anterior side of the proximal aortic arch (355.9 mPa [305.1–367.4 mPa] vs. 493.2 mPa [390.0–586.4 mPa], p<0.001).

Conclusions

Despite the small cohort and short follow-up time, displaced flow predicts the growth rate of AA dilatation in one-year follow-up. In addition, WSS was lower in AAs with significant grow as compared to unchanged AAs. Thus, 4D flow MRI might be useful when assessing the growth rate of AA dilatation.

Treatment success and its predictors as well as the complications of catheter ablation for atrial fibrillation in a high-volume centre

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Aims

Catheter ablation for atrial fibrillation (AF) is a standard procedure for maintaining sinus rhythm. The aim of this study was to evaluate treatment success and its predictors and to provide quality control data on complications and redo operations in a centre with an initially a low but currently high annual volume.

Methods

Data on patients (n = 1,253) treated with catheter ablation for AF in Tays Heart Hospital between January 2010 and May 2018 was evaluated (n = 1,178 ablation-naïve patients and n = 1,514 AF ablations). Comprehensive data on patient characteristics, treatment results, redo operations and complications were collected. Treatment success (maintenance of sinus rhythm at one year) was evaluated among patients residing within the hospital district (45% of the entire study population).

Results

Treatment success was observed in approximately 62.9% of the ablation-naïve patients. Preoperative predictors of treatment success were paroxysmal AF type, previous use of antiarrhythmic drugs, left atrium diameter and age. The experience at the centre did not associate with the one-year outcome. A relapse during the first three-month blanking period was associated with a nine-fold risk of failure at one year (unadjusted OR 9.1, 95% CI 5.5–15.1 $p < 0.001$). The major complication rate was 4.5% (68/1,514) with no deaths. Ten percent of the patients needed a redo procedure within the first year.

Conclusions

Patient-related factors are the most significant predictors of treatment success. A relapse during a three-month blanking period is associated with a very high risk of late failure.

Anna Numminen (MD)
Cardiology, Tampere University

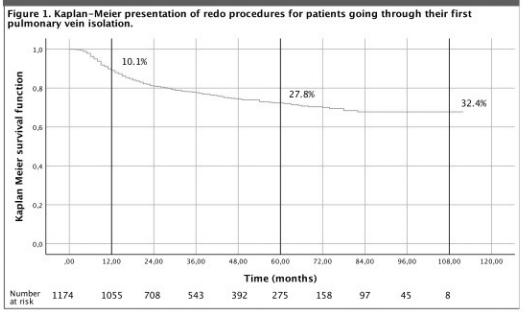
Retrospective study with 1253 AF ablation patients

With 1514 procedures

Major complication rate 4.5%
- no deaths

1178 ablation naive patients (first PVI)

Redo rate 10.1% at one year and 27.8% at five years



One year outcome available for patients living in Pirkanmaa N=531

Sinus rythm 62.9%
(no replapses 3-12 months after ablation)

After multivariate analysis previous use of AAD's, increased left atrium diameter and failure during first 3 months after ablation remained as significant predictors for failure

Previous use of AAD's
OR 0.50 for SR
(95% CI 0.313-0.808, p=0.005)

Left atrium diameter
OR 0.60 for SR for a one-centimeter increase in left atrium diameter
(0.40-0.91, p=0.016)

Paroxysmal AF
OR 1.49 for SR (0.97-2.22, p=0.051)

Documented failure during first 3 months after PVI
OR 8.49 for failure
(0.49-14.68, p<0.001)

Atrial inflammation on FDG-PET predicts atrial fibrillation in cardiac sarcoidosis

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Aim

Cardiac sarcoidosis (CS) is associated with increased risk of both ventricular and atrial arrhythmias. [18F]Fluorodeoxyglucose positron emission tomography (FDG-PET) is an accurate imaging modality for the detection of active myocardial inflammation in CS. We studied the association between atrial inflammation on FDG-PET and the risk atrial fibrillation (AF) in patients with CS.

Methods

The study population consisted of 123 patients with diagnosis of CS in Helsinki university hospital and without previously known AF. Patients underwent FDG-PET before or within 3 months of endomyocardial (n=34) or extracardiac biopsy (n=89). Atrial inflammation was retrospectively analyzed from FDG-PET images. Cardiac chamber volumes and function were also measured by cardiac magnetic resonance imaging (CMR). In addition, FDG-PET, CMR and single-photon emission tomography was used to quantify the extent of left ventricular inflammation and scar burden. Patient characteristics and laboratory results were collected from patient records. Cox-proportional hazards model and Kaplan-Meier analysis were used to assess the association between atrial inflammation measured by FDG-PET and the prevalence of AF during follow-up.

Results

Median follow-up time was 3 ± 4 years. The mean age was 49 ± 11 years and 81 (66%) were females. There were total of 38 AF diagnoses during follow-up. AF occurred more frequently in individuals with atrial uptake on FDG-PET compared to those without atrial uptake (46% vs. 24%, $p=0.01$). Atrial uptake on FDG-PET, left ventricular mass, right ventricular volume, left atrial volume, troponin elevation and the use of beta blocker were associated with AF in univariate analysis ($p<0.05$). In multivariate analysis, atrial uptake on FDG-PET and left atrial volume were independent predictors of AF ($p<0.05$). Left ventricular ejection fraction, late gadolinium enhancement, rest perfusion or the degree of left ventricular inflammation on FDG-PET were not associated with the occurance of AF during follow-up ($p>0.05$).

Conclusions

Atrial inflammation detected by FDG-PET and left atrium volume on CMR are independent predictors of atrial fibrillation in cardiac sarcoidosis. Extent of left ventricular scar or its inflammatory burden were not associated with atrial fibrillation during follow-up.

Juha Vähätalo (BM)
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Genetic variants associated with sudden cardiac death in victims with single vessel coronary artery disease and left ventricular hypertrophy with or without fibrosis

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Aim

Cardiac hypertrophy with varying degrees of myocardial fibrosis is commonly associated with coronary artery disease (CAD) related sudden cardiac death (SCD), especially in young victims among whom patterns of coronary artery lesions do not entirely appear to explain the cause of SCD. Our aim was to study the genetic background of hypertrophy, with or without fibrosis, among ischemic SCD victims with single vessel CAD.

Methods

The study population was derived from the Fingesture study, consisting of all autopsy-verified SCDs in Northern Finland between the years 1998 and 2017 (n=5,869). We carried out targeted next-generation sequencing using a panel of 174 genes associated with myocardial structure and ion channel function in 95 ischemic-SCD victims (mean age 63.6±10.3 years; 88.4% males) with single-vessel CAD in the absence of previously diagnosed CAD and cardiac hypertrophy with or without myocardial fibrosis at autopsy. Assessment for pathogenicity of detected variants was based on American College of Medical Genetics consensus guidelines.

Results

A total of 43 variants were detected in 43 subjects (45.3%). Five variants in 8 subjects (8.4%) were classified as pathogenic or likely pathogenic. We observed 38 variants of uncertain significance in 39 subjects (40.6%). Variants were detected in myocardial structure protein coding genes, associated with arrhythmogenic right ventricular cardiomyopathy, dilated cardiomyopathy, hypertrophic cardiomyopathy and left ventricular non-compaction cardiomyopathy. Also, variants were detected in RYR2, a gene associated with both cardiomyopathies and catecholaminergic polymorphic ventricular tachycardias. None of the subjects presented characteristic autopsy findings related to the inherited cardiomyopathies.

Conclusions

Variants associated with cardiomyopathies, in the absence of anatomic evidence of the specific inherited cardiomyopathies, were common findings among CAD-related SCD victims with single vessel disease and myocardial hypertrophy found at autopsies, suggesting that these variants may modulate the risk for fatal arrhythmias and SCD in ischemic disease.

Incidence of sudden cardiac arrests and sudden cardiac death after acute coronary syndrome

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Background and aims

Sudden cardiac arrests (SCA) and sudden cardiac death (SCD) are believed to account for a large part of deaths due to cardiac causes. The aim of this study was to form a comprehensive view of the epidemiology of these events among patients treated for acute coronary syndromes.

Methods

The incidence of SCAs (including SCDs) was studied retrospectively among 10,316 consecutive patients undergoing invasive evaluation for ACS between 2007 and 2018 in a center acting as a sole provider of specialized cardiac healthcare in the region of Pirkanmaa (catchment area of over 0,5 million inhabitants). Baseline information was collected by combining information from all electronic hospital health records and from full disclosure review of written patient records. Follow-up data for mortality and incident SCAs and SCDs was based on a review of death certificates and all written hospital records.

Results

The cumulative incidence of SCAs (including SCDs) was 12.4% during twelve years of follow-up (Figure1). SCAs and SCDs account for approximately one fifth of deaths occurring in this patient population. Almost half (45.4%) SCAs are classified as sudden cardiac deaths and 22.9% of SCAs are successfully aborted by successful resuscitation (Figure2). At baseline, SCA victims were younger, had lower left ventricular ejection fraction (LVEF) and more ST-elevation myocardial infarcts (STEMI) than other type of acute coronary syndromes (ACS) when compared to those who died of other reasons and to those who survived (Table1). Also, higher proportion of SCA victims were male. The proportion of SCAs of all deaths was highest among subjects below the age of 50 years (>50%) (Figure3). The vast majority of SCAs (95.3%) occur in patients with no previous implantable cardioverter defibrillator (ICD) device (95.3%) or subsequent hospitalizations for CAD (81.0%).

Conclusions

The cumulative incidence of SCA after ACS is low but almost half of the patients die SCD. SCAs account for over half of deaths occurring among patients who are 50 years or younger and the vast majority of these cases are not correctly predicted beforehand.

Table 1. Demographics, status, and events for SCA, death due to other causes or were alive in the end of the follow-up and did not suffer SCA.

	SCA (N=700)	Other deaths (N=2093)	Alive (N=7523)	p-value*	p-value**
Demographics					
Age (on admission)	70.1 ±11.5	75.8±9.7	66.0±11.5	<0.001	<0.001
Men (N)	72.7% (509)	62.4% (1305)	68.1% (5121)	<0.001	0.011
BMI (kg/m2)*	28.7 ±6.0	27.5 ±5.5	28.2 ±5.1	0.001	0.083
Diabetes (any) (N)*	33.3% (232)	33.6% (702)	22.3% (1667)	0.865	<0.001
Hypertension(N)*	61.0% (426)	67.4% (1408)	58.6% (4367)	0.002	0.215
Dyslipidaemia(N)*	55.5% (387)	56.3% (1172)	58.9% (4369)	0.723	0.086
CKD (N)*	7.3% (51)	7.8% (163)	5.7% (431)	0.672	0.091
VHD (N)	9.9% (69)	13.6% (285)	5.1% (381)	0.010	<0.001
Previous MI(N)	24.9% (174)	27.0% (566)	13.6% (1022)	0.257	<0.001
Previous PCI (N)	11.4% (80)	11.9% (250)	10.6% (795)	0.714	0.480
Previous CABG (N)	14.7% (103)	12.5% (261)	6.3% (476)	0.127	<0.001
PAD (N)	14.7% (103)	15.2% (318)	4.9% (369)	0.752	<0.001
Cancer (N)*	9.3% (64)	13.4% (277)	6.6% (465)	0.005	0.007
Dementia (N)*	2.5% (12)	6.3% (82)	0.9% (45)	0.005	0.003
Smoker (N)*	40.2% (131)	38.1% (381)	44.9% (2275)	0.510	0.098
Previous ICD (N)	1.0% (7)	0.3% (6)	0.2% (16)	0.016	<0.001
LVEF (%)	45.5±12.3	47.6±12.8	52.9±11.2	<0.001	<0.001
Status During Admission					
Haemoglobin (g/l)*	123.5 ±16.0	121.8 ±15.9	132.7 ±15.1	0.011	<0.001
Creatinine (µmol/l)*	107.2 ±93.1	105.7 ±84.2	81.2 ±42.3	0.705	<0.001
Killip class (N)*				0.287	<0.001
1	57.0% (326)	57.2% (930)	86.9% (4907)		
2	22.4% (128)	23.9% (389)	9.5% (538)		
3	14.0% (80)	14.4% (235)	3.2% (179)		
4	6.6% (38)	4.4% (72)	0.4% (21)		
Type of ACS				<0.001	<0.001
STEMI	44.7% (313)	36.3% (760)	34.5% (2594)		
NSTEMI	43.4% (304)	45.0% (941)	46.2% (3477)		
UAP	11.9% (83)	18.7% (392)	19.3% (1452)		
Treatment Modality					
PCI (N)	67.6% (473)	58.9% (1233)	68.4% (5148)	<0.001	0.640
Heart surgery (N)	9.7% (68)	13.2% (277)	10.3% (778)	0.014	0.601
Conservative (N)	24.3% (170)	29.7% (621)	22.5% (1692)	0.006	0.278

Percents are valid percents. Continuous variables are mean ± standard deviation. Categorical values are frequencies. BMI, Body Mass index; CKD, chronic kidney disease; VHD, valvular heart disease; PAD, peripheral arterial disease; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; ACS, acute coronary syndrome; STEMI, ST-elevation myocardial infarction; NSTEMI non-ST-elevation myocardial infarction; UAP, unstable angina pectoris; PCI, percutaneous coronary intervention. *Between SCA and other deaths.**Between SCA and alive.
**Missing data: <1% for diabetes, hypertension, dyslipidemia, CKD, haemoglobin, creatinine, 45.9% for BMI, 2.1% for cancer, 30.5% for dementia, 46.2% for smoking and 18.2% for Killip classification.

Figure 1. Cumulative incidence function for SCAs, other deaths and all deaths during the follow-up.

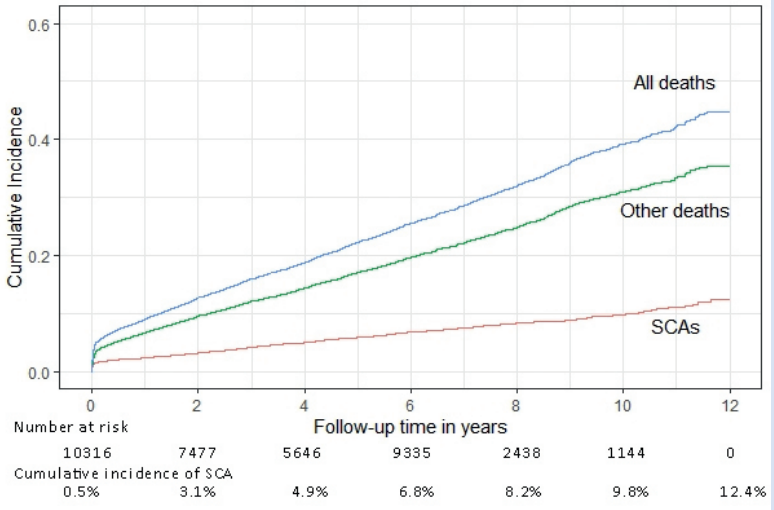


Figure 2. Sudden cardiac arrest subgroups in ACS patients.

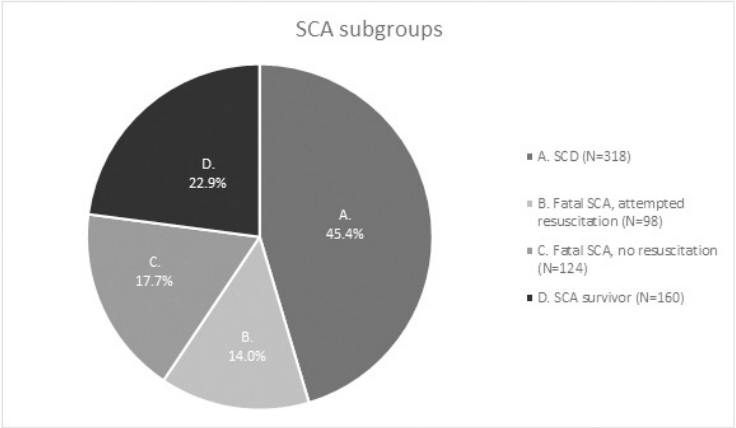
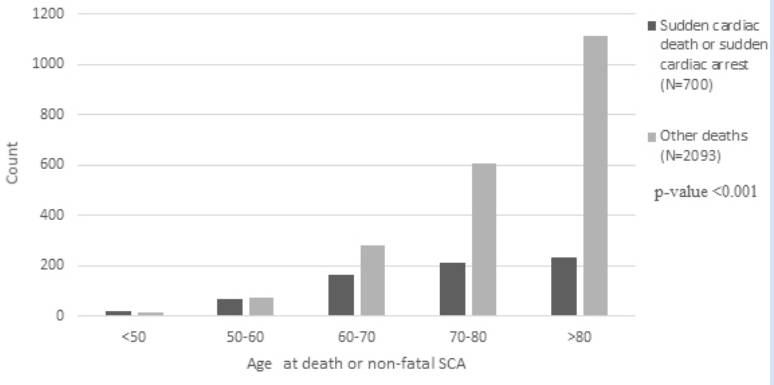


Figure 3. Sudden Cardiac Death or Arrest vs. Other Deaths by Age Groups



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Long-term safety and efficacy of intramyocardial VEGF-DΔNΔC gene therapy: an eight-year follow-up for phase 1 KAT301 study

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Aim

Vascular endothelial growth factor -based gene therapy (GT) targeted has been shown to increase myocardial perfusion in patients with coronary artery disease. In phase I KAT301 trial, intramyocardial VEGF-DΔNΔC (VEGF-D) encoding adenoviral GT resulted in a significant improvement in the myocardial perfusion reserve as well relieved angina group at 1-year follow-up. Most importantly, no major safety concerns were encountered. In this study, our objective was to investigate the long-term safety and efficacy of VEGF-D GT in KAT301 patients.

Methods

A total of 30 patients (24 VEGF-D and 6 controls) participated in the KAT301 trial. The mean follow-up time was 7.9 years (range 6.3 – 9.7 years). Patients were interviewed with questionnaires and by telephone to evaluate their current severity of symptoms (Canadian Cardiovascular Society class) and perceived benefit from GT. Medical records were reviewed to assess the incidence of major cardiovascular adverse events (MACEs) consisting of cardiovascular death, acute coronary syndrome, coronary angiography, percutaneous coronary intervention, coronary artery bypass grafting and stroke. In addition, the incidence the individual MACE components and new malignancies, diabetes, and proliferative retinopathy were assessed.

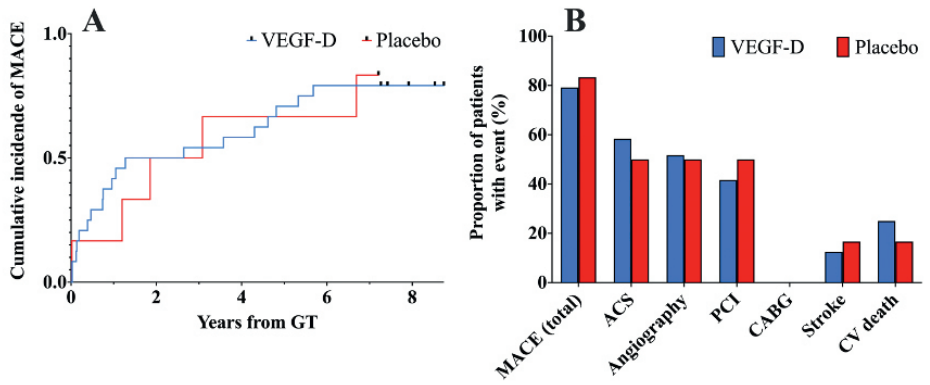

Figure 1. Incidence and the total amount of major adverse cardiovascular events composed of acute coronary syndrome, angiography, percutaneous coronary intervention, coronary artery bypass grafting, stroke, and cardiovascular death. The incidence was statistically equal in both groups (shown in **A**, $p = 0.93$), as was the number of total MACE and individual events (**B**). ACS, acute coronary syndrome; CABG, coronary artery bypass grafting; CV, cardiovascular, GT, gene therapy; MACE, major adverse cardiovascular event; PCI, percutaneous coronary intervention; VEGF-D, vascular endothelial growth factor D.

Results

Nine patients deceased during the follow-up. Mortality in the VEGF-D (33.3%) and control (16.7%) groups did not differ (p = 0.64). Neither the incidence of MACE as well as the other predefined endpoints differed between the groups. At the end of follow-up, angina symptoms (CCS) were less severe compared to baseline in the VEGF-D group (1.9±1.1 vs. 2.9±0.3, p = 0.006) but not in the control group (2.2 ± 1.3 vs. 2.6 ± 0.6, p = 0.414).

Conclusions

Our study indicates that intramyocardial VEGF-D GT is safe in the long-term. In addition, the relief of symptoms remained during the follow-up.

Exercise training enhances submaximal performance of young fontan-patients

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Aim

Univentricular heart defects are congenital malformations of the heart. Palliative surgery aiming to full cavopulmonary connection causes the systemic venous pressure to set to a high level predisposing the patient to serious long-term complications where interventions and medication have little effect. As means of self-care exercise may help preservation of transpulmonary flow. We investigated the effects of 6-month exercise prescription on pediatric Fontan patients. Specifically, we studied whether peripheral muscle pumps are important for cardiopulmonary performance and functional capacity.

Methods

18 stable Fontan patients (14 +/- 2.6 years, 160 +/- 11 cm, and 51 +/- 14 kg) were recruited. An interview of physical habits was performed, and body composition, cardiorespiratory performance, and muscle fitness were tested at entrance. An individualized plan for exercise drills emphasizing lower limb strengthening was prescribed and daily step goal was set. After six-months of regular practice the measurements were repeated.

Results

As expected, at entrance to the study Fontan patients had lower than normal maximal oxygen uptake (Vo2max) of 28.3 +/- 5.9 ml/kg/min (61% from matched reference). Vo2max significantly correlated with weekly amount of habitual exercise and muscle mass of the lower limbs ($p<0.001$ and $p<0,001$, respectively). After 6 months of training the patients had improved their anaerobic threshold (18 +/- 3,5 vs 20 +/- 4,8 ml/kg/min, $p=0.007$) and workload tolerance (119 +/- 39 vs 132 +/- 44 W, $p=0,001$). Of the EUROFIT testing, the parts measuring squats ($p<0.01$), standing broad jump ($p<0.001$), and shuttle run ($p<0.001$) significantly correlated with Vo2max.

Conclusions

Individualized exercise prescription enhances muscle fitness and submaximal performance of young patients with Fontan circulation. We would like to contemplate that physically active lifestyle improves functional reserves disposable for daily well-being, and helps in delaying inevitable chronic complications evolving after Fontan palliation. Further studies should measure the effects of regular exercise protocols on stroke volume regulation, transpulmonary flow, and elevated central venous pressure.