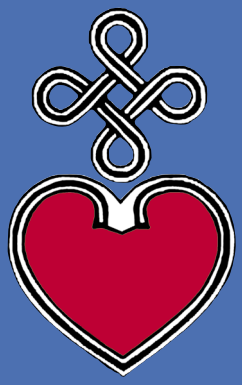
Suomen Kardiologinen Seura

Finnish Cardiac Society



40th Progress Report Meeting

March 19, 2014

Helsinki

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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 has 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	
2011	Markku Lähteenvuo	Aapo Aro
2012	1st Prize Kirsi Kujala 2nd Prize Maija Bry	
2013	Suvi Syväranta	Toni Grönberg

Early vascular healing after titanium-nitride-oxide-coated stent vs. platinum chromium everolimus-eluting stent implantation in patients with acute coronary syndromes

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Aim

Recent data suggests a paradigm shift in stent thrombosis (ST) occurrence as evidenced by lower rates of early and late ST in patients treated with platinum chromium everolimus-eluting stents (PtCr-EES) compared to traditional bare metal stents. Nevertheless, data on early vascular healing response of novel stent devices are scarce. In this randomized prospective trial, we sought to compare early healing and neointimal coverage of vessels treated with bioactive titanium-nitride-oxide–coated stents with thin strut platform (BAS) versus PtCr-EES at 2 months follow-up in patients presenting with ACS.

Methods

Thirty-eight patients with ACS were randomized to receive either BAS (n=19) or PtCr-EES (n=19). Neointimal stent strut coverage and apposition was examined by OCT and intravascular coronary flow reserve measurement (CFR) at 2-month follow-up. The primary endpoint was the percentage of uncovered struts.

Results

At a mean follow-up of 63 ± 8 days 302 cross-sections (3412 struts) were analyzed in the BAS group, and 324 cross-sections (3460 struts) in the PtCr-EES group. Mean ± SD neointimal thickness was 240 ± 127 µm and 65.4 ± 59.5 µm for BAS and PtCr-EES, respectively (p<0.001). Mean cross-sectional neointimal area was 1.94 ± 1.01 % vs. 0.427 ± 0.647 % (p<0.001). Median [interquartile range] percentage of uncovered struts was 1.2 {2.8] % vs. 11.3 [17.7] % (p<0.001). Median percentage of malapposed struts was 0 [1.20] % vs. 0.68 [3.59] % (p=0.026). CFR values between groups were comparable.

Table 1. Follow-up measurements of the two study groups at 2 months.

Variable	BAS (n=19)	PtCr-EES (n=19)	*p* value
Total number of cross-sections analysed	302	324	
Total number of struts analysed	3412	3460	
Struts per cross-section	11.4 ± 0.784	10.7 ± 1.20	<0.048
NIH area (mm^2)	1.94 ± 1.01	0.427 ± 0.647	<0.001
Mean NIH thickness (µm)	240 ± 127	65.4 ± 59.5	<0.001
Uncovered struts	66 (1.91)	510 (14.9)	<0.001
Percentage of uncovered struts	1.2 {2.8]	11.3 [17.7]	<0.001
Percentage of cross-sections with uncovered struts	8.6	54.0	<0.001
Malapposed struts	27 (0.791)	63 (1.82)	<0.001
% Malapposed struts	0 [1.20]	0.68 [3.59]	0.026
Percentage of cross-sections with malapposed struts	3.7	9.3	<0.001
Coronary flow reserve	2.92 ± 1.26	2.58 ± 1.36	0.450
Abnormal coronary flow reserve (≤2)	4 (26.7)	9 (47.4)	0.296

Continuous variables are presented as mean ± SD or as median [IQR], while categorical variables are presented as frequency (percentage).

Conclusions

BAS showed rapid and comprehensive neointimal coverage at 2 months as compared to PtCr-EES, with significant neointimal hyperplasia. Furthermore, less strut malapposision was found in BAS.

Sudden cardiac death during physical exercise: Characteristics of victims and autopsy findings

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Background

There has been little information about the risk factors and characteristics of victims of sudden cardiac death (SCD) occurring during physical exercise (PE).

Methods

We assessed the characteristics of subjects and findings obtained from the medico-legal autopsy of SCD victims of the FinGesture study population who had experienced a witnessed fatal cardiac arrest at rest (R) (n=876) or in relation to PE (n=328). The FinGesture study population was derived from autopsies of a consecutive series of 2667 victims of SCD in Northern Finland during 1998-2007.

Results

A total of 876 of witnessed SCDs occurred at R (73%) (mean age 63±11 y) and 328 (27%) SCDs during or immediately after PE (mean age 62±11 y). Male gender was more common in the PE-group compared to R-group (309/328, 94 % vs. 678/876, 77 %, $p<0.001$). Coronary artery disease (CAD) was a more common underlying structural heart disease at autopsy when death had occurred in relation to PE (299/328, 91 % vs. 657/876, 75 %, $p<0.001$). Myocardial scarring and cardiac hypertrophy at autopsy were associated with an increased occurrence among PE-related SCD (194/328, 59 % vs. 370/876, 42 %, $p<0.001$, and 243/328, 74 % vs. 585/876, 67%%, $p=0.012$, respectively). The type or location of coronary lesion at histological examination had no significant impact on the distribution of SCD between PE-group and R-group. Prior diagnosed heart disease in patient history was associated to neither PE-group nor R-group (134/316, 42 % vs. 350/842, 42 % p=NS).

Conclusions

Male gender, ischemic heart disease, myocardial scarring and hypertrophied heart at autopsy are more common findings among those who have suffered fatal cardiac arrest during or immediately after exercise compared to those dying at rest both in subjects with and without a known cardiac disease.

Ventricular conduction abnormalities as predictors of long-term survival in acute de-novo and decompensated chronic heart failure

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Aim

The role of ventricular conduction abnormalities in the survival of patients with acute heart failure (AHF) is still controversial. Our aim was to find prognostic factors in the admission electrocardiogram (ECG) in AHF, and compare them between patients with de-novo AHF and acutely decompensated chronic heart failure (ADCHF).

Methods

We analysed the admission ECG of 982 patients from a European multicentre cohort of AHF. The mean follow-up was 3.9 years and the end-point was all-cause mortality. In the multivariate models Cox proportional hazard ratios (HR) were adjusted for age, sex, clinically relevant comorbidities, renal function, smoking, and NT-proBNP.

Results

Patients with de-novo AHF (n=506) were younger and had less cardiac morbidities than those with ADCHF (n=476). In total, ventricular conduction abnormalities were more common in ADCHF than in de-novo AHF [IVCD (QRS width≥110ms, no bundle branch block) 20.6% vs. 13.2%, P=0.001; LBBB 17.2% vs. 8.7%, P<0.001; and RBBB 6.9% vs. 8.1%, P=NS; respectively]. Mortality during the follow-up was higher in patients with RBBB (85.4%) and IVCD (73.7%) compared to those with normal ventricular conduction (57.0%); P<0.001 for both. Figure 1 shows the unadjusted HRs for each conduction abnormality in all patients and in the two subgroups. The impact of RBBB on survival was driven by de-novo AHF [adjusted HR 1.93 (1.03-3.60); P=0.04], whereas IVCD was an independent predictor of death in ADCHF [adjusted HR 1.79 (1.28-2.52); P=0.001]. LBBB was not associated with increased mortality in either of the subgroups.

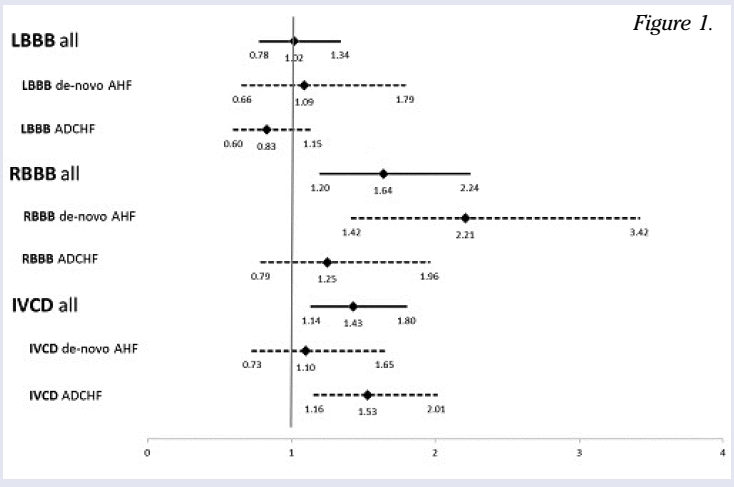

Figure 1.

Conclusion

Ventricular conduction abnormalities are more frequent in ADCHF compared to de-novo AHF. RBBB predicts poor long-term survival in patients with de-novo AHF, and IVCD in those with ADCHF.

The Ability of ECG Risk Variants to Predict Death in Asymptomatic Middle-Aged Subjects without a Known Cardiac Disease

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Aim

Recent general population based studies have noted many ECG variants as risk markers for increased mortality rates for sudden arrhythmic death (SAD). The importance of these findings has not been evaluated in asymptomatic subjects with no cardiac disease.

Methods

We assessed twelve-lead electrocardiograms of general population based study of 10904 middle-aged subjects (mean age [±SD], 44±8.5) with a follow-up of 30±11 years. Primary endpoint was death due to arrhythmia and secondary endpoints were death from cardiac causes and all-cause mortality. Abnormal ECG was defined as the presence of inferior early repolarization ≥0.1mV with horizontal/descending ST-segment, left bundle branch block, intraventricular conduction delay, abnormal QRST-angle, pathological Q-waves and/or T-inversions in other than leads V1-V3.

Results

The final population consisted of 9511 subjects (mean age 43±8.3 years, 52% men). Prevalence of any ECG abnormality was 7.7% (N=732, 64.9% men) subjects. Asymptomatic subjects with one or more ECG abnormality had an increased risk of arrhythmic death (adjusted relative risk [RR] 1.8; 95% confidence interval [95% CI], 1.4 to 2.3, P<0.001) as well as death from cardiac (adjusted RR 1.5; 95% CI, 1.3 to 1.8, P<0.001) and death from any cause (adjusted relative risk 1.2; 95% CI, 1.1 to 1.3, P=0.001, respectively) compared to those without.

Conclusion

The prevalence of abnormal ECG increasing the risk of SAD is substantial in asymptomatic middle-aged subjects. Future studies using more rigorous statistics, such as c-statistics, reclassification and cost-effectiveness analyses, will reveal the impact of routine ECG screening of middle-aged subjects for SAD.

Acute heart failure with and without concomitant acute coronary syndromes - patient characteristics, management and survival

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Aim

Acute coronary syndromes (ACS) may precipitate up to one third of acute heart failure (AHF) cases. As data are scarce, we assessed characteristics, initial management and survival of AHF patients with (ACS-AHF) and without concomitant ACS (nACS-AHF).

Methods

Data of 620 patients hospitalized due to AHF were prospectively collected in a multicenter study. All-cause mortality was assessed during five years follow-up. The data were compared between patients with and without ACS. Comparisons between groups were performed by $\chi 2$ test, t-test or Mann-Whitney U as appropriate. Survival analyses were performed using Kaplan-Meier method and multivariable logistic regression.

Results

ACS-AHF patients (32%) presented more often with de novo AHF (61% vs. 43% in nACS-AHF, p<0.001). While there were no differences between the two groups in mean blood pressure, heart rate or routine biochemistry on admission, cardiogenic shock and pulmonary oedema were more common manifestations in ACS-AHF (p<0.01 for both). The use of intravenous nitrates, furosemide, opioids, inotropes and vasopressors as well as non-invasive ventilation and invasive coronary procedures (angiography, PCI, CABG) was more frequent in ACS-AHF (p<0.001 for all). Although 30-day mortality was significantly higher in ACS-AHF (13 vs. 8%, p=0.03) survival at five years was similar between the two groups (figure; dashed line for ACS-AHF and solid line for nACS-AHF). Overall, ACS was an independent predictor of 30-day mortality (adjusted OR 2.0, 95% CI 1.07-3.79, p=0.03).

Conclusions

Despite differences in terms of medical history, manifestation and initial treatment, long-term survival is similar in ACS-AHF and nACS-AHF patients. Still, ACS is independently associated with increased short-term mortality in AHF. Special focus on ACS-AHF patients is warranted to improve outcomes.

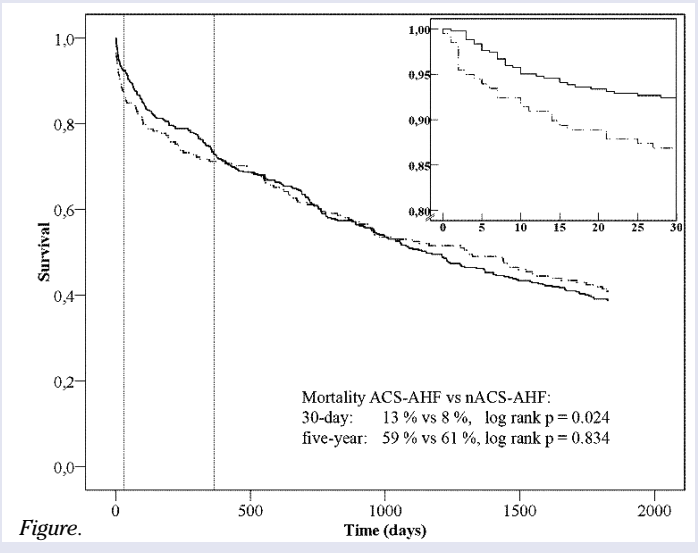

Figure.

Drug-eluting balloon in stable coronary artery disease and in acute coronary syndromes - an all-comers registry

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Aim

Drug-eluting balloon (DEB) has been found efficient for the treatment of in-stent restenosis (ISR) but little is known about its performance in other types of percutaneous coronary interventions (PCI) including de novo lesions of large vessels and in acute coronary syndromes (ACS). The aim of this registry study was to assess the efficacy and safety of PCI using DEB in real life patient population.

Methods

353 PCIs were performed to 332 patients using a paclitaxel-coated DEB between september 2009 and december 2012. The PCI registry data was retrospectively analyzed. The major cardiovascular adverse effects (MACE, the composite of death, non-fatal myocardial infarction and target lesion revascularization) and bleeding events were studied. The median follow-up time was 2 years and 9 months.

Results

Mean age of the patients was 68 years, 28% had diabetes and 25% had suffered prior myocardial infarction. 52%, 45% and 4% of the patients had PCI because of stable coronary artery disease (SCAD), ACS (unstable angina or non ST-elevation myocardial infarction) and ST-elevation myocardial infarction, respectively. 92% of the treated lesions were de novo and 8% involved ISR. Bailout stenting was needed in 15% of the PCIs. The 12 and 24 month MACE rate for the whole study population was 11% and 14% respectively. In SCAD MACE occurred in 7% and 11% by 12 and 24 months, respectively. In ACS, the respective MACE rates were 15% and 20%. The rate of target lesion revascularization (TLR) was 2% by 12 months and 3% by 24 months. The 12 and 24 month rate for bleeding was 6% and 7%, respectively.

Conclusions

In this all-comers registry of DEB in conventional indications for PCI both in SCAD and ACS the rates of MACE and TLR were lower than in many previous trials using bare-metal or drug-eluting stents. In conclusion, PCI using DEB appears a feasible alternative to stenting but randomized controlled trials are warranted to confirm these results.

Modeling hypertrophic cardiomyopathy with human induced pluripotent stem cells

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Aim

The two most predominant Finnish founder mutations for hypertrophic cardiomyopathy (HCM) are located in cardiac myosin binging protein C (cMYBPC, Q1061X) and in α-tropomyosin (TPM1, D175N). The functional consequences and the mechanisms by which mutations cause diverse phenotypes in HCM are still only partly understood. Here we have developed cell models for studying pathophysiological mechanisms of the Finnish HCM founder mutations by using human induced pluripotent stem cells (hiPSCs).

Methods

We have established hiPSC lines from HCM patients carrying cMYBPC (Q1061X) and TMP1 (D175N) mutations. We have studied the morphology, Ca2+ cycling and electrophysiological properties of hiPSC-derived HCM cardiomyocytes.

Results

We have observed dysregulated Ca2+ cycling and aberrant action potentials in hiPSC-derived HCM cardiomyocytes in single-cell level. The frequency of abnormalities in Ca2+ cycling increases during the maturation of cardiomyocytes.

Conclusions

The electrophysiological properties of hiPSC-derived HCM cardiomyocytes differ from the properties of cardiomyocytes derived from healthy controls. Our HCM hiPSC models can be used to studying pathophysiological mechanisms of the HCM disease in humans and to drug screening regarding the two Finnish founder mutations in TPM1 and cMYBPC.

Association of Late Gadolinium Enhanced Cardiac MRI Measured Interstitial Myocardial Fibrosis, Biomarkers of Fibrosis and Diastolic Dysfunction

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Aim

Patients with coronary artery disease (CAD) and diastolic dysfunction have higher mortality and incidence of hospitalization due to heart failure. We studied the association of cardiac MRI markers of myocardial fibrosis, galectin-3 and PIIINP biomarker levels and echocardiographically measured diastolic dysfunction.

Methods

We determined the galectin-3 and PIIINP levels and performed cardiac MRI on 64 subjects with preserved left ventricular systolic function from the highest and lowest septal E/E' groups derived from large CAD study population; ARTEMIS study. We compared the extracellular volume assessed from myocardial late gadolinium enhancement T1 relaxation time as a marker of myocardial fibrosis, galectin-3 and PIIINP levels with diastolic dysfunction assessed by E/E'.

Results

There was a significant correlation between T1 relaxation time and galectin-3 ($r2 = -0{,}33$, $p = 0{,}012$) and also between E/E' and galectin-3 ($r2 = 0{,}39$, $p < 0.001$) and between E/E' and PIIINP ($r2 = 0{,}33$, $p < 0.001$). The lowest T1 relaxation time tertile had significantly higher galectin levels ($p = 0{,}009$) and higher E/E' values ($p = 0{,}046$) compared to the highest T1 relaxation time tertile.

Conclusions

Radiological evidence of myocardial fibrosis is associated with biomarkers – especially with galectin-3. Additionally, diastolic dysfunction was strongly associated with biomarkers of fibrosis. These findings suggest that interstitial myocardial fibrosis is a major determinant of myocardial relaxation capacity among subjects with CAD.

p38a regulates SERCA2a function

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Aims

cAMP-dependent protein kinase (PKA) regulates the L-type calcium channel, the ryanodine receptor, and phospholamban (PLB) thereby increasing inotropy. Cardiac contractility is also regulated by p38 MAPK, which is a negative regulator of cardiac contractile function. Aim of this study was to identify the mechanism mediating the positive inotropic effect of p38 inhibition.

Methods

Isolated adult and neonatal cardiomyocytes and perfused rat hearts were utilized to investigate the molecular mechanisms regulated by p38.

Results

PLB phosphorylation was enhanced in cardiomyocytes by chemical p38 inhibition, by overexpression of dominant negative p38α and by p38α? RNAi, but not with dominant negative p38β. Treatment of cardiomyocytes with dominant negative p38α significantly decreased Ca2+-transient decay time indicating enhanced sarco/endoplasmic reticulum Ca2+-ATPase function and increased cardiomyocyte contractility. Analysis of signaling mechanisms involved showed that inhibition of p38 decreased the activity of protein phosphatase 2A, which renders protein phosphatase inhibitor-1 phosphorylated and thereby inhibits PP1.

Conclusion

Inhibition of p38α enhances PLB phosphorylation and diastolic Ca2+ uptake. Our findings provide evidence for novel mechanism regulating cardiac contractility upon p38 inhibition.

Stroke is often the first clinical manifestation of atrial fibrillation. The FibStroke Study

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Aim

Atrial fibrillation (AF) is often asymptomatic and may remain undiagnosed and lead to stroke when no anticoagulation is used.

Methods

We analyzed the timing of 1,471 ischemic strokes and transient ischemic attacks (TIA) in relation to the diagnosis AF in 1,310 patients treated in 4 centers during 2003-2012. The patients were divided into 2 groups according to the history of AF: (1) patients with a history of AF and (2) patients with a new diagnosis of AF at the presentation of stroke or TIA.

Results

AF was diagnosed for the first time at the time of stroke/TIA in 384 (26.1%) patients. Patients with a history of AF were significantly older and they had more often heart failure, vascular disease, history of stroke and chronic AF (Table).

Conclusions

Stroke is often the first manifestation of AF. More effective measures to screen for asymptomatic AF are needed.

	Previous AF n (%)	New AF n (%)	p
N (% of all events)	1087 (73.9)	384 (26.1)	
Age, yr (95% CI)	76.7 (9.3)	74.8 (9.3)	.001
Female gender	601 (55.3)	204 (53.1)	.5
Heart failure	221 (20.3)	37 (9.6)	<.001
Diabetes	241 (22.2)	76 (19.8)	0.3
Hypertension	698 (64.2)	245 (63.8)	0.9
Vascular disease	432 (39.7)	91 (23.7)	<.001
History of stroke	359 (33.0)	60 (15.6)	<.001
Paroxysmal AF	406 (44.0)	197 (80.1)	<.001