Suomen Kardiologinen Seura

Finnish Cardiac Society

38th Progress Report Meeting

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Contents

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	

Coronary artery bypass surgery versus percutaneous coronary intervention in patients on chronic anticoagulation for atrial fibrillation

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***Andrea Rubboli**, Cardiac Catheterization Laboratory, Maggiore Hospital, Italy*
***Axel Schlitt**, Department of Cardiology, Paracelsus-Harz-Clinic Bad Suderode, Germany*
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Aim

The aim of this study was to evaluate the outcome after coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) in patients on oral anticoagulation for atrial fibrillation (AF).

Methods

This study includes 120 patients who underwent CABG and 170 patients who underwent PCI. Propensity score was employed for risk adjustment and for one-to-one matching.

Results

Thirty-day postoperative outcome after PCI or CABG was similar. Multivariate analysis showed that PCI was associated with significantly poorer 3-year survival (71.9% vs. 86.2%, RR 3.046), freedom from combined major adverse cardiovascular and cerebrovascular (MACCE) events (61.3% vs. 79.7%, RR 2.196), freedom repeat revascularization (85.4% vs. 97.3%; RR 4.454) and freedom from myocardial infarction (83.8% vs. 94.5%; RR 2.858). When adjusted for propensity score, PCI was still significantly associated with an increased risk of late mortality (RR 3.342), MACCE (RR 2.945), repeat revascularization (RR 5.729) and myocardial infarction (3.523). Results in 59 one-to-one matched pairs showed that 3-year survival (68.7% vs. 91.3%, log-rank test: p=0.005) and freedom from MACCE (58.6% vs. 84.2%, log-rank test: p=0.002) were significantly lower in PCI-patients compared with CABG.

Conclusions

This is the first study comparing the outcome after CABG versus PCI in patients on OAC for AF. These results suggest that CABG is associated with significantly better outcome compared to PCI in these patients and should be considered the treatment of choice in patients with 2- and 3-vessel disease. Further studies are needed to confirm these findings.

Increased left atrial or left atrial appendage volume: an independent risk factor for cardioembolic stroke in patients without atrial fibrillation? – Cardiac computed tomography study

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Aim

Intracardiac thrombus is an established high risk finding for cardioembolic stroke. We studied whether increased left atrium (LA) or left atrial appendage (LAA) volumes detected with cardiac computed tomography (cCT) constitute an additional risk factor in patients with suspected cardioembolic stroke without atrial fibrillation.

Methods

Consecutive patients (n=136, 92 male, mean age 60.0 years) with acute stroke of suspected cardioembolic origin underwent cCT. In cCT cardiogenic risk factors (cardiac or aortic thrombus, LV aneurysm or tumor) were evaluated and LA and LAA volumes were calculated using Simpson's method. The control population constituted of 124 patients with low pre-test probability of coronary artery disease and no significant (<50 %) coronary artery stenosis in cCT. A pairwise comparison was performed with 56 patients and 56 controls matched for age and gender.

Results

The upper limits (mean + 2SD) for normal LA and LAA volumes were 97.5 ml and 10.8 ml in control subjects. By these criteria 76 (55.1 %) stroke patients had enlarged LAA and 47 (34.0 %) patients had enlarged LA. In pair-wise comparisons, both LA (83.8 ml vs. 61.6 ml; $p < 0.001$) and LAA (11.1 ml vs. 6.3 ml; $p < 0.001$) volumes were significantly larger in patients with suspected cardioembolic stroke than in control subjects. Twenty-two patients proved to have established cardiogenic risk factors for stroke. Sixty-one of the 76 patients (80.3 %) with LAA dilatation had none of the previously described established risk factors for stroke.

Conclusions

LA and LAA volumes in patients with suspected cardiogenic stroke are significantly increased. Enlarged LA and/or LAA volume measured with cCT may constitute an independent risk factor for cardioembolic stroke.

Speckle Tracking improves the assessment of myocardial function in systemic sclerosis

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Background

Systemic sclerosis (SS) is a connective tissue disease characterized by vascular inflammation and fibrosis. Myocardial involvement is related to repeat focal ischaemic injury causing subsequent irreversible myocardial fibrosis. Clinically evident cardiac involvement is a poor prognostic factor.

Aims

The aim of this study was to evaluate the usefulness of Speckle Tracking (ST) in detecting left ventricular (LV) contraction abnormalities in SS patients.

Methods

29 patients without history of myocardial infarction or heart failure and normal LV ejection fraction (EF) and blood pressure were compared with 11 healthy controls. LV function was studied by tissue doppler imaging and ST analyses. All patients underwent also Cardiac Resonance Imaging (MRI).

Results

There was no significant difference in the LV EF between the study groups. However, SS patients had reduced longitudinal contraction of the LV as measured by echocardiography Global Strain four chamber(4C) view ($p < 0.05$). Echocardiographic Global Strain 4C had also a good correlation with the MRI global strain ($r= 0.459$ $p = 0.006$). No subject showed late enhancement or perfusion defects on MRI. Conventional echocardiography and TDI showed no significant diastolic dysfunction. Blood tests S-ENA ($p < 0.05$), S-ANA ($p < 0.05$) and proBNP ($p = 0.001$) separated SS patients clearly from healthy controls.

Conclusion

Speckle Tracking is a new sensitive method to detect subclinical contraction abnormalities in SS patients. This enables the detection of possible myocardial involvement in SS earlier compared to conventional ultrasound methods used in the clinical practice. Impaired LV strain in SS may be due to interstitial myocardial fibrosis.

Thrombin formation and effect of unfractionated heparin during pediatric cardiac catheterization

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Aim

Unfractionated heparin (UFH) reduces thrombotic risk related to catheterization but the effects of UFH on coagulation system in children and proper monitoring of UFH remain unclear. The purpose of our study was to assess the strength of thrombin formation and to determine effects of UFH in pediatric patients during cardiac catheterization. We also wished to assess the extent of heparinization using a new method, prothrombinase-induced clotting time (PiCT).

Methods

We studied 42 patients aged 3-12 years. Twenty-seven patients undergoing percutaneous closure of atrial septal defect or patent ductus arteriosus received a UFH bolus of 100 IU/kg (group A), and 15 patients undergoing venous catheterization did not receive UFH (group B). Anticoagulation was assessed by measuring plasma prothrombin fragment F1+2, thrombin-antithrombin complexes (TAT), D-dimer, activated partial thromboplastin time (APTT), anti-FXa, and PiCT.

Results

Markers for thrombin generation remained low during catheterization in group A. In group B, both F1+2 and TAT increased significantly by the end of the procedure when compared with baseline or with group A. D-dimer levels remained low in both groups. F1+2, TAT and D-dimer increased in both groups by the first postoperative day as compared to baseline. In group A, 15 minutes after heparinization, APTT was over 180 s, anti-FXa in median 1.5 U/ml and PiCT 1.6 U/ml, and there was a correlation between anti-FXa and PiCT ($R=0.84$, $p<0.0001$). No thrombotic or bleeding complications were observed in either group.

Conclusions

Thrombin generation was enhanced in patients not receiving UFH, which may increase risk for thrombotic complications. In patients who received UFH, routine heparinization seemed excessive by all monitoring methods. PiCT seems to be a viable method of monitoring heparinization in children. Further studies are needed to clarify adequate heparin dosing for children during cardiac catheterization to prevent thrombotic complications without predisposing the patient to bleeding complications.

Human induced pluripotent stem cell -based model for catecholaminergic polymorphic ventricular tachycardia

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Aim

Catecholaminergic polymorphic ventricular tachycardia (CPVT) is an inherited cardiac disorder characterized by stress-induced ventricular tachycardia and risk of sudden death with a structurally normal heart. Here we investigate whether the electrophysiological characteristics of CPVT can be mimicked in vitro by using induced pluripotent stem cell (iPSC) -derived human cardiomyocytes.

Methods

Cardiomyocytes were differentiated from iPSC lines derived from a CPVT patient carrying the P2328S mutation in the cardiac ryanodine receptor (RyR2) and from a healthy control donor. Ca2+ handling and electrophysiological properties were studied by comparing mutation-specific and control cardiomyocytes.

Results

We found substantial defects in electrical activity and calcium signaling in CPVT cardiomyocytes, presumably reflecting the cardiac phenotype observed in the patients. In Ca2+ imaging studies, catecholaminergic stress in CPVT cardiomyocytes led to abnormal Ca2+ transients and induced arrhythmias. CPVT cardiomyocytes displayed reduced sarcoplasmic reticulum (SR) Ca2+ content, implicating leakage of Ca2+ from the SR. Patch-clamp recordings of CPVT cardiomyocytes showed early afterdepolarizations (EADs), delayed afterdepolarizations (DADs), irregular beating, and tachycardiac bursts, due to catecholaminergic stress.

Conclusions

Our cell model displayed aberrant Ca2+ signaling consistent with CPVT characteristics as well as abnormal electrophysiological properties that have not been reported before. Thus, this cell model for CPVT provides a promising platform to study basic pathology, to screen drugs safely, and to optimize drug therapy in a patient-specific manner.

Prenatal diagnosis improved the postnatal cardiac function in population based cohort of infants with HLHS

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Background

Prenatal diagnosis of hypoplastic left heart syndrome (HLHS) enables planning of perinatal care and is known to be associated with more stabile preoperative hemodynamics. The aim was to determine whether prenatal diagnosis of HLHS has an impact on postnatal myocardial function.

Methods

We blindly reviewed a consecutively encountered cohort of 66 HLHS infants born between 2003 and 2010 in Finland. Postnatal global and segmental right ventricular fractional area change (FAC), strain rate (SR) and myocardial velocity (V) were analyzed from the apical 4-chamber view using Velocity-Vector- Imaging technique. Mechanical synchrony was measured between six cardiac segments by mean standard deviation of time to peak SR and peak V. Intra- and interobserver correlations were good ($R>0.8$, $p<0.05$).

Results

Twenty-five infants (38%) had prenatal diagnosis. No differences in maternal age, gestational weeks, birth weight or Apcar score were detected between prenatally and postnatally diagnosed groups. Prenatally diagnosed infants had less asidosis (pH 7.30±0.04 vs 7.25±0.09, p=0.005) and end organ failure (alanine aminotransferase 33±38 vs 139±174 U/l, p=0.0001; creatinine 78±18 vs 81±44 umol/l, p=0.05). Global right ventricular function was better in prenatally diagnosed patients than in those diagnosed postnatally both in systole and diastole (FAC 27.9±7.4 vs 21.1±6.3%, p=0.0004; SR 1.1±0.6/1.3±1.0 vs 0.7±0.2/0.7±0.3 1/s, p=0.004/0.003; V 1,6±0.6/2.0±1.1 vs 1,3±0.4/1,4±0.4cm/s, p=0.004/0.0009, respectively). In segmental analysis, there was a difference in every area. Mechanical synchrony was not different between groups (mean standard deviation to peak SR 27.4±15.3ms vs 32.5±17.3ms, p=0.3 and peak V 28.6±24.4ms vs. 31.1±23.2ms, p=0.7). Thirty-day mortality after Norwood operation was 0% in prenatally diagnosed children and 10% (4 children) in those diagnosed postnatally (p=0.15).

Conclusions

Prenatal diagnosis of HLHS is associated with improved postnatal right ventricular function, less metabolic acidosis and end-organ dysfunction, and better early survival.

Vascular endothelial growth factor-B expands the coronary arterial tree and protects against ischemic damage in the rat heart

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Background

Vascular endothelial growth factor-B (VEGF-B) is abundantly expressed in the heart, but its biological function is poorly understood. Here we have investigated the cardioprotective role of VEGF-B in the heart.

Methods

VEGF-B was overexpressed in rats either via a heart-specific transgene or systemically using adeno-associated viral vectors, and biochemical, microarray and morphological analyses were performed. Transgenic rats were subjected to experimental myocardial infarction via LCA ligation, and positron emission tomography (PET) imaging was used to assess myocardial perfusion, oxygen consumption and efficiency of work in infarcted hearts.

Results

Overexpression of VEGF-B protected the heart via adaptive cardiac hypertrophy and increased coronary arterial reserve. Micro-computed tomography (CT) analysis showed that the coronary arterial tree was dramatically expanded in VEGF-B transgenic rats. Also systemic delivery of VEGF-B induced cardiomyocyte hypertrophy and increased myocardial capillary size. Erk1/2, Akt and mTORC1 pathways were activated in the VEGF-B transgenic hearts, and angiogenic and cytoskeletal gene programs were upregulated. After myocardial infarction, transgenic (TG) rats demonstrated better cardiac performance and perfusion and had smaller infarcts than wildtype (WT) rats (Figure).

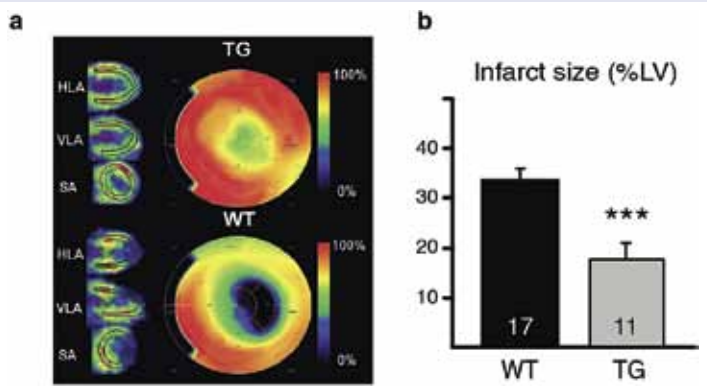

*Figure. (a) Representative PET images and polar maps of left ventricle myocardial perfusion using [11]C-acetate four weeks after myocardial infarction. (b) Quantification of the infarct size in [11] C-acetate PET perfusion images. n=17+11; ***p<0.001.*

Conclusions

These results indicate that VEGF-B protects the myocardium from ischemic damage, making VEGF-B an attractive tool for the development of new therapies for the treatment of ischemic heart disease.

Coronary plaque imaging in patients with unstable angina pectoris using dual gated (18F)-FDG PET/CT

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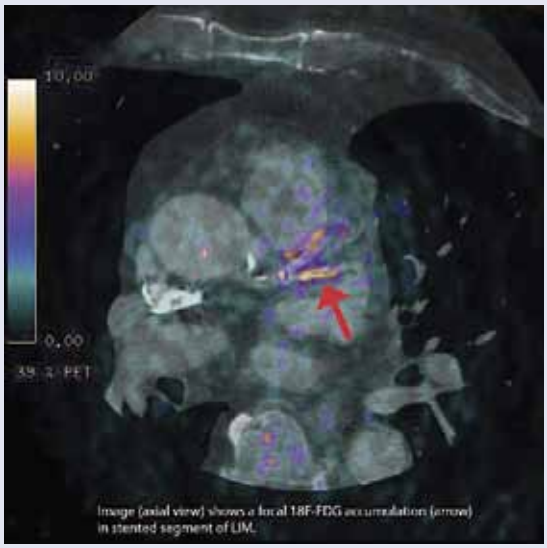
Background

[18F]-FDG(fluorodeoxyglucose)-PET imaging has been proposed as a tool to assess inflammatory activity in atherosclerotic plaques, but its feasibility for imaging coronary arteries remains unknown. The purpose of the study was to test whether it is possible to visualize FDG uptake in coronary arteries using respiratory- and cardiac-gated PET together with metabolic intervention (high fat diet) to reduce myocardial FDG uptake in patients with acute coronary syndrome (ACS) without ST-elevation.

Methods

A total of 16 patients (4 women, 12 men; age 61 ±10 years) with ACS were included and studied within 72 hours of hospital admission either prior or after invasive angiography. The subjects followed a VHFLCPP (a very high fat, low-carbohydrate, protein-permitted) diet on the previous day of the examinations. After an overnight fast, the patients underwent coronary CT-angiography, a low-dose ECG gated CT imaging followed by [18F]-FDG-PET imaging with monitoring of ECG and respiratory motion. After the dual gated reconstruction, the gated PET images were fused manually with gated low-dose CT images and visually analyzed for the presence of focal FDG accumulation related to coronary arteries. The peak FDG activity in lesions was normalized to activity in the LV cavity blood and expressed as target-to-background ratio (TBR).



Results

The VHFLCPP diet was successful in reducing myocardial [18F]-FDG accumulation in most patients. We identified 16 coronary lesions in 12 out of 16 patients (75%) that showed focal [18F]-FDG accumulation. These lesions were located in the proximal LM/LAD (n=3), LCX (n=6), RCA (n=4), and 3 in other segments, and were found in both stented and non-stented lesions. Maximal TBR in these lesions was 3.2±1.3 (from 1.75 to 5.42).

Conclusions

Dual gated PET/CT together with diet intervention is a potential method for visualization of focal [18F]-FDG accumulation in coronary plaques in patients with acute coronary syndromes without ST-elevation.

Lentivirus-mediated SERCA2a gene transfer improves left ventricular function in heart failure

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Background

Despite significant treatment advances, severe heart failure carries a dismal prognosis, underscoring the need for novel therapeutic approaches. In the heart, during relaxation, calcium is reaccumulated in the sarcoplasmic reticulum by the sarcoplasmic reticulum Ca2+ ATPase pump (SERCA2a). It has been shown that SERCA2a expression and activity is decreased in cardiac dysfunction leading to diminished calcium uptake and release by sarcoplasmic reticulum, thus providing a rationale for SERCA2a-based gene therapy for heart failure.

Methods

Lentiviral vector LV-SERCA2a-GFP expressing human SERCA2a gene and GFP reporter gene was constructed. A GFP-expressing vector LV-GFP was used as a control. Heart failure was induced by administrating Doxorubicin intraperitonially to adult C57Bl male mice. LV-SERCA2a-GFP, LV-GFP or saline was delivered by ultra-sound guided direct intramyocardial injection into the anterior wall of the left ventricle (7 mice per group). Several functional parameters were measured by echocardiography 7 and 28 days after injection, after which the mice were sacrificed. RNA and protein were extracted for Western blot and RT-PCR, and tissue sections were prepared for immunohistochemical analysis.

Results

The in vivo method was shown to be feasible and intramyocardial injections were well tolerated. Reporter gene analysis from frozen tissue samples exhibited robust GFP expression confirming that cardiomyocytes had been transduced by the viral vector (figure 1). Echocardiography analyses demonstrated a significant change in the ejection fraction (EF), end-diastolic volume (EDV) and end-systolic volume (ESV) from day 7 to day 28 in SERCA2a group when compared to control virus group (GFP) or saline-injected group (table 1).

Conclusions

SERCA2a-based gene therapy resulted in significant improvement in left ventricular function in experimental heart failure. These results encourage further clinical development of SERCA2a gene therapy.

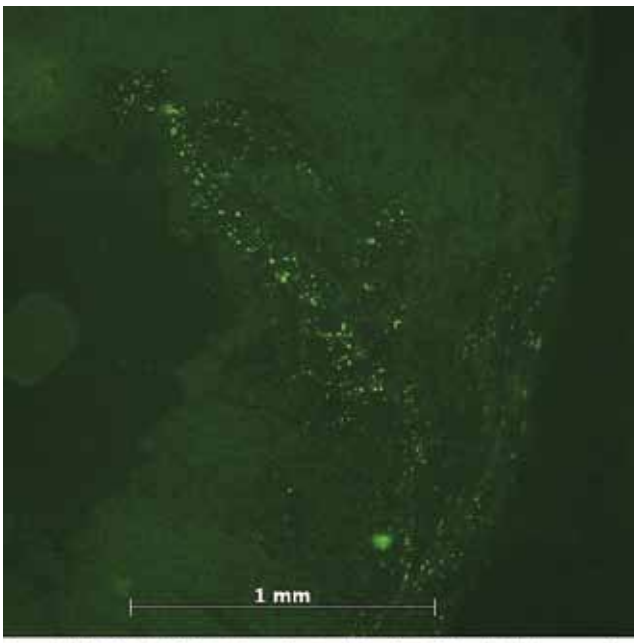

Figure 1. LV-SERCA2a-GFP injected mouse heart exhibit robust GFP signal in the frozen section obtained from the left ventricle.

Table 1. M-mode echocardiography, percentual change from day 7 to day 28. (SERCA2a vs GFP or saline *P<0.05; **P<0.01)

	SERCA2a	GFP	Saline
Ejection Fraction	8,3	-9,3 **	-6,1 *
End Systolic Volume	4,9	47,6 *	46,0 *
End Diastolic Volume	10,9	34,1	37,2

Predicting sudden cardiac death with exercise-stress test Combining cardiorespiratory fitness with myocardial ischemia

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Background

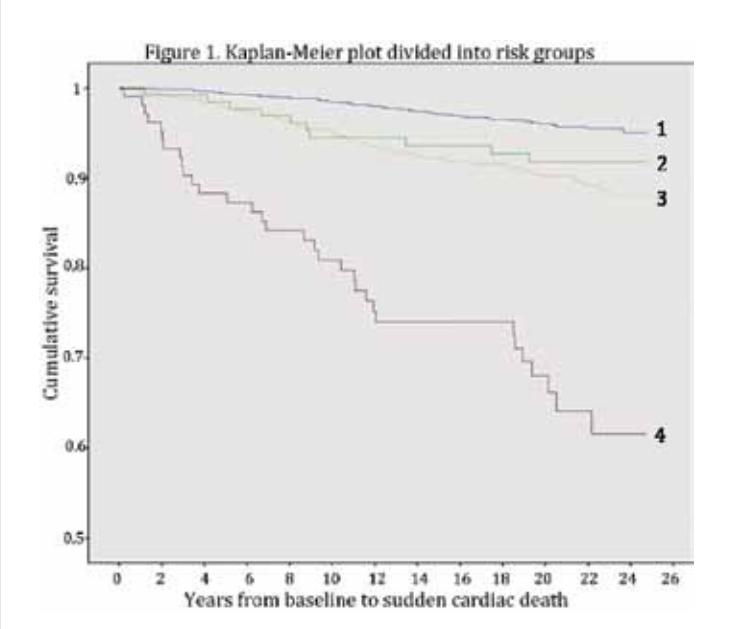
To investigate how exercise-stress test can be used to assess more accurately the risk of sudden cardiac death (SCD). Low cardiorespiratory fitness (CRF) and exercise-induced myocardial ischemia in electrocardiogram have previously been shown to increase the risk of SCD. More information is needed in how these risk factors when combined can be used to assess the risk of SCD.

Methods

A total of 2328 randomly selected men aged 42–60 in Kuopio, Finland, participated in this population based follow-up study. At baseline (1984–89) exercise stress test was performed and a large amount of risk factors were collected. The population was divided into four groups according to CRF (Metabolic equivalent (MET) 8 as cut-off point) and the presence of exercise-induced myocardial ischemia in electrocardiogram (defined as atleast 1.0mm ST depression). Cox Regression analysis was used to calculate the risk ratio. SCD was defined as cardiac death within 24 hours after onset of symptoms.

Results

During the mean follow-up time of 19 years 165 SCDs occurred. The risk of SCD was considerably higher in the men who had low CRF together with the presence of exercise-induced myocardial ischemia. The risk ratio was 4.8 (95% CI 2.9-7.9), after adjusting for conventional covariates. As a continuous variable 1 MET increase in CRF was related to a decreased risk of SCD by 19% (p<0.001). The results remained when SCD was defined as 1h after onset of symptoms. Figure 1 is a Kaplan-Meier plot of the cumulative incidence of SCD divided into risk groups 1. High CRF and no ischemia 2. Low CRF and no ischemia 3. High CRF and ischemia 4. Low CRF and ischemia.



Conclusion

By combining these risk factors derived from exercise-stress test, more accurate risk assessment can be made. On basis of these findings this high risk combination of low CRF and exercise-induced myocardial ischemia should be taken into account when considering treatment for patients in risk of SCD.