Suomen Kardiologinen Seura

Finnish Cardiac Society

48th Progress Report Meeting

March 23, 2022, Oulu

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48th Progress Report Meeting Programme

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Chairperson Mika Laine, HUS Heart and Lung Center

Meeting is supported by unrestricted educational grant from Boehringer Ingelheim

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Elina Hynninen (BM), Heart and Lung Center, Cardiology, Helsinki University Hospital

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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
2021	1st Pfize Aleksi Leikas	2nd Prize Minna Koivunen

Fibrillatory wave amplitude and thromboembolic risk in non-anticoagulated atrial fibrillation patients

Samuli Jaakkola, Heart Center, Turku University Hospital and University of Turku, Turku, Finland, Hilla Virri, Heart Center, Turku University Hospital and University of Turku, Turku, Finland, Eelis Niemelä, Heart Center, Turku University Hospital and University of Turku, Turku, Finland, Tuija Vasankari, Heart Center, Turku University Hospital and University of Turku, Turku, Finland, Ilpo Nuotio, Department of Medicine, Turku University Hospital and University of Turku, Turku, Finland, Juhani Airaksinen, Heart Center, Turku University Hospital and University of Turku, Turku, Finland, Tuomas Kiviniemi, Heart Center, Turku University Hospital and University of Turku, Turku, Finland

Aim

The benefit of oral anticoagulation (OAC) in atrial fibrillation (AF) is well established for patients at elevated stroke risk but less clear for those at low risk. We sought to better identify patients at risk for stroke and systemic embolisms (SSE) using the electrocardiogram derived atrial fibrillatory waves (F-waves).

Methods

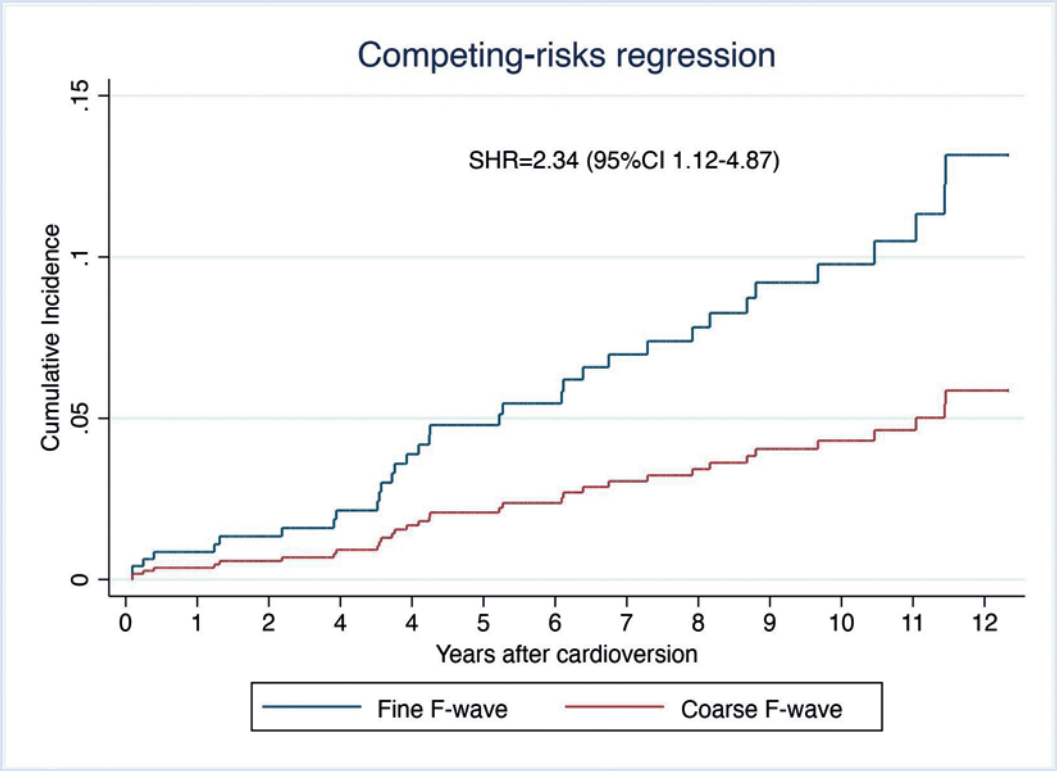
Finnish Cardioversion 1 (FinCV1) study included patients not on permanent OAC who underwent a cardioversion for an acute AF episode. We identified 739 individuals and measured the maximum amplitudes of F-waves in leads II and V1 manually from the electrocardiogram preceding the procedure. F-waves were categorized as coarse (≥ 0.05mV) or fine (<0.05mV). SSE were retrospectively identified from the patient medical records until either OAC prescription, AF was deemed chronic, patient had deceased or the end of follow up.

Results

Overall 37 (5.0%) patients suffered SSE during the median follow-up time of 5.4 years (IQR 1.9–10.8). In lead V1, fine F-wave was found on 112 (15.2%) patients. Baseline characteristics were similar between the groups. Kaplan-Meier estimates of SSE occurrence at 12 years were 8.9% and 3.8% (p=0.043) for patients with fine and coarse F-waves, respectively. Fine F-wave was an independent predictor for SSE in a competing risk analysis (SHR 2.34, 95%CI 1.12–4.87, p=0.023).

Conclusions

Fine F-wave in lead V1 predicted SSE in patients not on OAC for AF. Electrocardiographic F-wave amplitude may give additional information on stroke risk in patients with paroxysmal AF and borderline indications or contraindications to anticoagulation.


Competing-risks regression
SHR=2.34 (95%CI 1.12-4.87)
Cumulative Incidence
0
.05
.1
.15
0 1 2 4 4 5 6 7 8 9 10 11 12
Years after cardioversion
Fine F-wave
Coarse F-wave

Sorafenib induces cardiotoxicity via reversible injury to cardiac endothelial cells

Manar Elmadani, University of Oulu, Oulu, Finland, Zoltan Szabo, University of Oulu, Oulu, Finland, Lin Ruizhu, University of Oulu, Oulu, Finland, Tarja Alakoski, University of Oulu, Oulu, Finland, Jarkko Piuhola, Oulu University Hospital, Oulu, Finland, Andrey Anisimov, Wihuri Research Institute, University of Helsinki, Helsinki, Finland, Raisa Yrjölä, University of Oulu, Oulu, Finland, Ilkka Miinalainen, Biocenter Oulu, University of Oulu, Oulu, Finland, Pirjo Åström, University of Oulu, Oulu, Finland, Olli Tenhunen, University of Oulu, Oulu, Finland, Kari Alitalo, Wihuri Research Institute, University of Helsinki, Helsinki, Finland, Johanna Magga, University of Oulu, Oulu, Finland, Risto Kerkelä, University of Oulu, Oulu, Finland

Aim

Sorafenib is a multitargeted kinase inhibitor used for treatment of hepatocellular and renal cell carcinoma. It has been associated with cardiovascular adverse effects such as hypertension, myocardial ischemia, thrombosis and pulmonary embolism, whereas incidence of left ventricular (LV) dysfunction appears less common. Here we aimed to further characterise sorafenib cardiotoxicity.

Methods

Healthy mice (n=4–10/group) were treated with sorafenib (50 mg/kg/d) or vehicle for 2–4 weeks. Echocardiography and invasive hemodynamic analysis were used to evaluate LV systolic function. Electron, light and fluorescence microscopy were used to analyse endothelial cell (EC) death, proliferation and capillary rarefaction. Angiopoietin-1 overexpression in mice was achieved with a AAV9-vector.

Results

Echocardiography showed no difference in LV systolic function, whereas invasive hemodynamic analysis showed attenuated response to βadrenergic stimuli ($p<0.01$) in sorafenib treated mice. Hearts of sorafenib treated mice showed decreased EC proliferation, increased EC apoptosis and capillary rarefaction. In keeping with this, electron microscopy and TUNEL analysis showed that a short-term treatment with sorafenib was sufficient to induce EC death. The cardiotoxicity of sorafenib was abolished after 4 weeks of drug free period indicating reversibility of the toxicity. Overexpression of angiopoietin-1 induced protective signalling pathways in hearts of mice treated with sorafenib but did not rescue from acute EC injury. Treatment of angiopoietin-1 overexpressing mice with sorafenib for 4 weeks further reduced EC proliferation and resulted in heart failure. This also induced cardiac EC senescence evidenced by significantly increased expression of p21 in ECs and increased expression of senescence associated genes.

Conclusions

Sorafenib induces cardiotoxicity via rapid induction of EC damage in the heart. Overexpression of angiopoietin-1 in sorafenib-treated mice induces EC senescence and reduces EC proliferation resulting in heart failure.

Kristiina Harju (PhD student)
A.I. Virtanen Institute, University of Eastern Finland

From pathophysiological mechanisms to novel biomarkers of atrial fibrillation

Suvi Linna-Kuosmanen, Computer Science and Artificial Intelligence Lab, Massachusetts Institute of Technology, Boston, United States, Jari Halonen, Heart Center Kuopio University Hospital, University of Eastern Finland, Kuopio, Finland, Tomi Tuomainen, A.I. Virtanen Institute, University of Eastern Finland, Kuopio, Finland, Olli Kärkkäinen, School of Pharmacy, University of Eastern Finland, Kuopio, Finland, Marko Lehtonen, LC-MS Metabolomics Center Core facility, University of Eastern Finland, Kuopio, Finland, Juha Hartikainen, Heart Center Kuopio University Hospital, University of Eastern Finland, Kuopio, Finland, Pasi Tavi, A.I. Virtanen Institute, University of Eastern Finland, Kuopio, Finland

Aim

AF is a growing medical condition associated with significant morbidity and mortality, but its pathophysiology has remained widely unknown. In our study we aim to identify clinically relevant AF-related biomarkers and to unravel the complex pathophysiological mechanisms of AF by combining metabolomics and single cell level transcriptional profiling. The overall aim is to find diagnostic and treatment options for AF to contribute the quality of healthcare and patient safety.

Methods

Patients recruited were undergoing cardiac surgery at the University Hospital of Kuopio, due to valve defects, coronary artery disease, or a combination of these. Biopsy from the right atrial appendage, pericardial fluid and blood samples were collected from 149 patients (Fig. 1). Liquid chromatography mass spectrometry (LC-MS) was used to identify metabolites and multiplexed snRNA-seq and snATAC-seq to infer cell-type-specific transcriptional alterations.

Results

Untargeted MS metabolite analysis identified altogether 15751 molecular features divided unequally between the sample types (Fig.2). According to the identified metabolites, AF was associated with a clear metabolite signature of the atrial tissue including signs of altered purine metabolism, antioxidant defense and DNA methylation. Altogether, we found 48 statistically significant ($p<0.0007$) metabolites from the heart tissue, 15 from the pericardial fluid and 3 from the blood.

We have allocated 20 atrial tissue and pericardial fluid cell fraction samples from patients with permanent AF and their 21 age and gender matched controls to transcriptional analysis at the single nuclei level. Based on the snRNAsec, human atrial muscle contains 12 main cell types and AF is associated with cell type specific changes in the expressions of subsets of genes involved in mitochondrial respiration, reactive oxygen species formation and scavenging as well as signalling pathways associated with mitochondrial biogenesis and adaptation to hypoxia.

Conclusions

We describe novel metabolites associated directly with AF. Combination of transcriptional profiling with the metabolomics reveals new information of the pathways associated with chronic AF and yields novel circulating biomarkers that can be traced back to the cellular mechanisms of the disease.

Kristiina Harju (PhD student)
A.I. Virtanen Institute, University of Eastern Finland

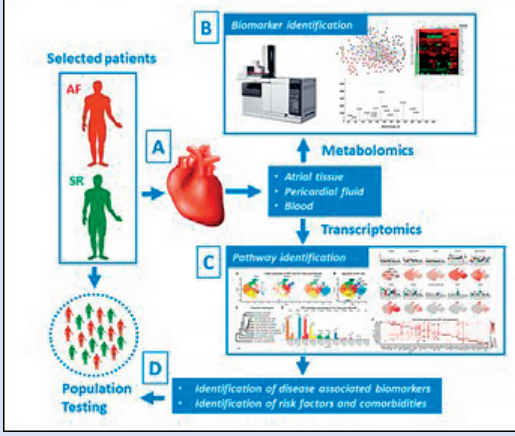


Figure 1. Overview of the study. A) The atrial tissue, pericardial fluid, and blood samples of patients with permanent AF and clinically significant heart-loading valve defect and/or coronary artery disease are collected from open-heart surgery. The samples are divided into **B)** untargeted MS metabolite analysis and **C)** transcriptional profiling with single-cell RNA-sec, single-cell ATAC-sec (atrial tissue and pericardial fluid cell suspension). **D)** The general usefulness of the identified potential AF biomarkers will be elucidated by measuring the amount of the molecules in biobank (Finnish Biobank Cooperative; FINBB) blood samples of AF and control patients. Depending on the type of molecules we will use targeted MS profiling, enzyme-linked immunoassay (ELISA), or quantitative PCR for quantification.

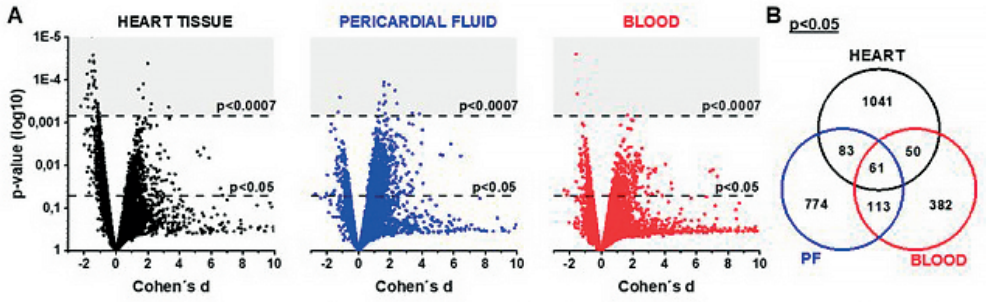


Figure 2. Analysis of AF associated metabolites in atrial tissue, pericardial fluid, and blood. A) Volcano plots with p-values (y-axis) and sample sizes (Cohen´s d, x-axis) showing differences in the detected metabolites between atrial tissue (**black**), pericardial fluid (**blue**) and blood (**red**) collected from patients with permanent AF (n=16) and sinus rhythm (control, n=17). Dotted lines in each plot show significance levels (0.05 and 0.007). The light grey backgrounds highlight the areas wherein the dots represent metabolites with qualifiable difference at multivariate α-level (0.0007). **B)** Venn diagram showing the numbers of specific and common metabolites within and between sample types associated with AF at the significance level p<0.05. Venn diagram has the same colour coding as in **A)**.

Janna Kauppila (MD)
Research Unit of Internal Medicine, University of Oulu

Use of psychotropic medication in victims of nonischemic sudden cardiac death

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Introduction

Nonischemic heart disease (NIHD) is the underlying pathology in about 20 % of all sudden cardiac deaths (SCDs). Psychotropic medication has been reported as a risk marker for SCD among patients with coronary artery disease, but similar information concerning NIHD are scarce. We evaluated the use of psychotropic medication in nonischemic SCD victims and compared it to the general medication use in Finland.

Methods

Study population was derived from the Finnish Genetic Study of Arrhythmic Events (Fingesture) (n = 5,869, mean age 65 ± 12, 79 % males). All deaths occurred in Northern Finland during 1998–2017. All victims underwent a medico-legal autopsy. Information on use of medication was defined using post-mortem toxicology results of medication concentrations in femoral blood. Subjects of SCD due to ischemic heart disease (n = 4,392) and subjects with no toxicological analysis (n = 218) were excluded. Information on general medication use was derived from Finnish Statistics on Medicines 2018 and presented as defined daily dose/1000 inhabitants/day.

Results

1,259 victims of nonischemic SCD (mean age 57 ± 12, 77 % males) were included in the study. 483 (38 %) of the subjects had psychotropic medication in post-mortem blood, whereas in the general population only 15 % were estimated to use psychotropic medication. The results were similar in subgroups of psychotropic medication (24 % vs 2.3 % for benzodiazepines, 16 % vs 7.5 % for antidepressants and 16 % vs 2.2 % for antipsychotics).

Conclusions

Use of psychotropic medication is common in victims of SCD due to NIHD compared to the general population. Use of psychotropic medication might be a risk factor for SCD in patients with NIHD.

CYP2C19 loss-of-function alleles and the use of omeprazole or esomeprazole increase the risk of cardiovascular outcomes in patients using clopidogrel – a real-world study

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Aim

Patients carrying loss-of-function (LOF) variants of CYP2C19 or using the CYP2C19-inhibitors omeprazole or esomeprazole cannot fully bioactivate clopidogrel, and thus are lacking optimal thrombosis prevention. Our aim was to investigate in a real-life prospective patient cohort how LOF CYP2C19 variants and omeprazole or esomeprazole influence the incidence of cardiovascular events (cardiovascular deaths, reinfarction and strokes) in patients using clopidogrel.

Methods

A cohort of prospective patients (N=1972) with acute coronary syndrome (ACS) (N=1302) or symptomatic chronic coronary disease (N=670) were followed for 365 days. Information of purchased prescription drugs, hospital discharge, and death registry was available for all patients. The patients were retrospectively genotyped for the CYP2C19*2, CYP2C19*3, and CYP2C19*8 LOF variants.

Results

A total of 608 (30.8%) patients carried CYP2C19 LOF alleles. During the 365 days follow-up, 252 patients had a recurring ischaemic vascular event, either myocardial infarction (N=189), stroke (N=24) or cardiovascular death (N=39). Vascular events were significantly more frequent among carriers of CYP2C19 LOF alleles [14.8% (95% CI 11.7–17.8)] than in non-carriers [10.8% (95% CI 9.0–12.6)], p=0.016. Omeprazole or esomeprazole use was similar among the LOF allele carriers and non-carriers, but inclusion of their use in the analysis strengthened the association. Vascular events were significantly more common in a composite group of carriers of CYP2C19 LOF alleles and non-carriers who were using omeprazole or esomeprazole than in non-carriers who were not using omeprazole or esomeprazole 14.8% (95% CI 12.2–17.3) vs 9.9% (95% CI 8.0–11.9) p=0.002. There was a tendency towards lower risk of hemorrhagic complications in carriers of LOF alleles than in non-carriers (p=0.07).

Conclusions

Patients with impaired clopidogrel bioactivation due to loss-of-function CYP2C19 variants or concomitant omeprazole or esomeprazole use are at increased risk of cardiovascular events. For relevant patient care both genetics and concomitant medication should be considered.

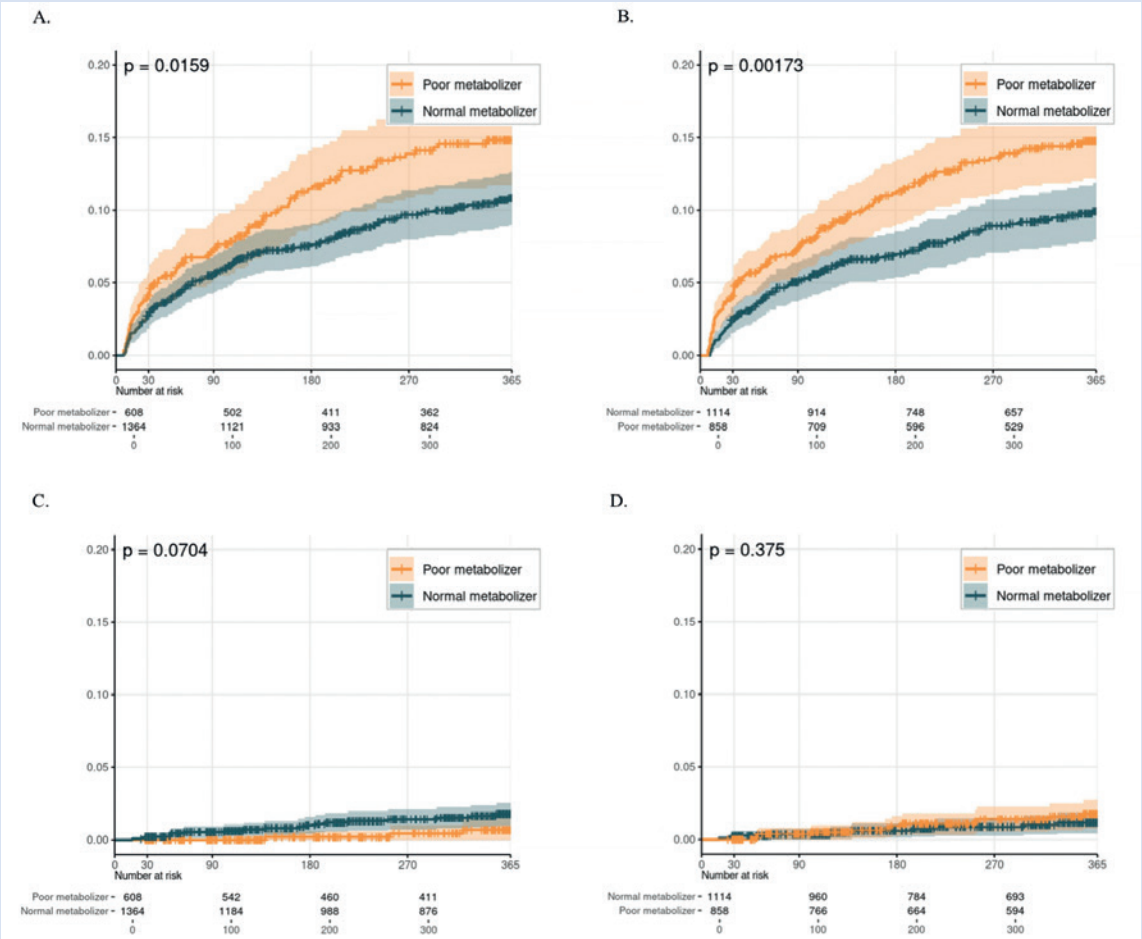

Figure 1. Shadowed area represents 95% confidence interval (CI).
A. Cardiovascular events in *CYP2C19* loss-of-function (LOF) allele carriers (poor metabolizers) and non-carriers (normal metabolizers).
B. Cardiovascular events in *CYP2C19* LOF carriers and non-carriers with omeprazole or esomeprazole use (poor metabolizers) and non-carriers without omeprazole or esomeprazole use (normal metabolizers).
C. Hemorrhagic events in in *CYP2C19* LOF carriers (poor metabolizers) and non-carriers (normal metabolizers).
D. Hemorrhagic events in *CYP2C19* LOF carriers and non-carriers using omeprazole or esomeprazole (poor metabolizers) and non-carriers without omeprazole or esomeprazole use (normal metabolizers).

Konsta Teppo (MD)
UTUGS, University of Turku

Socioeconomic disparities in use of rhythm control therapies in patients with incident atrial fibrillation: a Finnish nationwide cohort study

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Aims
In patients with atrial fibrillation (AF), socioeconomic disparities have been reported in the use of oral anticoagulant therapy and outcomes, but whether socioeconomic status also affects the utilization of antiarrhythmic therapies (AATs) for rhythm control is unknown. We assessed the hypothesis that AF patients with higher income are more likely to receive AATs.

Methods
The nationwide retrospective registry based FinACAF cohort study covers all patients with AF from all levels of care in Finland. Patients were divided in AF diagnosis year and age-group specific income quintiles according to their highest annual income during 2004–2018. The primary outcome was the use of any AAT, including cardioversion, catheter ablation, and fulfilled antiarrhythmic drug (AAD) prescription.

Results
We identified 188 175 patients (mean age 72.6±13.0 years; 49.6% female) with incident AF during 2010–2018. Patients in higher income quintiles had consistently higher use of all AAT modalities (Figure). When compared to patients in the lowest income quintile, the adjusted incidence rate ratios (95% CI) in the highest quintile were 1.53 (1.48–1.59) for any AAT, 1.71 (1.61–1.81) for AADs, 1.43 (1.37–1.49) for cardioversion, and 2.00 (1.76–2.27) for catheter ablation. Patients in the highest income quintile had a 3-fold higher crude catheter ablation rate when compared to the lowest quintile. No temporal change during study period was observed in the magnitude of income disparities in AAT use, except for a decrease in income-related differences in the use of AADs.

Conclusions
Clear income-related disparities exist in AAT use among patients with AF in Finland, especially in the use catheter ablation.

Konsta Teppo (MD)
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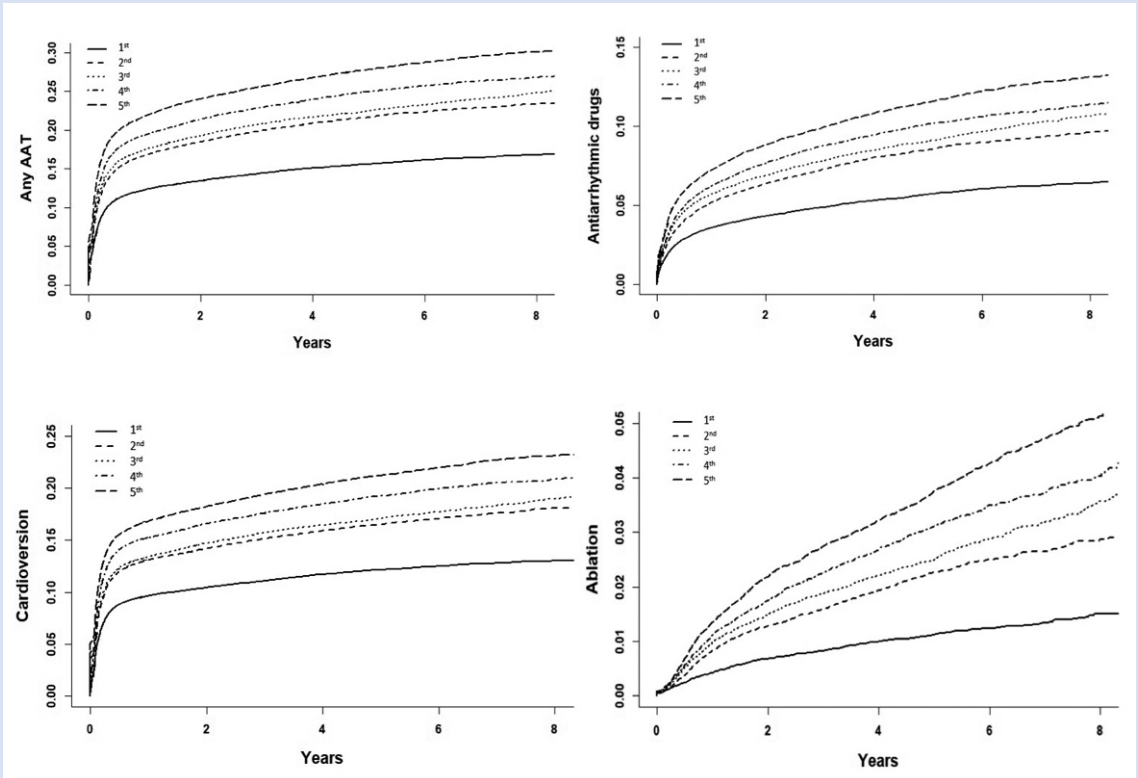

Valtteri Muroke (MD)
Department of Cardiology, Helsinki University Hospital

Long-term mortality and late causes of death in atrial septal defect patients: a nationwide cohort study

Mikko Jalanko, Department of Cardiology, Helsinki University Hospital, Helsinki, Finland, Jari Haukka, Department of Public Health, University of Helsinki, Helsinki, Finland, Juha Sinisalo, Department of Cardiology, Helsinki University Hospital, Helsinki, Finland

Background
Atrial septal defect (ASD) is a common congenital heart defect, which is known to cause excess mortality. ASD's excess mortality is thought to be consequence of right heart strain and increased stroke risk. However, there are no large data sets reporting cause-specific mortality of ASD patients.

Objectives
This study evaluated the long-term mortality and cause-specific mortality of ASD patients in a nationwide cohort.

Methods
All patients diagnosed with simple ASD in the hospital discharge registry during 1969–2019 were included in the study. Complex congenital defects were excluded. Each subject was matched with five controls according to sex, age, and municipality at the index time. We calculated Kapplan-Meier estimates from the time of diagnosis, and adjusted odds ratios were calculated using Poisson regression models.

Results
The Median follow-up time was 11.1 years. During follow-up, ASD patients had increased overall mortality, with an adjusted mortality risk ratio (MRR) of 1.64 (95% CI: 1.54–1.75). Closed atrial septal defects also had increased total mortality (MRR = 1.22, 95% CI: 1.04–1.43). In transcatheter closed defects the mortality was decreased compared to the control cohort (MRR = 0.62, 95% CI: 0.40–0.96).

ASD patients had significantly more deaths to malformations (MRR 54.90), Other diseases of the circulatory system (MRR 2.87), ischemic heart disease (MRR 1.57), stroke (MRR 1.94), Diseases of the endocrine (MRR 1.73), and respiratory system (MRR 1.63), and accidents (MRR 1.41).

Conclusions
ASD patients had increased overall mortality compared to a matched general population cohort. Increased cause-specific mortality was seen in malformations, stroke, and heart diseases. Patients applicable for transcatheter closure have an excellent prognosis.

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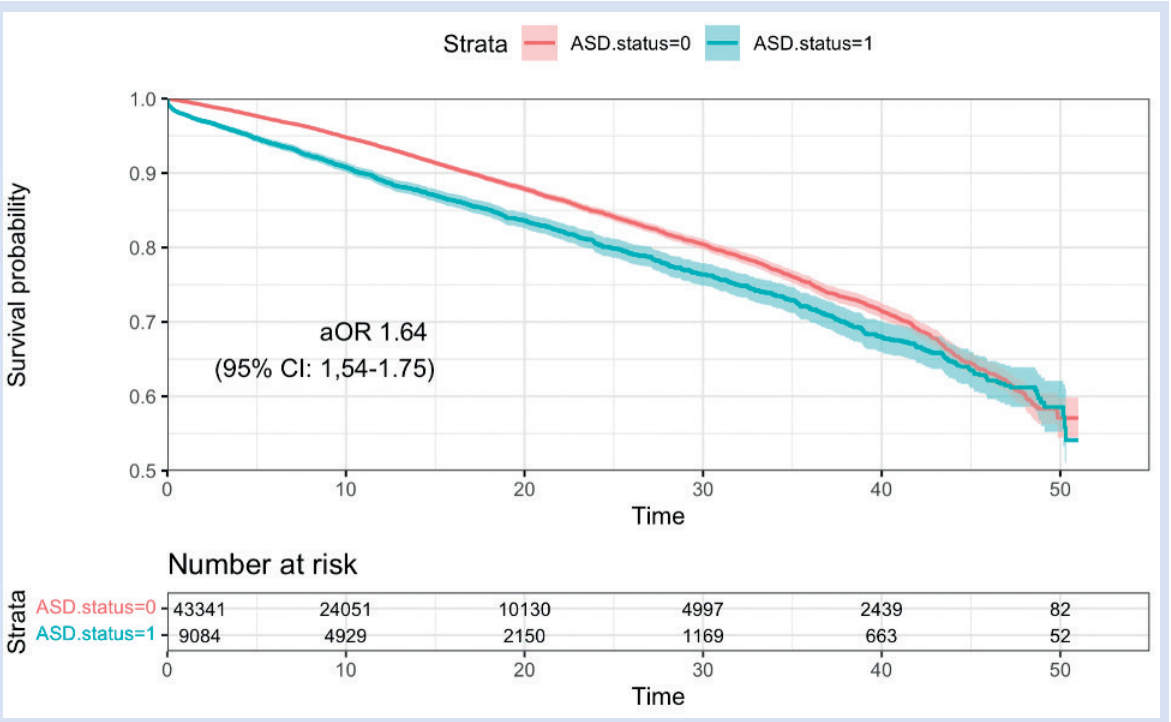

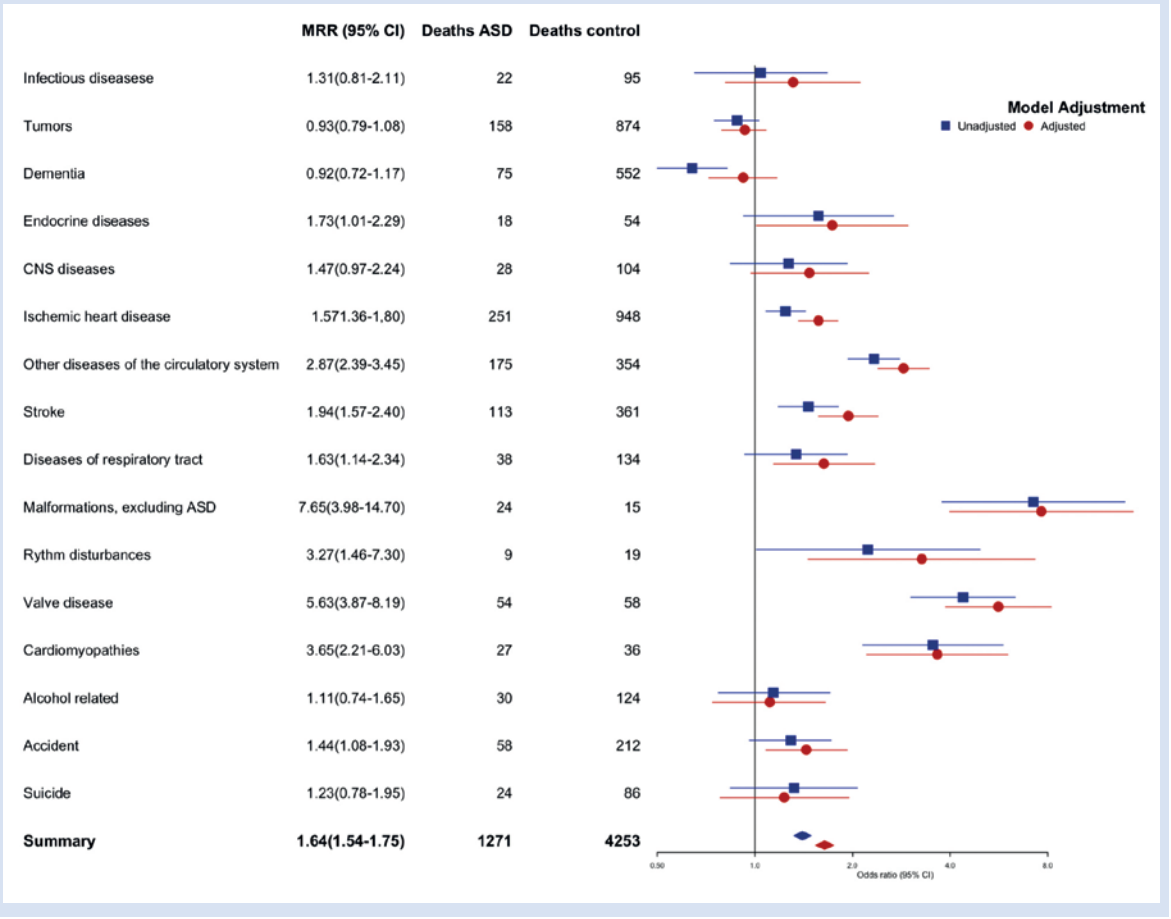

Association of atrial depolarization variability and cardiac autonomic regulation with sudden cardiac death in coronary artery disease

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Background

P-wave abnormalities have been shown to predict sudden cardia death (SCD) in general population and in patients with coronary artery disease (CAD). However, the prognostic significance of the temporal variability of P-wave morphology, specifically in relation to cardiac autonomic regulation, is not well understood.

Methods

In the present study, we analyzed the standard deviation of P-wave residuum (PWRSD) from 5 consecutive beats of the standard 12-lead ECG in 1,236 patients with angiographically verified CAD. We evaluated the prognostic value of PWRSD, of PWRSD and PWR in relation to the 24-hour standard deviation of normal-to-normal intervals (PWRSD/SDNN and PWR/SDNN). The primary endpoint of the present study was SCD/resuscitated sudden cardiac arrest (SCA).

Results

After 8.7±2.2 years of follow-up on average, 43 patients (3.5%) experienced SCD or were resuscitated from SCA, 34 (2.8%) succumbed to non-sudden cardiac death (NSCD) and 113 (9.1%) to non-cardiac death (NCD). In the Cox regression analysis, PWRSD (≥ 0.002727) had a significant univariate (uv) (HR 4.27, 95% CI 2.26–8.08, p=0.000008) and multivariate (mv) (2.58, 95% CI 1.31–5.08, p=0.006) association with SCD/SCA, but not with NSCD (uv p=0.76, mv p=0.33) or NCD (uv p=0.57, mv p=0.66). All the studied P-morphology parameters retained a significant association with the risk of SCD/SCA after relevant adjustment (mv p-values from 0.00003 to <0.05), but not with NSCD or NCD. When dichotomized PWRSD, PWR, PWRSD/SDNN and PWR/SDNN were added to the clinical risk model for SCD/SCD, the C-index increased from 0.799 to 0.834 and integrated discrimination index (IDI) and net reclassification index (NRI) improved significantly (p<0.001).

Conclusions

Variability of P-morphology representing temporo-spatial heterogeneity of atrial depolarization, specifically when combined with cardiac autonomic regulation, independently predicts the risk of SCD in patients with CAD.

Evaluation of cerebrovascular incidents via retinal angiography during transcatheter aortic valve replacement

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Aim

Patients receiving transcatheter aortic valve replacement (TAVR) usually are elderly with multiple comorbidities and are at increased risk of perioperative cerebrovascular incidents. Retinal vasculature presents the circulation of central nervous system and is noninvasively achievable by retinal imaging. The aim of this study was to evaluate the applicability of retinal angiography imaging of microvascular complications during TAVR. The aim was also to evaluate the mechanisms of cerebral ischemic events by visualizing retinal vasculature during TAVR.

Methods

One hundred patients (male 54 %, age: median 82 years, range 64 - 95 years) undergoing TAVR were recruited for this study. Imaging of retinal vasculature was evaluated with handheld fundus camera in all patients, before and after the procedure. Additionally, long-term changes in retinal vasculature were imaged after 1 month in most of the patients. Cerebrovascular incidents were determined as a part of contemporary clinical evaluation with cerebral CT and CTA imaging when symptoms occurred.

Results

We examined successfully 79/100 patients (79 %) before, 67/100 (67 %) immediately after and 65/100 (65 %) one month after the TAVR. Altogether 66/100 patients (66 %) were included in the analysis. In-hospital ischemic event (transient ischemic attack, cerebral infarction) was observed in 1/66 patient (1.5 %). Retinal vascular abnormalities occurred in 8/66 patients (12.1 %); 4/66 patients (6.1 %) were detected with a cholesterol plaque in the central artery, 2/66 (3 %) a capillary leakage, 1/66 (1.5 %) an optic disc hemorrhage and 1/66 (1.5 %) a leakage of microaneurysm. Most of the retinal vascular abnormalities (7/8, 87.5 %) were detected right after the TAVR. Most of the patients with retinal vascular abnormalities (6/8, 75 %) received self-expanding bioprosthesis. No significant association between retinal vasculature abnormalities and cerebrovascular incidents was detected mainly due to the low event rate.

Conclusions

Perioperative evaluation of cerebrovascular ischemia with noninvasive imaging of retinal vasculature is possible in most patients undergoing TAVR. More data is needed to evaluate the association of cerebrovascular incidents and retinal microvascular abnormalities during the procedure.

Validation of the novel biomarker-based risk score, the CLIP score, for mortality prediction in cardiogenic shock: comparison with CardShock and IABP-SHOCK II risk scores

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Aim

Accurate risk prediction is crucial in clinical decision-making and in planning future clinical trials for cardiogenic shock (CS). We aimed to validate the CLIP score, a novel biomarker-based risk score for CS and to compare its predictive value with the previously published CardShock and IABP-SHOCK II risk scores.

Methods

The CardShock patient cohort is a multicentre cohort of CS patients including various aetiologies of CS. The biomarkers in the CLIP score are cystatin C, lactate, interleukin-6 and NTproBNP. The CLIP score was calculated from biomarkers measured at 12 hours from study inclusion (CLIP12h). ROC-analyses were conducted to assess the predictive value of the CLIP score compared to the CardShock and the IABP-SHOCK II risk scores at baseline. Mortality was assessed at 90 days. Risk stratification was assessed by constructing Kaplan-Meier curves.

Results

Patients (n=126) were on average 66 years old and 24% (n=30) were women. Acute coronary syndrome accounted for 79% of cases. The overall mortality at 90 days was 43% (n=54). Patients with a CLIP score above median (0.2987), had a 90-day mortality of 67% compared to 19% in patients with a CLIP score below median (log rank $p<0.001$). The CLIP score appeared to be a good predictor for 90-day mortality (area under the curve [AUC] 0.855). The discriminative performance of the CLIP score was superior to that of the CardShock (AUC 0.771) or the IABP SHOCK II (AUC 0.767) risk scores. Based on the Youden index, the optimal cut-off for risk stratification (0.2839) was very close to the median value. The CLIP score improved risk stratification in the CardShock risk score categories, especially in the intermediate-risk group (Figure).

Conclusions

The CLIP score may be useful for early risk stratification of mortality in CS patients. Moreover, the CLIP score seems to further refine risk stratification of patients classified by the CardShock risk score.

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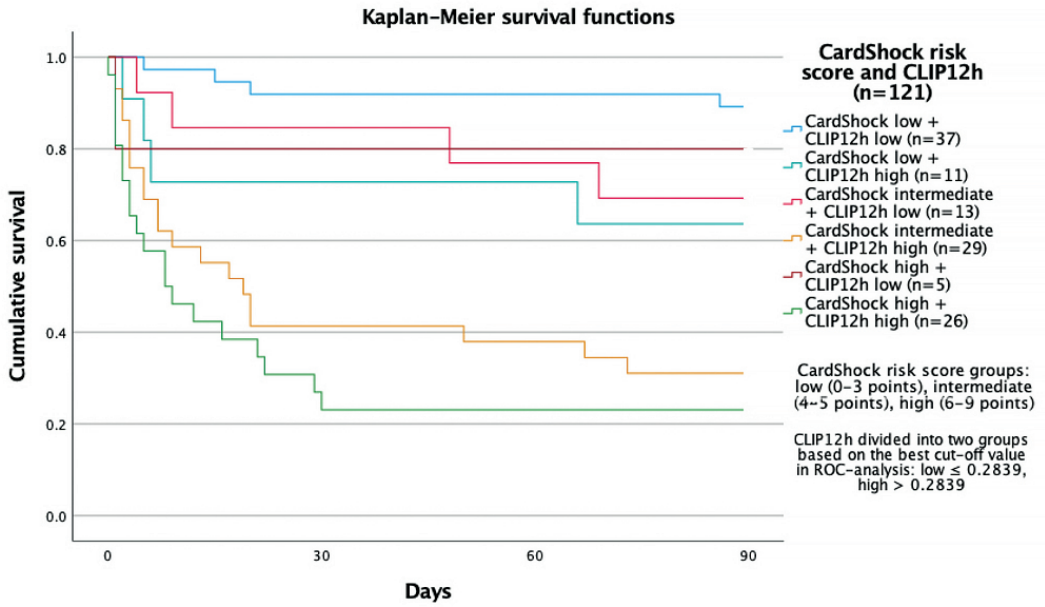

Figure. Kaplan-Meier survival curves for patients categorized into six groups by different combinations of the CardShock risk score and the CLIP score (CLIP12h).