

Prevalence and prognosis of patients with myocardial infarction with nonobstructive coronary arteries ; a nationwide registry based study

Authors:

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On behalf: Hungarian Myocardial Infarction Registry Study Group

Citation:

Background: There are conflicting data about the proportion and prognosis of patients (pts) with acute myocardial infarction (AMI) with nonobstructive coronary arteries (MINOCA).

Purpose: to define the incidence and prognosis of MINOCA pts in different types of AMI.

Methods: The Hungarian Myocardial Infarction Registry (HUMIR) is a nationwide, mandatory database in which the clinical and demographic informations of patients with AMI are recorded. Between January 1, 2014 and June 30, 2018, a total of 45,223 AMI (ST-elevation myocardial infarction (STEMI) n=22,469) pts were registered. After excluding pts with previous AMI, PCI, CABG, and congestive heart failure, 2003 MINOCA pts were found (MINOCA group), while 43,220 AMI pts had obstructive coronary artery disease (MI-CAD group).

Results: The proportion of pts with MINOCA disease was 4.4% among the total pts with AMI. The prevalence was higher in the non ST-elevation myocardial infarction (NSTEMI) group (n=1546, 6.8%) than in the STEMI (n=457, 2.0%) group. The pts with MINOCA disease were slightly younger compared to the pts with MI-CAD (mean age 64.0±14.4 vs. 65.5 ± 12.2 years respectively). The proportion of women was higher in the MINOCA group than in the MI-CAD group (55.7% vs. 36.5%). At discharge, pts with MINOCA disease were less likely to be prescribed certain drugs compared to the pts with MI-CAD. These include aspirin (85.4% vs. 95.6%), RAAS blockers (83.8% vs. 90.4%), statins (86.2% vs. 94.7%), β-blockers (86.8% vs. 89.8%) for the MINOCA and MI-CAD groups respectively. At the 1-year follow-up, the incidence of new AMI events was 1.6% in the MINOCA group compared with 5.0% in the MI-CAD group (HR=2.79). All-cause mortality was higher among the pts with MI-CAD compared to the pts with MINOCA disease. In the MINOCA group, among the pts with NSTEMI, men and women had similar outcomes at 30 days, but men had somewhat higher mortality at one and two years. In contrast, in the STEMI group, women had higher mortality compared to men at all time points during the study (Table 1).

Conclusion: The population-level incidence of MINOCA disease was 4.4% in AMI; the incidence was higher in the NSTEMI group compared to the STEMI group (6.8% vs. 2.0%). Despite the benign anatomy, the long-term prognosis is poor, especially in women after STEMI: 1 out of 4 pts died at the two-year follow up.

Mortality	MINOCA (n=2003)	MI-CAD (n=43,220)	MINOCA - STEMI - Men (n=218)	MINOCA - STEMI - Women (n=239)	MINOCA - NSTEMI - Men (n=669)	MINOCA - NSTEMI - Women (n=877)
30-day	5.9% [4.9-7.0]	8.4% [8.1-8.7]	8.7% [4.9-12.4]	13.4% [9-17.6]	4.3% [2.8-5.9]	4.4% [3.1-5.8]
1-year	12.5% [11.0-14.0]	15.6% [15.3-16.0]	12.1% [7.6-16.4]	20.3% [15-25.2]	12.2% [9.6-14.7]	10.8% [8.7-12.8]
2-year	16.7% [14.9-18.5]	19.9% [19.5-20.3]	18.2% [12.4-23.6]	23.6% [17.8-29]	16.9% [13.8-20]	14.3% [11.7-16.7]

(95% confidence interval in parenthesis)

Resveratrol improves cardiac function and exerts an anti-inflammatory effect in systolic heart failure patients

Authors:

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Citation:

Introduction

The positive effects of resveratrol on heart failure have already been evaluated in several experimental animal models, however, in a human clinical trial it was not yet confirmed. The aim of our study was to assess the effect of resveratrol supplementation on left ventricular structure and function in patients with heart failure with reduced ejection fraction (HFrEF).

Methods and materials

60 HFrEF patients (age: 66.7±11.04 years, 17 women and 43 men) were enrolled into our study. They were randomized into two groups, in the first group (n=30) daily 2x50 mg resveratrol was administered orally and placebo was given in the other group (n=30). 56% of the enrolled patients had ischemic HFrEF. During the whole study period, patients were taken the optimal medical therapy of HFrEF (ACEI/ARB, BB, MRA) in the same dose as before the randomization. On the day of randomization and 3 months later echocardiography, six minutes walking test (6MWT) and quality of life questionnaire (QoL) test were performed. Besides the routine lab tests, the levels of biomarkers (NT-proBNP,

galectin-3) and inflammatory cytokines (IL-1, IL-6) were also measured.

Results

After the 3-month-long follow-up period left ventricular ejection fraction improved significantly in the resveratrol group comparing to the placebo group ($p < 0.001$). The function of the right ventricle (RV) improved ($p < 0.05$), moreover the RV dimensions, as well as atrial volumes decreased significantly in the resveratrol group ($p < 0.05$). In the case of 6MWT ($p < 0.05$) and QoL test ($p < 0.05$) a significant improvement could be observed in the resveratrol group versus the placebo group ($p < 0.05$). Lab test analysis showed that resveratrol supplementation reduced significantly the total cholesterol level ($p < 0.05$) and LDL-C level ($p < 0.05$) and had no overt effect on other metabolic parameters. NT-proBNP level increased significantly in the placebo group ($p < 0.05$) by the end of the trial, however, in the resveratrol group we could see a slight improving tendency (NS). In the case of Galectin-3, no significant changes could be seen.

Conclusions

Our results revealed that resveratrol supplementation in systolic heart failure patients adding to the standard medical therapy resulted in an improvement of echocardiographic parameters, functional status and decreased the level of inflammatory cytokines.

Cardiac magnetic resonance characteristics of the transplanted heart: first results of the prospective Heart-Timing CMR substudy

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Citation:

Background: In case of heart transplantation (HTX) the heart is affected by several factors e.g. ischaemia/reperfusion, denervation, immunosuppression. During the adaptation, the heart may show marked temporal changes in terms of myocardial mechanics, function and tissue characteristics. To better understand temporal characteristics after orthotopic bicaval HTX we started the prospective Heart-Timing (Transplantation Imaging) trial in January 2018 including standard 12-lead ECG, 24-hour Holter monitor, endomyocardial biopsy, transthoracic echocardiography, invasive coronary angiography with intravascular ultrasound and optical coherence tomography and cardiac magnetic resonance (CMR).

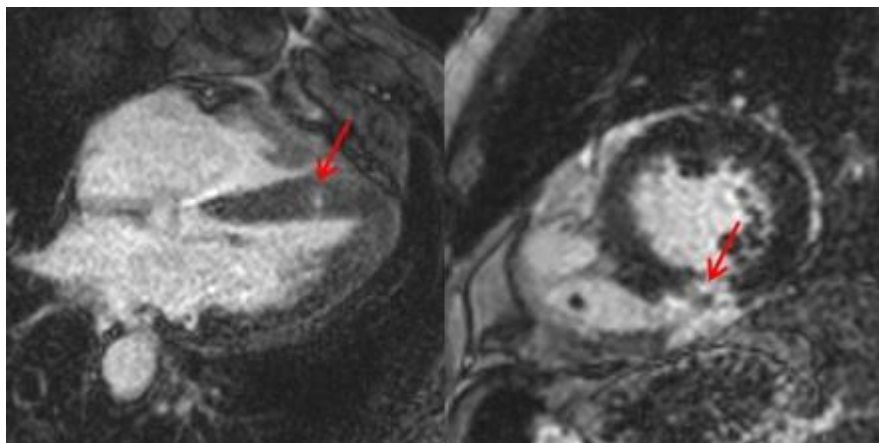
Aim: In our CMR substudy we aimed to evaluate the physiological structural and functional left and right ventricular characteristics and their temporal changes after HTX using CMR.

Methods: As part of the study HTX patients underwent CMR at 1, 3 and 6 months after HTX (n=31; 52±10.5y, 25 male). Cine images, T2-weighted, late gadolinium enhancement (LGE) and adenosine stress perfusion (at 1 month) images were acquired. In order to describe physiological characteristics of the transplanted heart we excluded pts with significant coronary artery disease, ischaemic scar, =Grade II allograft rejection from this present study (n=6). We assessed the left (LV) and right ventricular (RV) ejection fractions, volumes, masses (M) and LV strain. We assessed the global strain values: longitudinal, circumferential (GCS) strain and the standard deviation (SD) of the peak longitudinal strain (LS) and the left ventricular mechanical dispersion. We compared baseline volumetric and strain parameters to age matched healthy controls (n=20; 47±11.4y, 15 male), and the temporal changes between one, three and 6 months.

Results: Comparing the HTX patients' CMR parameters at one month with normal controls, HTX patients had lower LV and RV end-diastolic volumes (LVEDVi: 76.6±15.9 vs 90.6±11.6ml/m²; RVEDVi 74.5±17.5 vs 90.3±12.1ml/m²p<0.05), stroke volumes (p<0.05) and higher LVMi (67.6±14.4 vs 57.2±11g/m², p<0.05). CMR based strain analysis of the HTX pts showed hyperkinetic GCS (-40.5±6.3% vs -35.2±4.8%,p<0.05), increased SD of peak LS and more pronounced mechanical dispersion (p<0.001) compared to the controls. Examining temporal changes in HTX pts we found a decrease in LVMi (69.57±16.4 vs 61.7±9.8g/m², p<0.05) already at three months, normalization of GCS (-37.7±5.5% vs -32.6±4.9%, p<0.05) and decrease in SD of peak LS (13.5±2.3 vs 11.4±2.4, p<0.05) at 6 months. Oedema was present in all pts at one month after HTX, and disappeared after three months. LGE with aspecific pattern was present in 42%.

Conclusions: Understanding the temporal changes of LV mechanics, function and tissue characteristics, furthermore the establishment of physiological values may help in the early, noninvasive identification of pathological changes in HTX pts.

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Results from the Hungarian Cardiac Magnetic Resonance Registry of Structural Heart Disease and Aborted Sudden Cardiac Death in Athletes

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Citation:

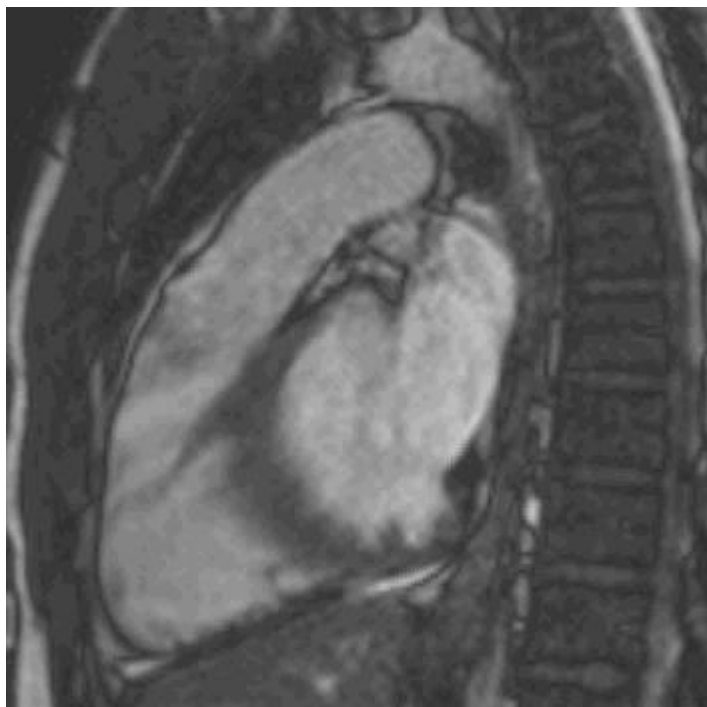
Introduction: Sudden cardiac death (SCD) is the most common cause of death in athletes occurring usually during intensive training. Cardiac magnetic resonance (CMR) has a crucial role in the detection of structural myocardial abnormalities.

Aims: Our aim was to investigate the etiology of SCD and to estimate the prevalence of myocardial structural heart diseases among Hungarian athletes using CMR.

Methods: Between January 2011 and January 2019 we performed CMR scans on 228 athletes (199 males, age: 29.1±13.2) with suspected structural myocardial disease. Twelve athletes were investigated after aborted sudden cardiac death and normal coronary angiography.

Results: CMR confirmed the diagnosis of structural myocardial disease in 62 athletes (26.2%) (28.8±9.1 years, 59 male): hypertrophic cardiomyopathy (HCM) in 14 cases (22.6%), arrhythmogenic right ventricular cardiomyopathy (ARVC) in 9 cases (14.5%), noncompaction (NCCMP) in 6 cases (9.7%) and dilated cardiomyopathy (DCM) in 5 cases (8.1%). Subendocardial late gadolinium enhancement (LGE), reflecting myocardial scar, was typical of previous myocardial infarction (post MI) in 3 cases (5.5%). Acute myocarditis was found in 2 cases (3.6%). Nonischaemic LGE pattern was found in 20 cases (32.2%): patchy subepi-midmyocardial LGE suggesting previous myocarditis in 8 athletes, and with aspecific pattern in 12 athletes. Athletes with nonischaemic LGE had normal clinical and laboratory parameters without wall motion abnormalities, in their cases further investigations ruled out systemic disease. One athlete was diagnosed with Fabry-disease, one with coronary artery abnormality (anomalous origin of the left main coronary artery from the right sinus of Valsalva), one athlete showed pheochromocytoma-related Tako-Tsubo cardiomyopathy (each 1.6%). Five athletes with confirmed structural heart disease were investigated after sustained ventricular tachycardia, seven athletes after aborted SCD: ARVC (n=6), aspecific LGE pattern (n=4), HCM (n=1) and pheochromocytoma-related Tako-Tsubo cardiomyopathy (n=1) were diagnosed.

Conclusion: In our national CMR registry the most common structural alteration was nonischaemic fibrosis, the most common cardiomyopathy was HCM, and the leading cause of SCD in Hungarian competitive athletes was ARVC. The national registers are highly important for a better understanding the etiology and the geographical differences of SCD in athletes.



Differential diagnosis of MINOCA patients: the contribution of early cardiac magnetic resonance imaging to the final diagnosis in patients with normal coronary angiography

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Citation:

Introduction: The diagnostic value of cardiac magnetic resonance (CMR) imaging has been suggested in determination of the cause behind Myocardial Infarction with Non-obstructive Coronary Arteries (MINOCA). According to the current STEMI Guideline CMR is considered to

have the best diagnostic performance, when CMR timing is within its optimal =2 weeks.

Purpose: The aim of our study was to establish the prevalence of the underlying pathologies using early (1-7 days) CMR examination in patients with signs of troponin positive acute coronary syndrome (ACS) but normal coronary angiography (NCA). We also aimed to investigate how early CMR changes the provisional diagnosis, and to provide detailed information of CMR characteristics of our pts and to compare laboratory parameters and risk factors of each group.

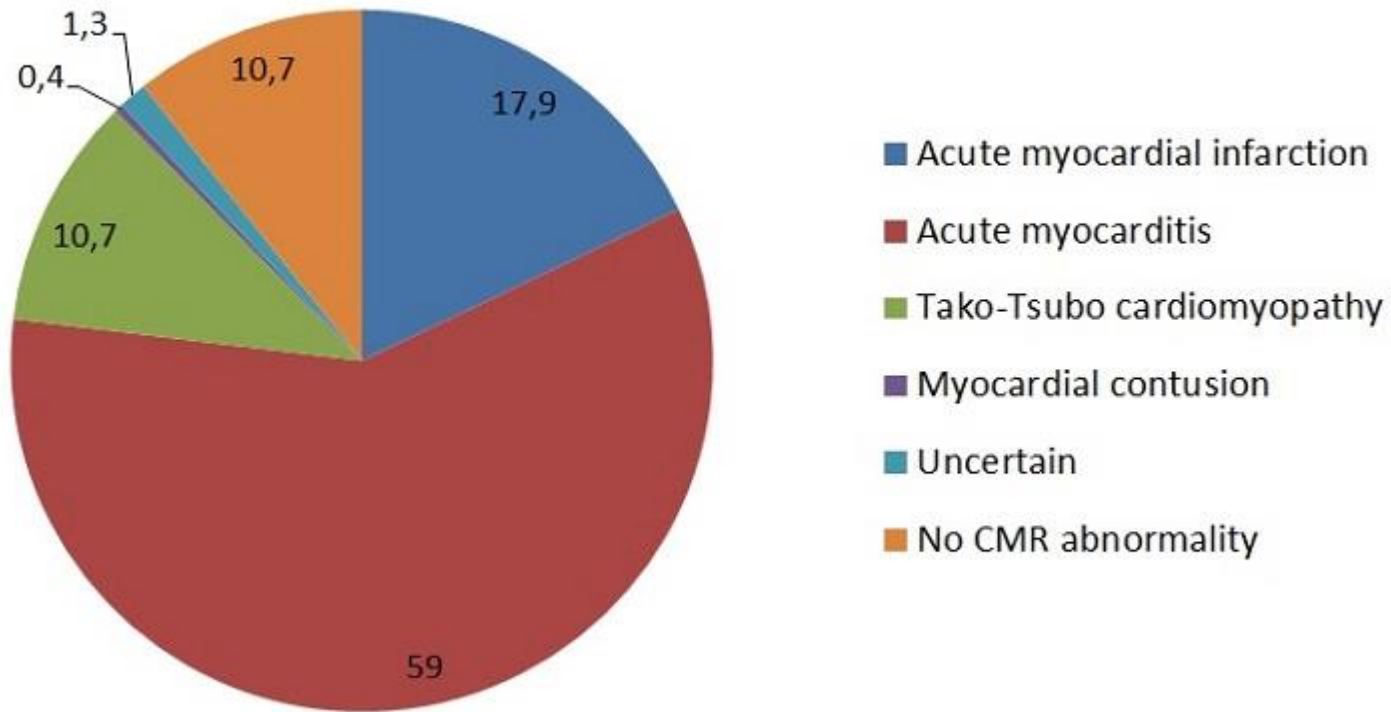
Methods: Between 2010-2018 (n=234) consecutive pts (40.2±12.1y, 159 male) with troponin positive ACS underwent CMR examination following NCA (=20% stenosis), in a mean length of time of 2.5 days. Cine movie, T2-weighted and late gadolinium enhanced images (LGE) were performed. Left ventricular end-diastolic and end-systolic volumes (LVESVi), ejection fraction (LVEF), mass (LVM) and myocardial necrosis were evaluated. We analysed the risk factors and laboratory values of our patients.

Results: CMR proved acute myocardial infarction (MI) in 42 pts (52% male), acute myocarditis in 138 pts (89% male), Tako-Tsubo cardiomyopathy (TTC) in 25 woman, myocardial contusion in one case, in three cases CMR raised the suspicion of sarcoidosis and in 25 pts (56% male) there was no CMR abnormality. LVEF was lower, LVESVi was elevated in TTC patients compared to MI and myocarditis (LVEF: 44±9.1 vs 56.5±7 vs 55±6.6%; LVESVi: 52.5±12.9 vs 41±16.8 vs 42.1±8.9 ml/m² p<0.001). The most frequently affected areas of the myocardium by LGE were the basal and mid inferolateral segments in case of myocarditis (69% of pts). In MI pts the anterior wall was affected only in 16%, while the involvement of inferior wall was visible in 57% of the pts. Early CMR examination established a definitive diagnosis in 88% of the cases, in 11% there was no CMR abnormality and it remained inconclusive in only 1% of the cases. CMR changed the provisional diagnosis in 47% of the pts.

Myocarditis pts were younger (myocarditis: 32.5±10.8 vs MI 47.6±15.5 vs TTC 65.5±9.6 y; p<0.001) and lower percentage had hypercholesterinaemia (myocarditis: 18.8 vs MI: 40 vs TTC: 54.5%, p<0.01) or hypertension (myocarditis: 14.3 vs MI: 38.7 vs TTC: 55.6%, p<0.001). Laboratory values showed significant elevation of hsTroponin and CKMB of MI and myocarditis pts compared to other groups (p<0.05), but there was no difference between these two groups.

Conclusion: In patients with the working diagnosis of MINOCA and normal coronary angiography early CMR established a definitive diagnosis in 88% of our patients and changed the provisional diagnosis in 47% of the pts.

Prevalence of the underlying pathologies in MINOCA patients (%)



Patients adherence with fixed dose combinations of renin-angiotensin-aldosterone system inhibitors in hypertension.

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Citation:

Introduction:

The latest ESC/ESH guidelines recommended fixed dose combinations (FDC) for first therapy in hypertension. Preferred two-drug combinations are a RAS (renin-angiotensin system) blocker with a CCBs (calcium channel blockers) or a diuretic. There are no available data about these FDCs adherence in hypertension.

Aim:

To assess one year persistence of recommended FDCs (RAS-inhibitors/CCBs or diuretics) in hypertensive patients.

Method:

Prescriptions database of National Health Insurance Fund in Hungary on pharmacy-claims were analysed between October 1, 2012 and September 30, 2013. We identified patients who filled prescriptions for FDCs of RAS-inhibitors/CCBs or diuretics prescribed for the first time in hypertensive patients who have not received similar drugs during one year before. To model the persistence, the apparatus of survival analysis was used, where "survival" was the time to abandon the medication.

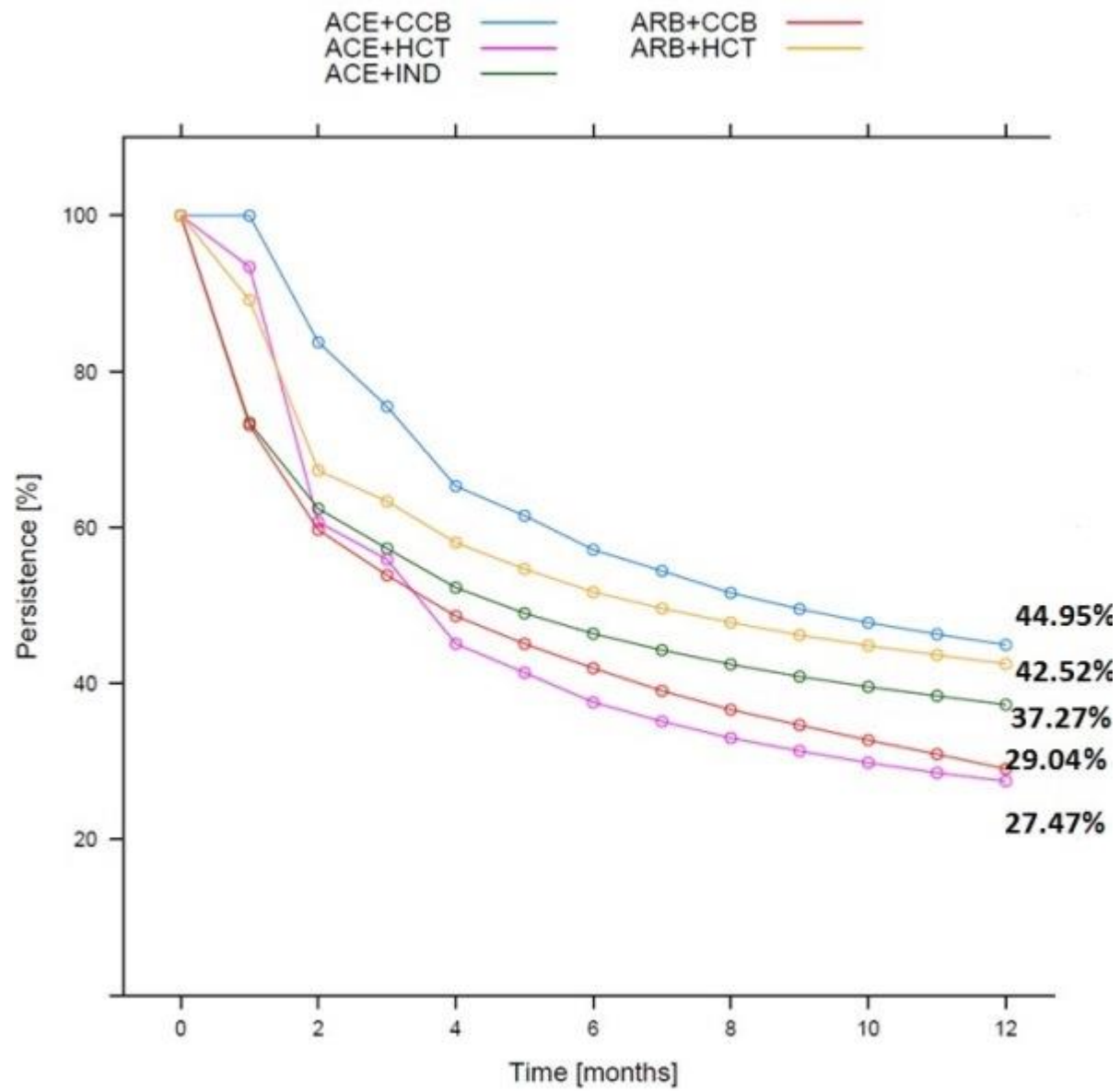
Results:

443,149 patients met the inclusion criteria. One-year persistence rate and hazard ratio (HR) of discontinuation (reference was ACEi/indapamide FDC) in patients with ACEi/CCB FDCs (n=124,154) was 44,95% (HR=0.69, [CI: 0.68-0.69], p<0.0001), ARB/HCT FDCs (n=109,707) was 42,52% (HR=0.80, [CI: 0.81-0.83], p<0.0001), ACEi/indapamide FDC (n=127,757) was 37,27% (HR=1.00, reference), ARB/CCB FDCs (n=13,542) was 29.04% (HR=1.19, [CI: 1.17-1.22], p<0.0001) and ACEi/HCT FDCs (n=67,989) was 27.47% (HR=1.17, [CI: 1.15-1.18],

p<0.0001).

Conclusions:

We have found significant difference between FDC s of RAS-inhibitors in hypertensive in relation of patients adherence. Our result demonstrated that ACEi/CCBs FDC therapy has the best one year persistence rate.



Magic mirror on the wall, can we reach our LDL-C goal? Comparison of calculated LDL-C and direct measured LDL-C levels in atherogenic dyslipidemia condition.

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Background: LDL-C represents the primary lipoprotein target for reducing cardiovascular risk. LDL-C can either be calculated or measured directly. Friedewald equation has certain limitations especially with high triglyceride and low LDL-C levels. Although a number of automated direct LDL-C assays are commercially available, non of them is considered to be equivalent to the „gold standard" of direct LDL-C, beta quantitation, a complex and expensive process that is unavailable in routine clinical practice. In atherogenic dyslipidemia condition (ADC) (triglycerides=2.3 mmol/L and HDL-C<1.0 mmol/L) non-HDL-C and remnant cholesterol are proven additional risk factors. Purpose: We compared one of the direct homogeneous assays with the widely used Friedewald's and the new Martin/Hopkins methods of estimation of LDL-C to see the differences in average LDL-C, remnant cholesterol and non-HDL-C levels and in availability of less than 1.8 mmol/L of LDL-C in atherogenic dyslipidemia condition.

Methods: We investigated 14 906 lipid profiles from fasting blood samples of Hungarian individuals with triglycerides <4.5 mmol/L. Total cholesterol (TC), HDL-C, triglycerides (TG) and direct LDL-C (D-LDL-C) were measured directly by the enzymatic assays. We also estimated calculated LDL-C by the Friedewald's formula (F-LDL-C) and by using the new Martin/Hopkins estimation (MH-LDL-C). We have now prepared first a variant of Martin/Hopkins table in mmol/L, in which the modified adjustable factors of 2.2 are included. We determined also non-HDL-C and remnant cholesterol (RC) as a difference of non-HDL-C and F-LDL-C (F-RC), MH-LDL-C (MH-RC), D-LDL-C (D-RC).

Results: In the investigated population 19.25 % was F-LDL-C, 15.48 % MH-LDL-C and 7.92 % D-LDL-C below 1.8 mmol/L. ADC occurred at 8.12 %. For ADC, when F-LDL-C<1.8 mmol/L (A), mean values for F-LDL-C, MH-LDL-C, D-LDL-C and non-HDL-C were 1.23±0.4; 1.65±0.39; 2.06±0.4 and 2.46±0.5 mmol/L respectively. These mean levels were 1.01±0.36; 1.4±0.3; 1.83±0.3 and 2.15±0.34 mmol/L for MH-LDL-C<1.8 mmol/L (B). For D-LDL-C<1.8 mmol/L (C), mean values were 0.79±0.35; 1.13±0.26; 1.54±0.19 and 1.83±0.25 mmol/L respectively. The average RC values (in mmol/L) for A were F-RC: 1.23±0.36; MH-RC: 0.81±0.18; D-RC: 0.4±0.17, for B 1.14±0.33; 0.74±0.14; 0.32±0.13, and for C 1.04±0.27; 0.70±0.1; 0.29±0.12 respectively. Conclusions: The Friedewald equation tends to underestimate and the homogeneous enzymatic direct LDL-C assays to overestimate the LDL-C levels compared to the new, accurate, calculated LDL-C values in atherogenic dyslipidemia condition. Based on the data presented in our investigation we should like to propose that more realistic vasculo-protective lipid status can be attained if we calculate LDL-C using the Martin/Hopkins estimation.

Characteristic of sympathetic nerve activity in two subgroups of patients with heart failure (HF_rEF and HF_{mr}EF)

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Citation:

Introduction

Sympathetic overactivity is a well documented in severe heart failure (HF) with reduced ejection fraction (HF_rEF). The European Society of Cardiology has recently introduced a new HF category, i.e. HF with mid-range ejection fraction (HF_{mr}EF), characterized by left ventricular EF of 40–49%. The sympathetic regulation in this new category has not been thoroughly described.

Aims

Characterization of the sympathetic regulation in patients with HF_{mr}EF compared with data obtained from HF_rEF patients and healthy volunteers.

Method

14 HF_rEF patients, 22 HF_{mr}EF patients and 10 control subjects were enrolled (table 1). Muscle sympathetic nerve activity, (MSNA) was recorded in the superficial peroneal nerve by microneurography, and processed by the Nerve Traffic Analyzer System (Model 662C-3, Iowa). Continuous ECG and non-invasive blood pressure (Finapres 2300) were digitized online (500 Hz/channel). Sympathetic burst frequency (bursts/minute) and burst incidence (bursts/100 heartbeats) were determined. The 6 min walking distances (6MWD) and NT proBNP levels in the HF subgroups were also assessed.

Results

Both burst frequency and incidence were significantly elevated in the HF subgroups compared to controls, and significant differences were also seen between the HF_rEF and HF_{mr}EF groups. The sympathetic burst activity in the HF populations significantly correlated with the NT proBNP level ($R=0.53$, $p=0.003$) and inversely correlated with the ejection fraction ($R=-0.38$, $p=0.03$).

Conclusion

Sympathetic activity is elevated in heart failure as compared to healthy controls. In patients with HF_rEF both parameters of sympathetic activity were significantly higher as compared to patients with HF_{mr}EF.

		EF < 40 %	EF: 40-49 %	Healthy control group (HC)	p	p	p
		(n=14)	(n=22)	(n=10)	EF < 40 % vs. EF: 40-49 %	EF < 40 % vs. HC	EF: 40-49 % vs. HC
NYHA	I-II.	8	21	–	–	–	–
	III-IV.	6	1	–	–	–	–
Age		58.36±12.31	62.23±9.74	52.44±10.41	0.302	0.247	0.019
BMI		29.65±3.77	29.84±4.19	–	0.895	–	–
NT proBNP [ng/L]		1574.75±1415.06	300.20±247.35	–	0.002	–	–
6MWT [m]		476.88±63.53	496.53±76.59	–	0.503	–	–
EF [%]		44.47±3.34	26.78±8.58	–	–	–	–
Baseline	burst/min	59.29±14.18	39.55±9.48	25.78±8.47	<0.001	<0.001	0.001
	burst/100	84.64±12.63	65.68±15.48	35.78±11.27	0.001	<0.001	<0.001

Distal radial artery access using slender technique for superficial femoral artery intervention

Authors:

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Citation:

Purpose: The purpose of this pilot study was to evaluate the acute success and complication rate of the distal radial artery access for femoral artery intervention.

Methods and results: The clinical and angiographic data of 195 consecutive cases with symptomatic superficial femoral stenosis, treated via distal radial (DR) or proximal radial (PR) access using 6F sheathless guiding between 2014 and 2018, were evaluated in a pilot study. Secondary access was achieved through the pedal artery. Primary endpoint: major adverse events (MAE), rate of major and minor access site complications. Secondary endpoints: angiographic outcome, procedural factors, cross-over rate to femoral access site, and duration of hospitalization. Overall technical success was achieved in 186 patients (95.4%) with 25/26 (96.1%) success in DR and 161/169 (95.2%) success in PR group (ns). The cross over rate to femoral access site was 3.8 % in DR and 4.7 % in PR group (ns), while dual (transradial and transpedal) access was used in 9/26 (34.6%) patients in DR and 39/169 (23%) patients in PR group (p<0.05). Stent implantation was necessary in 8/26 (30.7%) cases in DR and in 42/169 (24.8%) cases in PR group (ns). CTO recanalization was performed in the DR and PR group with 94.1% (16/17) and 92.6% (79/81) technical success rate. The mean contrast consumption, fluoroscopy time and procedure time was in the DR and PR group was: 93.4 [78-108]ml vs 120 [108-131]ml, 662 [501-822]vs 769 [671-866]min, and 33.4 [27-39]vs 36.5 [32-40]min (ns), respectively. The rate of access site complications in the DR and PR group was 0% and 4.7% (0% major, 4.7% minor) (p p<0.001), respectively. The cumulative incidence of MAE at 3 months in the DR and PR group was 3.8 % vs 10.6% (p<0.05).

Conclusion: Femoral artery intervention can be safely and effectively performed using distal transradial access and distal radial access is associated with lower access site complications.

Feasibility of distal radial access for carotid interventions: the RADCAR-DISTAL pilot study

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Citation:

Aims:

The aim of our study was to demonstrate the feasibility and safety of the distal transradial approach (DTRA) for carotid artery stenting (CAS).

Methods and results:

We included 209 consecutive patients (151 Trans-Radial Access (TRA) and 58 DTRA) treated in a single center by CAS with cerebral protection between 2016 and 2018. DTRA punctures were performed by ultrasound guidance, and the carotid artery cannulations were done using a 6.5 F coronary sheathless guiding catheter. The groups showed similar demographic profile regarding age, gender and comorbidities, however the proportion of symptomatic patients was significantly higher in the DTRA cohort (DTRA: 75,86 % vs. TRA: 46.36% $p < 0.001$). Procedural success rate was similarly high in both groups, while the overall complication rate was very low, with no major adverse events and only a few vascular complications. The cannulation times were similar, while the overall procedure length was slightly higher in the DTRA group. The cumulative X-ray dose was similarly low regardless the access used.

Conclusion:

DTRA is a safe and effective alternative of conventional trans-radial approach for CAS, with a potential to further improve the patient comfort.

Transpedal access for below-the-knee lesions in critical limb ischemia

Authors:

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Citation:

Background: Traditional access for the treatment of below-the-knee (BTK) lesions is the femoral approach, but in failed antegrade cases transpedal access can be utilized. The aim of the study was to evaluate the safety and technical and clinical success of endovascular BTK artery revascularization by a primarily retrograde transpedal access.

Methods: The clinical and angiographic data of 115 consecutive patients treated via transpedal access with symptomatic BTK stenosis were evaluated two cardiovascular centers (Europe and USA). We have selected patients with good distal run-off and non-infected distal puncture zone. The distal pedal artery was punctured by ultrasound guidance, and the procedural guidance was done by transpedal (TPA) or transradial angiography (TRA). Distal pressure at the end of the pedal sheath was also measured before and after the intervention. The primary endpoint was a composite of procedural success, major adverse events, and rate of access site complications. Secondary endpoints were: angiographic result of BTK intervention, fluoroscopy time, X-ray dose, procedure length, cross over rate to another puncture site and duration of hospitalization.

Results: The indication of the intervention was critical limb ischemia in all patients. Overall technical success was achieved in 99.1% of the

patients at least in one BTK artery. The distal puncture was successful in 114/115 patients 99.1% of the patients and the access site was anterior tibial artery in 96 patients (83.55), posterior tibial artery in 15 patients (13%) and peroneal artery in 4 patients (3.5%). Pedal to femoral access site cross over was 0.5%. Control angiography was done in 73 patients (63.5%) from radial and in 42 patients (36.5%) from transpedal access. The average contrast, procedure and fluoroscopy time was 109.9 [97-123]vs 31.4 [27-35]ml ($p<0.001$), 43.2 ± 22.3 vs 47.8 ± 25.5 min and 581 ± 448.7 vs 788 ± 605 sec in the TR and TP group. The average systolic transpedal pressure has been increased from $100.1 \text{ mmHg} \pm 44$ to 131 ± 36.4 mmHg after the procedure. Major adverse event at one month was detected in six patients (5.2%). Radial and pedal artery access site complications were encountered by ultrasound in 3/73 (4.1%) and 3/115 patients (2.6%) during follow up.

Conclusion: Below-the-knee artery angioplasty can be safely and effectively performed using radial and transpedal access in selective patient population.

B-lines and left atrial strain in outpatients with suspected Heart Failure with Preserved Ejection Fraction

Authors:

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Citation:

Background: Heart Failure with Preserved Ejection Fraction (HFpEF) is a growing healthcare burden and its prevalence is increasing. Diagnosing HFpEF is challenging. Lung ultrasound (LUS) and left atrial strain are promising tools to assess pulmonary congestion and left atrial dysfunction in outpatient settings in patients with suspected HFpEF.

Aim: To evaluate the correlation of LUS B-lines with left atrial strain in patients with HFpEF.

Methods: Thirty-six consecutive patients (24 women, mean age 70 ± 6 years) with clinical signs of heart failure were prospectively enrolled. Exclusion criteria were: ejection fraction $<55\%$, more than mild mitral and/or aortic valve disease, pulmonary disease, pulmonary arterial hypertension. Within one hour all patients underwent comprehensive echocardiographic evaluation including left atrial strain analysis (peak atrial longitudinal strain-PALS), lung ultrasound assessment of B-lines on the antero-lateral and posterior chest wall, and NT-proBNP levels.

Results: The mean ejection fraction was $65.5 \pm 8.6\%$. In 28 patients (85%) a significant number of B-lines (=15) was observed. We found a positive correlation between the number of B-lines and NT-proBNP levels ($p<0,0001$, $r: 0,76$, Figure 1.), left atrial volume ($p<0,05$, $r 0,45$), and

PALS ($p < 0,05$, $r = 0,5$, Figure 2.). We didn't find any correlation between the number of B-lines and E/e' ratio ($p = 0,1$, $r = 0,28$), or between E/e' ratio and NT-proBNP level ($p = 0,2$, $r = 0,2$).

Conclusion: LUS is a simple, feasible tool to detect pulmonary congestion in HFpEF and it seems to better characterize these patients. B-lines correlate well with NT-proBNP values and with parameters of left atrial dysfunction. PALS is a promising tool which better reflects pulmonary congestion and elevated NT-proBNP values than the conventional echocardiographic parameter E/e'.

Cardiopulmonary exercise testing normal values for young athletes and non-athletes

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Introduction:

Cardiopulmonary exercise testing (CPET) is an important diagnostic method to evaluate athletes and non-athletes, however we do not have widely accepted normal values for correct evaluation and interpretation in the young.

Goals:

Our aim was to compare CPET parameters of young athletes and non-athletes and determine reference values.

Methods:

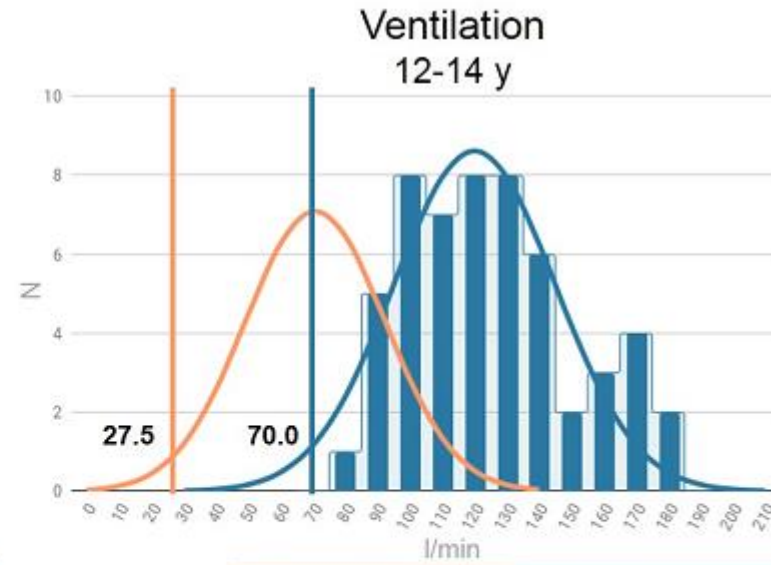
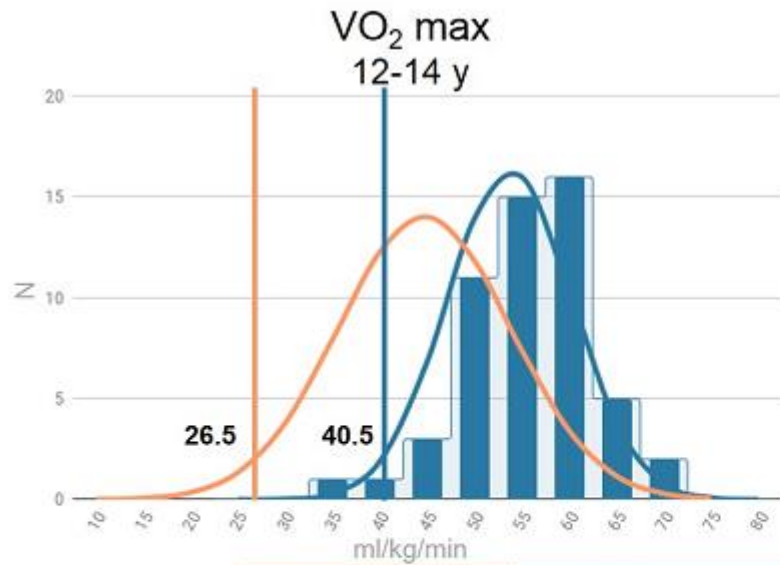
Exercise tests were performed in young non-athletes, aged < 18 years between 2011 to 2016 at Mayo Clinic. Athletes underwent detailed sports cardiology screening including CPET at Semmelweis University Heart and Vascular Center between 2016 and 2018. Individuals with cardiovascular disease were excluded. We created 2 subgroups in both sexes: 12-14 years (Group 1), 15-17 years (Group 2). Statistical analysis was performed using SAS with analysis of variance under the general linear model adjusting for age, body mass index and test effort based on peak respiratory exchange ratio (RER).

Results:

A total of 212 athletes (92% male, 15.5±0.6ys) and 207 non-athletes (68% male, 15.0±0.7ys) were included in the analysis. In Group 1 boys, athletes have higher peak HR (200.0±9.2 vs 188.5±16.8 bpm, p<.0001), HR reserve (117.1±14.5 vs 108.9±19.8 bpm p<.05), VO2 max (53.7±6.6 vs 44.7±9.1 mL/kg/min p<.0001), ventilation (VE) (120.3±25.0 vs 70.7±21.6 L/min p<.0001) and RER (1.12±0.0 vs 1.07±0.08, p <.001) compared to controls. In Group 2 boys, there was no difference in peak HR and HR reserve, but athletes have higher VO2 max (57.2±4.7 vs 45.3±9.3 mL/kg/min, p<.0001) and VE (150.7±23.7 vs 104.1±25.9 L/min, p<.0001), similarly as Group 2 girls: VO2 max (46.3±3.6 vs 34.9±8.5 mL/kg/min p<.0001), VE (118.7±12.5 vs 68.4±20.6 L/min, p<.0001). In male athletes, peak HR (200.6±9.2 vs 196.5±7.4 bpm p<.05) and HR recovery (34.2±9.8 vs 29.8±11.1 bpm p<.05) decreases with age, while VO2 max (53.7±6.6 vs 57.2±4.7 mL/kg/min, p<.001) and VE (120.3±24.9 vs 150.7±23.7 L/min, p<.0001) increases. Lower cut-off values were determined in each group (Figure).

Conclusion:

We created a unique Mayo-Semmelweis database of young athletes and non-athletes. As a result of intensive training, athletes show higher levels of CPET variables vs non-athletes. Our study provides CPET reference values in the pediatric age group, applying them could contribute to correct evaluation and interpretation of CPET, increasing its diagnostic potential.



	Non-athletes	Athletes
12-14 y boys	26.5 ml/kg/min	40.5 ml/kg/min
15-17 y boys	26.7 ml/kg/min	47.8 ml/kg/min
15-17 y girls	17.9 ml/kg/min	39.1 ml/kg/min

	Non-athletes	Athletes
12-14 y boys	27.5 l/min	70.0 l/min
15-17 y boys	52.3 l/min	103.3 l/min
15-17 y girls	27.2 l/min	93.3 l/min

The impact of highest doses of ACEi/ARB therapy on mortality of patients suffering from heart failure with reduced ejection fraction: a long-term follow-up, propensity-matched cohort study

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Citation:

The angiotensin-converting enzyme inhibitors (ACEi) as cornerstone of neurohormonal drug regime reduce mortality and morbidity in heart failure with reduced ejection fraction (HFrEF) hence these drugs are recommended for every HFrEF patients without presence of contraindication or intolerance. However, there are controversial results regarding the incremental survival benefit of higher doses of these drugs used in HFrEF. In addition, achieving the highest doses (TD1) (20 mg < enalapril daily dose=40 mg, or dose equivalent ACEi/ARB), of these drugs often accompanies side effects related to the up-titration, which may make it impossible to start other therapies proven to result in undoubtful mortality benefit (i.e. sacubitril/valsartan).

Aim: to assess the effect of TD1 of ACEi/ARB on mortality of HFrEF patients followed at a heart failure outpatient clinic (HFOC).

Methods: Data of 579 consecutive HFrEF patients, who hadn't been treated with an ACEi/ARB or were receiving = 50% of doses equivalent with 20mg enalapril daily (TD2) at the time of initiation of care (NYHA:3.1±0.8; LVEF:27.5±6.6%; age:61.1±13.0years; male:76.1%; ischemic:46.8%; atrial fibrillation:27.6%; diabetes:34.9%; hypertension:72.5%), followed at our HFOC was analysed. After therapy optimization (TO) ACEis/ARBs were applied in 96.5% and at least TD2 was reached in 55.9% of the total cohort, while TD1 of an ACEi/ARB was applied in 111 patients (19.2% of total cohort). BBs in 88.4%, target doses of BBs in 46.8%, MRAs in 57.0% of total cohort were used. To adjust for possible confounders, patients were matched based on the ACEi/ARB doses reached during TO applying propensity score matching (PSM) using the nearest neighbor matching (caliper: 0.2). All-cause mortality (ACM) was assessed using the Kaplan-Meier method and compared with the Cox proportional hazard model.

Results: After 7.1±4.7 years follow-up ACM of patients treated with TD1 of ACEis/ARBs was significantly lower than those treated with lower doses in the total cohort (HR=0.67; 95% CI=0.50-0.89; p=0.005). Applying multivariate Cox regression analysis the use of TD1 of an ACEi/ARB didn't remain independent predictor of survival; creatinine, NYHA f.c., age, sex, ischemic etiology were proved to be significant predictor of mortality. After PSM the survival of patients receiving TD1 of an ACEi/ARB didn't differ from those treated with lower doses (HR=0.84; 95% CI=0.61-1.14; p=0.27).

Conclusions: The current ESC guidelines recommend the use of target doses or maximal tolerated doses of ACEis or ARBs in HFrEF. In a real-world patient cohort whom all the effort was made to reach the target doses, ACM of patients treated with TD1 of an ACEi/ARB was significantly lower than those treated with lower doses, however this result wasn't independent from the patient characteristics. Beside that, after PSM the survival of patients treated with TD1 or with lower doses of an ACEi/ARB did not differ significantly.

Machine-learning defined predictors of mortality in ischemic and non-ischemic heart failure patients undergoing CRT-P or CRT-D implantation

Authors:

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Citation:

Background: Both Cardiac Resynchronization Therapy Pacemakers (CRT-P) and CRT Defibrillators (CRT-D) improve mortality in heart failure patients with reduced ejection fraction and wide QRS complex. However, not every patient benefits equally from each type of treatment and determinants of mortality may vary across the subgroups of patients with different etiologies and devices.

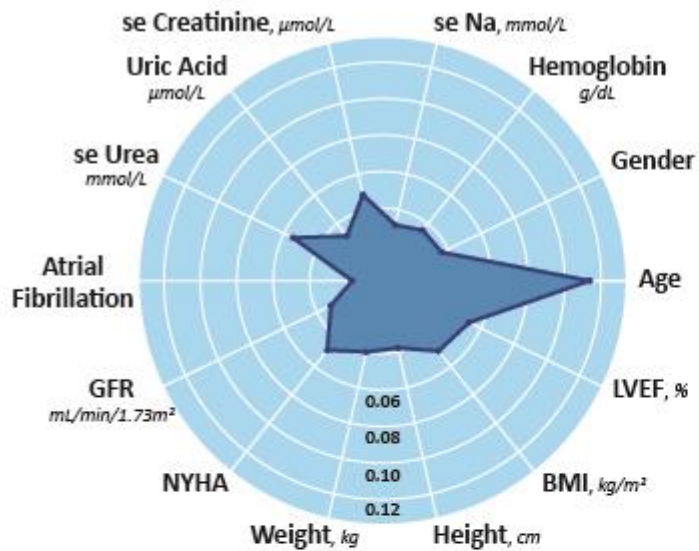
Purpose: Our aim was to investigate the differences in the predictors of long-term mortality in heart failure patients with different etiologies undergoing CRT-P or CRT-D implantation using machine learning.

Methods: We created 4 separate random forest models to predict 5-year all-cause mortality (models for ischemic and non-ischemic etiology in both CRT-P and CRT-D subgroups). A registry of 1650 patients (66±10 years, 1258 [76%] males, 751 [46%] CRT-D) was used as the training cohort for the prediction models. Forty-seven pre-implant parameters including cardiovascular risk factors and clinical variables were utilized to train our models. For each clinical parameter, we calculated the mean decrease in Gini impurity (dG). Based on the extent of decline, the 10 most important features were selected for each model. To keep the data comparable between the different models, we took the union of these features and plotted the results on radar charts.

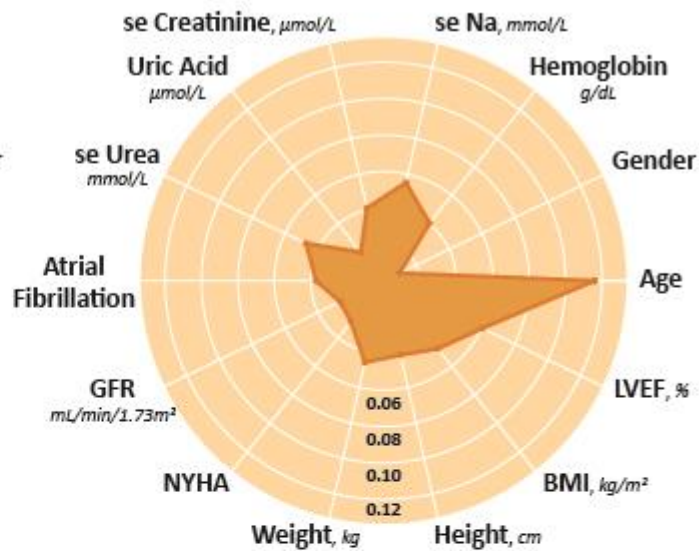
Results: There were 879 (53%) deaths during the follow-up period. The mortality benefit of adding an Implantable Cardioverter Defibrillator could be observed only in ischemic patients (Hazard Ratio = 0.83, 95% Confidence Interval: 0.72-0.97, p<0.005), but not in the entire cohort or in patients with non-ischemic etiology. In patients with non-ischemic etiology, the pattern of mortality predictors were almost similar: in CRT-P patients the most important predictors were age, serum urea levels and left ventricular ejection fraction (LVEF) (dG: 0.114, 0.054 and 0.053, respectively) whereas in the CRT-D subgroup these factors were age, LVEF and serum sodium (dG: 0.116, 0.060 and 0.052, respectively). In CRT-P patients with non-ischemic etiology, the most relevant variables were age serum urea and LVEF in decreasing order (dG: 0.085, 0.060 and 0.050, respectively). The strongest predictors of mortality were age, hemoglobin and serum creatinine in ischemic patients with CRT-D (dG: 0.088, 0.060 and 0.052, respectively).

Conclusions: In patients with ischemic heart failure, CRT-D was associated with a mortality benefit compared to CRT-P. Our results also suggest that machine-learning may identify distinct patterns in clinical characteristics for a better mortality prediction. Taking these factors into consideration during the management of heart failure patients with CRT, risk stratification and outcomes could be improved.

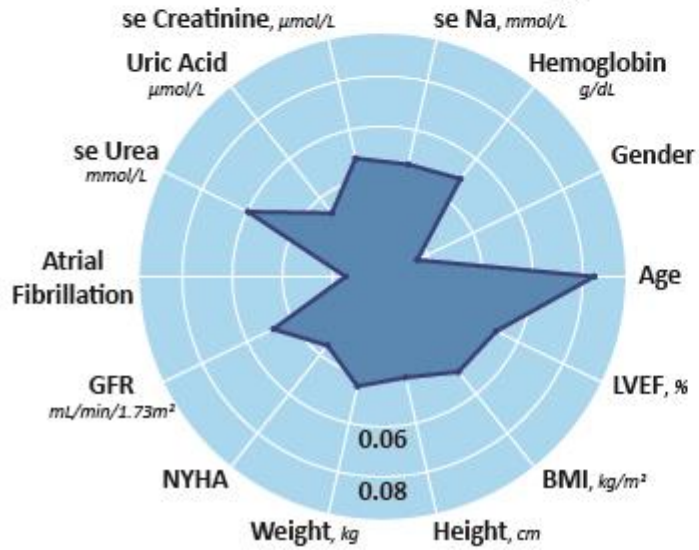
CRT-P – Non-Ischemic Etiology



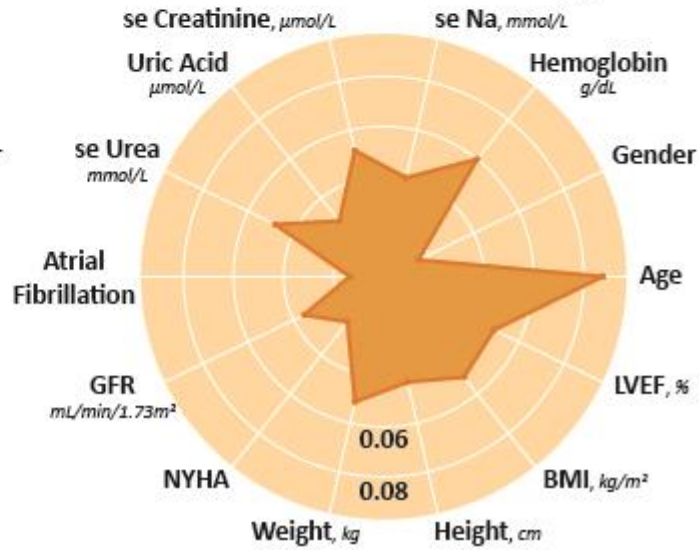
CRT-D – Non-Ischemic Etiology



CRT-P – Ischemic Etiology



CRT-D – Ischemic Etiology



Aortic pulse wave velocity measured by an oscillometric device independently predicts all-cause mortality in a cohort of 4146 subjects

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Citation:

Objectives. Assessment of carotid-femoral pulse wave velocity by applanation tonometry independently predicts all-cause and cardiovascular mortality. However, there has been a need for a simpler, user-independent measurement with a validated device, that is applicable even in the primary care setting.

Methods and subjects. 4146 subjects (49% men) aged 35-75 years were measured in multiple centers in Hungary. Subjects visited the outpatient department of these centers on their own initiative. The measurement of aortic pulse wave velocity (PWV_{ao}) with Arteriograph was performed in addition to taking past medical history, physical examination and laboratory tests. The mean follow-up time of the study was 5.5 years. The number of events (all cause mortality) were provided by the Hungarian National Health Insurance Fund. Cox regression analyses were used to identify predictive factors for this endpoint.

Results. The mean age of the study population was 53 years, brachial systolic and diastolic blood pressure were 137 ± 20 and 82 ± 11 mmHg, and heart rate was 70 ± 10 1/min. The mean value of SCORE was 3 in this large cohort. 410 subjects had a registered cerebro-or cardiovascular event before the measurement, the number of smokers was 656 (16%), 1974 subjects were treated with at least one anti-hypertensive drug (48%), while the number of subjects on lipid-lowering, antidiabetic or antiplatelet medication were 807 (19%), 352 (8%) and 398 (17%), respectively. There were 116 fatal events during a mean follow-up of 5.5 years. According to the Cox regression, PWV_{ao} is a significant and independent predictor of all cause-mortality and in univariate analysis, a 1.0 m/s increase in PWV_{ao} was associated with HR 1.7 [1.47–1.98; $p < 0.001$], for this endpoint.

Conclusion. Aortic pulse wave velocity measured by an invasively validated, simple, oscillometric device predicted all-cause mortality in a large cohort of relatively young subjects of the general population that may improve risk stratification even in the everyday clinical practice or primary care setting.

Right ventricular function and long-term outcomes in cardiac resynchronization therapy patients enrolled in MADIT-CRT

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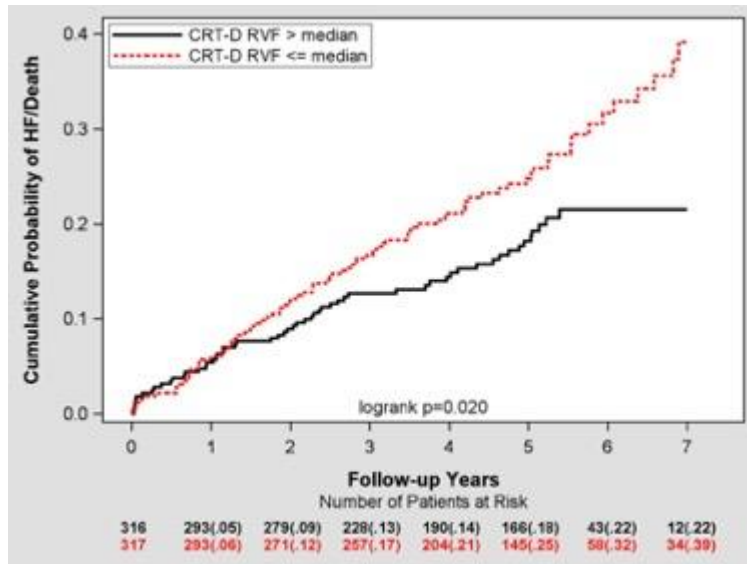
Citation:

Background: Long-term predictive value of baseline right ventricular (RV) function and CRT-induced changes of RV function for the clinical outcomes, mortality or heart failure are not well understood, especially in mild HF patients implanted with CRT-D.

Methods: MADIT-CRT enrolled 1,820 patients at 110 centers worldwide, with either ischemic cardiomyopathy (New York Heart Association [NYHA] functional class I or II), or non-ischemic cardiomyopathy (NYHA functional class II only), sinus rhythm, ejection fraction of 30% or less, and a QRS duration of 130 ms or more. We assessed right ventricular function (RVF) as RV fractional area change by echocardiography at baseline and after 1 year of therapy in patients with LBBB assigned to CRT arm (n=633). Kaplan-Meier survival analyses and multivariate Cox models were utilized to identify RV parameters predicting long-term outcomes of HF or death events.

Results: During the median follow up of 5.6 years 192 (30.3 %) patients had heart failure or death. CRT-D LBBB patients with below or above median RV end-systolic area (RVS) had lower cumulative probabilities of HF/death (p=0.02). Lower, than the median value of both RVS and RVF were associated with higher risk of HF events alone (p=0.004; p=0.01 respectively). In multivariate analysis, after adjustment of relevant clinical covariates more RV reverse remodeling in the terms of RV end-diastolic area (RVD) decrease proved to be an independent predictor for 5-year all-cause mortality (HR: 0.4; p=0.03).

Conclusions: Based on our results RV geometry and function before CRT implant and also significant RV reverse remodeling at 12 months follow up are significant predictors of long-term outcomes.



Predictors of mortality following extracorporeal membrane oxygenation support in a large unselected critically ill patient population

Authors:

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Citation:

Background: Mechanical circulatory support (MCS) has been established as a means of augmenting circulation in critically ill patients due to a variety of underlying clinical reasons. Different methods of MCS may be applied with the venous-arterial extracorporeal membrane oxygenation (VA-ECMO) system being one of the most utilized in everyday care.

Objectives: Our aim was to determine independent predictors of mortality following VA-ECMO therapy in a large, unselected, adult, critically ill patient population requiring MCS.

Methods: Data on 181 consecutive, real-world VA-ECMO treatments have been assessed. Analysis was conducted for all subjects requiring MCS with the VA-ECMO as first instalment, regardless of underlying cause or eventual upgrade. All potential clinical factors influencing mortality were examined and evaluated.

Results: Overall mortality amounted to ~65% at a median follow-up of 28 days and depended upon: glomerular filtration rate of <60 ml/min/1.73 m² (HR: 1.53; p=0.03) and age ≥ 65 years (HR: 1.65; p=0.02) based on multivariate Cox regression analysis. However, prolonged ECMO time, conversion of the ECMO to longer duration MCS, diabetes, prior ACS or revascularization, reduced left ventricular ejection fraction (EF) had no effect on adverse mortality outcomes (all p>0.05). Surprisingly, neither the need for resuscitation during MCS nor any ECMO implantation indication influenced mortality by itself (p>0.05).

Conclusions: We have found that mortality in critically ill patients requiring VA-ECMO use remains very high. Decreased renal function and advanced age were found to influence mortality in our all-comers patient population, while traditional predictors of cardiovascular mortality did not have a significant effect on survival.

Figure 1: B-lines vs NT-proBNP level

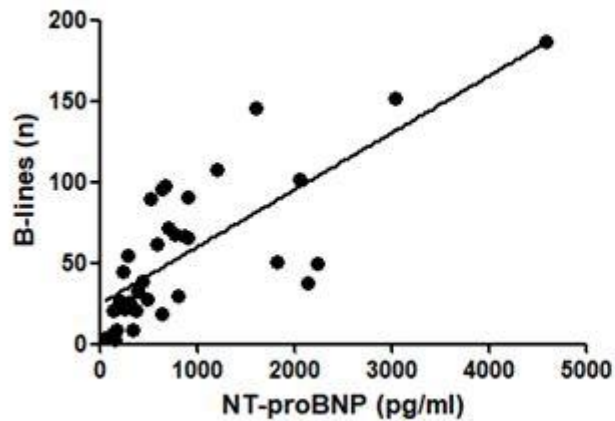
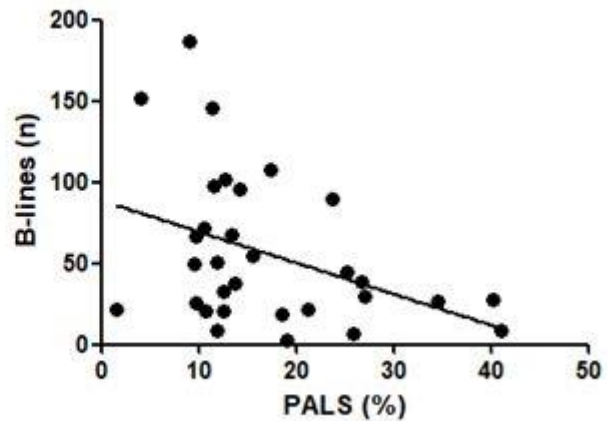


Figure 2.: B-lines vs PALS



Equal significance of longitudinal and radial wall motion represents the normal right ventricular mechanical pattern: 3D echocardiographic study in 231 healthy volunteers

Authors:

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Citation:

Three main mechanisms contribute to right ventricular (RV) pump function: (1) shortening of the longitudinal axis with traction of the tricuspid annulus towards the apex; (2) inward (radial) movement of the RV free wall, which is often referred as the "bellows effect"; and (3) bulging of the interventricular septum into the RV during the left ventricular contraction and stretching of the free wall over the septum (causing shortening

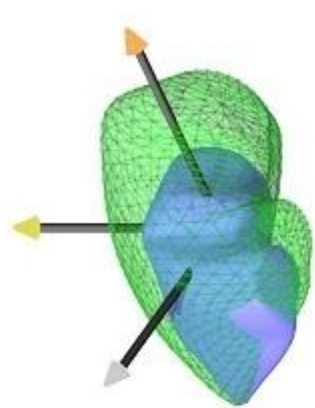
in the anteroposterior direction). Despite the established clinical value of the functional changes among the aforementioned components, their relative importance remains to be quantified during physiological conditions.

Accordingly, the aim of our study was to evaluate the relative contribution of the different RV motion directions to global RV function on both global and segmental level in a large set of healthy individuals.

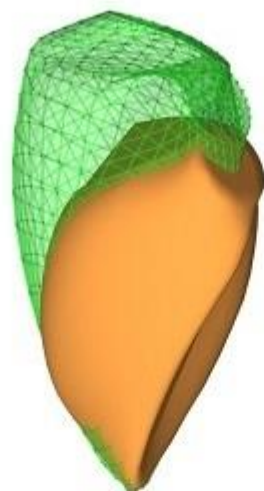
We have recruited 231 healthy volunteers (44% female, with a wide and balanced age range from 8 to 81 years) from two experienced centers performing transthoracic 3D echocardiography (3DE) on a routine basis. 3DE datasets focused on the RV were obtained using multi-beat acquisition. We determined RV volumes and subsequent ejection fraction (RVEF) by dedicated software. Using the ReVISION method, we have decomposed the motion of the RV to determine longitudinal (LEF), radial (REF) and anteroposterior ejection fraction (AEF). Their ratio to RVEF quantifies the relative contribution of the given component to global RV function. Moreover, regional subvolumes were also analyzed in a 15-segment model.

Mean value of RVEF was significantly higher in female subjects compared to male subjects (60 ± 7 vs. $56\pm 7\%$, $p<0.001$). The relative contributions of LEF and REF to RVEF were comparable, while the contribution of AEF was significantly lower (LEF/RVEF vs. REF/RVEF vs. AEF/RVEF: 0.48 ± 0.08 vs. 0.49 ± 0.07 vs. 0.39 ± 0.11 , $p<0.001$) in the pooled population as well as in the genders separately. In line with higher RVEF found in women, female gender was associated with a higher longitudinal and radial contribution compared to males, however, AEF was similar (women vs. men; LEF/RVEF: 0.49 ± 0.08 vs. 0.47 ± 0.07 , $p<0.05$; REF/RVEF: 0.50 ± 0.07 vs. 0.48 ± 0.06 , $p<0.01$; AEF/RVEF: 0.38 ± 0.12 vs. 0.40 ± 0.10 , $p=NS$). Interestingly, AEF/RVEF showed a significant deterioration with age ($r=-0.354$, $p<0.001$), while age-dependency of the longitudinal and radial contributions were not observed concerning both genders. An age-related decrease could be demonstrated by the volume fractions of the 5 septal volumetric segments ($r=-0.229$, $p<0.001$).

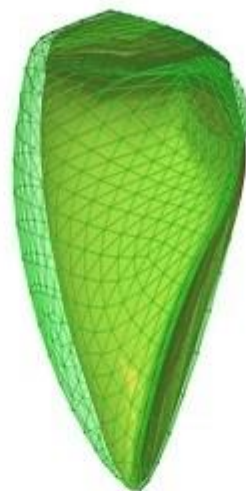
In physiological conditions, the relative importance of longitudinal and radial wall motions is similar in determining global RV function. Aging accompanied by a decrease in anteroposterior shortening, which may point to a deteriorating systolic LV-RV interaction. Our results may facilitate further research concerning the alterations of RV mechanical pattern in various disease states.



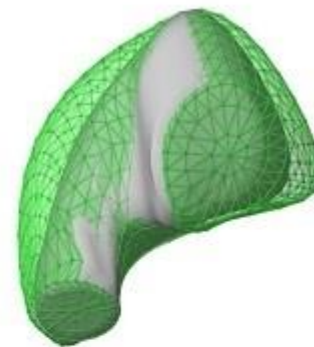
Global



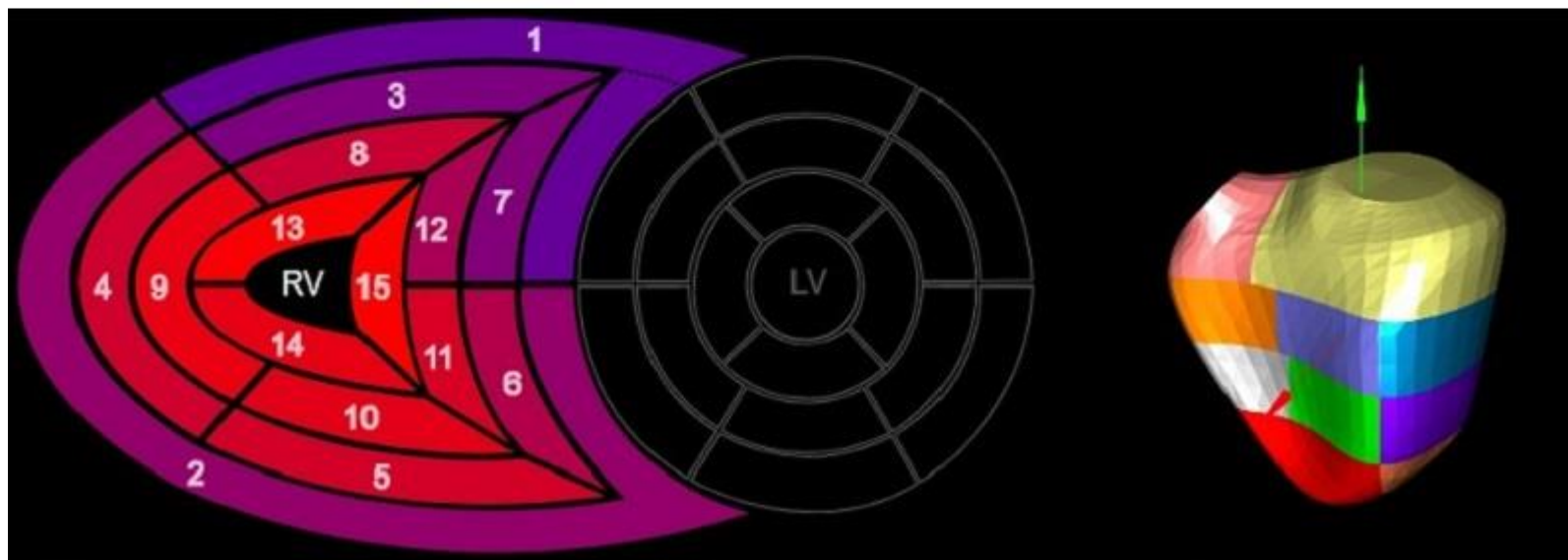
Longitudinal



Radial



Anteroposterior



Hemodynamic management of resistant hypertension

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Citation:

Background: Hypertension is the most prevalent chronic disease worldwide and is related with high probability of cardiac disease, kidney disease and cerebrovascular events. Blood pressure measurement was used in the last decades to diagnose and guide antihypertensive therapy; however blood pressure is the result of interaction of more complex hemodynamic parameters previously reserved to experimental studies or critical care patients management using invasive methods. Since 1996 few studies has proposed the use of hemodynamic parameters to classify and guide hypertension therapy with good results. Purpose: the present study purpose was to measure hemodynamic parameters in patients with non-controlled resistant hypertension and use it to guide pharmacologic treatment in order to archive control blood pressure values according to the European Society of Cardiology guidelines. Methods: a total of 84 patients between 32 and 95 years old diagnosed with non-controlled primary resistant hypertension were recruited and after previous therapy washout hemodynamic parameters were measured using noninvasive methods: preload by central venous pressure (CVP) using inferior vena cava diameter, cardiac index and systemic vascular resistance using Lyljestrang & Zander modified formula. Patients were classified in 3 basic groups depending on which parameter was above normal value: hyperdynamic (HD) for high cardiac index $>3,5L/min/m^2$, fluid overload (FO) for $CVP > 8cmH_2O$ and high systemic vascular resistance index (HSVRi) $>2500dynes/sec/m^2/cm^{-5}$, also 3 combined groups were a patient had 2 simultaneous hemodynamic alterations (HD+FO, HD+HSVRi and FO+HSVRi), according to this classification pharmacotherapy was guided indicating Bisoprolol in HD group, Amlodipine to HSVR patients and Hydrochlorothiazide to FO patients, in combined groups, combined therapy was given. Patients were observed for 6 months period taking as primary endpoint blood pressure control, acute cardiovascular events and hypotension. Results: a significant reduction of hemodynamic parameters and blood pressure was observed since the first month of treatment obtaining a 100% hemodynamic and blood pressure goals in all patients at the third month of therapy without hypotension or acute cardiovascular event during this period, the HD+FO group reach goals at the 6th month of treatment without reported complications. Conclusions: in this preliminary studied we observed that hemodynamic guided high blood pressure control may be a useful tool to a better understanding, classifications and treatment in patients with resistant hypertension; however a larger outcome studies to confirm this hypothesis.

Detailed characterization of atrial remodeling induced by exercise training in a rodent model of exercise-induced cardiac hypertrophy

Authors:

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Citation:

Introduction Atrial fibrillation and heart failure share common risk factors and frequently coexist as atrial fibrillation leads to impaired myocardial function. Although regular exercise training is associated with cardiovascular benefits, the increased risk of atrial arrhythmias has been observed, with differences regarding prevalence between genders. While multiple mechanisms are likely, the atrial alterations induced by long-term physical exercise still need to be elucidated.

Purpose We aimed at investigating exercise-induced atrial remodeling in a rat model of athlete's heart and determining sex-specific differences.

Methods Age-matched young adult rats were divided into female exercised (FEx), female control (FCo), male exercised (MEx) and male control (MCo) groups. After exercised animals completed a 12-week-long swim training protocol, echocardiography was used to describe atrial alterations. In vivo electrophysiologic investigation was performed by programmed stimulation with an octapolar catheter inserted into the right atrium and atrial gene expression analysis was carried out.

Results Post-mortem atrial weight data revealed marked atrial hypertrophy (atrial weight to tibial length: 18.6±2.7g/cm FEx, 10.3±1.0g/cm FCo, 23.7±2.2g/cm MEx, 15.8±1.9g/cm MCo pex<0.01), while echocardiography data showed slight atrial dilatation and improved contraction in both exercised groups. Exercise training was associated with bradycardia, P-wave enlargement and prolonged right atrial effective refractory period (RAERP: 45.7±4.3ms FEx, 40.2±5.9ms, FCo, 49.8±4.2ms MEx, 43.1±4.6ms MCo pex<0.01). Sinus node recovery time (SNRT) did not differ between groups and we could not induce significant number of arrhythmias by programmed stimulation (double extrastimulation, burst pacing) in any groups. We found increased atrial gene expression of antioxidant enzymes (e.g. NADPH oxidase 2, superoxide dismutase 2) in both genders. Despite the marked atrial hypertrophy, no gene expression alteration was found regarding markers that describe pathological remodeling (atrial natriuretic factor), proinflammatory (tumor necrosis factor- α) and profibrotic [e.g. transforming growth factor- β (TGF- β), matrix metalloproteinase-2 (MMP-2)] processes. While exercise training did not affect on the expression of profibrotic markers, female gender was associated with lower TGF- β and MMP-2 expression. We found altered expression of ion channels participating in atrial depolarization and repolarization.

Conclusions Our data suggests that long-term exercise-induced atrial hypertrophy is not associated with harmful electrical remodeling and no inflammatory or profibrotic response was observed in the atrium of exercised rats.

Cerebral venous congestion promotes blood brain barrier disruption and neuroinflammation, impairing cognitive function in mice

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Background: Cognitive impairment is one of the most common co-occurring chronic conditions among heart failure patients (incidence: 25-80%), however, the underlying mechanisms are not completely understood. It is hypothesized that in addition to decreased cardiac output increases in central – and consequentially, cerebral - venous pressure (backward failure) may also contribute significantly to the genesis of cognitive impairment. To test this hypothesis and elucidate the specific pathogenic role of venous congestion in the brain we have established a novel model of increased cerebral venous pressure: mice with jugular vein ligation.

Methods: To test the hypothesis that increased venous pressure in the brain contributes to the development of cognitive deficits by causing blood brain barrier disruption, dysregulation of blood flow and/or promoting neuroinflammation, bilateral ligation of external and internal jugular veins were performed in 10 month old male C57BL/6 mice. 7 days after the operation cognitive function was tested with radial arm water maze. Gait function and motor coordination were also tested. Neurovascular coupling responses were assessed by measuring changes in cerebral blood flow in the whisker barrel cortex in response to contralateral whisker stimulation by laser speckle contrast imaging through a closed cranial window. Blood brain barrier integrity (IgG extravasation) and microglia activation (CD68/Iba1 staining) were assessed in brain slices by immunohistochemistry. Neuroinflammation-related gene expression profile was assessed by a targeted qPCR array.

Results: After the ligation of jugular veins, mice exhibited impaired spatial learning and memory, altered motor coordination and impaired gait function, mimicking important aspects of altered brain function observed in human heart failure patients. Jugular vein ligation did not alter neurovascular coupling responses. In the brains of mice with jugular vein ligation significant extravasation of IgG was detected, indicating blood brain barrier disruption, which was associated with histological markers of neuroinflammation (increased presence of activated microglia) and a pro-inflammatory shift in gene expression profile.

Conclusion: Cerebral venous congestion *per se* can cause blood brain barrier disruption and neuroinflammation, which likely contribute to the genesis of cognitive impairment. These findings have relevance to the pathogenesis of cognitive decline associated with heart failure, and venous congestion due to arteriovenous malformations as well as increased venous reflux in human patients.

Effect of anthropometrics, serostatus, medication and cocaine use on quantified coronary plaque volumes in patients with human immunodeficiency virus

Authors:

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Citation:

Introduction

The effect of human immunodeficiency virus (HIV) and its medications on coronary artery disease (CAD) is controversial. Furthermore, illicit drug use such as cocaine occurs more often in these populations, however its potential modulating impact on CAD poorly understood.

Purpose

We sought to assess the effect of anthropometrics, serostatus, HIV medications and cocaine use in HIV patients on coronary plaque volumes assessed using coronary CT angiography (CTA).

Methods

We randomly selected 100 HIV patients without known CAD, but with coronary CTA confirmed coronary stenosis. All major epicardial vessels were segmented. Total plaque volume, low-attenuation non-calcified plaque volume and calcified plaque volumes were quantified from vessel portions which contained coronary atherosclerosis. We used linear regression analysis to assess the association between anthropometric (age, sex, body mass index), traditional risk factors (hypertension, diabetes, positive family history, HDL, LDL, cholesterol, triglycerides levels, years of alcohol and smoking), HIV associated parameters (years of HIV infection, months of protease inhibitor, nucleoside reverse transcriptase inhibitor, non-nucleoside reverse transcriptase inhibitor, antiretroviral therapy medication use, hepatitis virus C infection, endothelin 1 levels, CD4 levels and viral load), years of cocaine use and coronary plaque volumes.

Results

Among anthropometric and traditional risk factors age ($\beta=10.35$, $p=0.006$) and smoking years ($\beta=2.72$, $p=0.044$) showed a significant association with total plaque volume, while all other parameters did not. Among HIV related parameters non-showed a significant association with the total

plaque volume. However, the years of cocaine use significantly increased the amount of plaque volume ($\beta=4.51$, $p=0.024$). The amount of low-attenuation non-calcified plaque volume was only associated with the years of cocaine use ($\beta=0.30$, $p=0.031$), while all other parameters were non-significant. The amount of calcified plaque volume was associated with age ($\beta=2.82$, $p=0.047$) and years of cocaine use ($\beta=1.52=0.043$).

Conclusions

Cocaine use significantly increases the amount of low-attenuation non-calcified plaque volume, calcified plaque volume and overall plaque volume in HIV patients. Our results suggest the importance of cocaine use prevention in HIV patients as it increases plaque volumes which have been shown to be associated with poor cardiovascular outcomes.

Cardiac magnetic resonance characteristics of professional athletes and hypertrophic cardiomyopathy patients in the grey zone of hypertrophy

Authors:

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Citation:

Differentiation between athlete's heart and hypertrophic cardiomyopathy (HCM) may cause difficulties especially in patients in the grey zone of hypertrophy.

We aimed to determine conventional cardiac magnetic resonance (CMR) parameters such as left ventricular (LV) ejection fraction (EF), BSA-corrected end-diastolic (EDVi), end-systolic and stroke volume (SVi), mass (Mi), derived CMR parameters such as maximal end-diastolic wall thickness to LVEDVi ratio (EDWT/LVEDVi), LVM to LVEDV ratio (LVM/LVEDV), and CMR based strain values (global longitudinal (GLS), radial (GRS) and circumferential strain (GCS)) in male HCM patients and athletes.

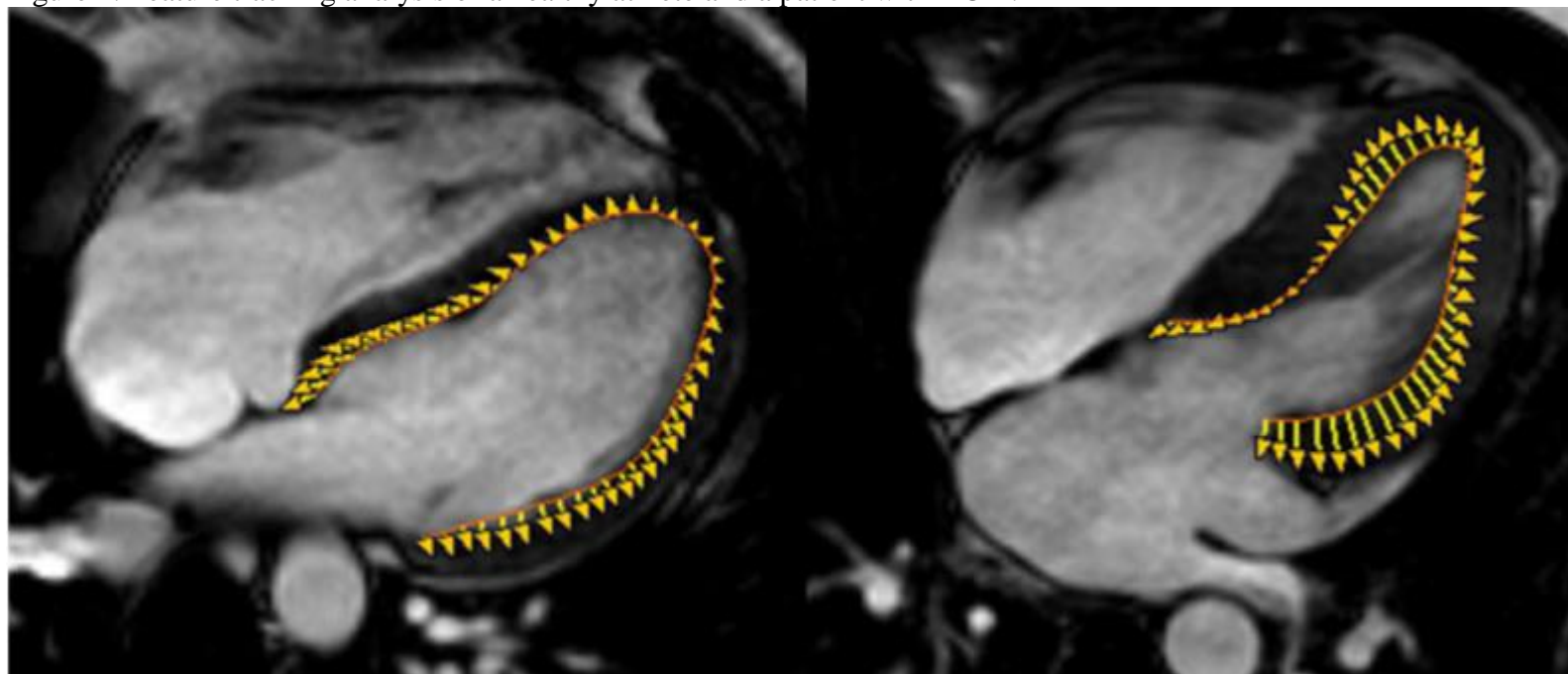
We consecutively enrolled male HCM patients with only slightly elevated EDWT (13-18 mm) and highly trained healthy athletes (n=30, 18.7±1.2 training hrs/week) with marked LV hypertrophy. HCM patient group was divided into sedentary (n=30, <7 training hrs/week) and athletic HCM group (n=10; >7 h/week, 12.7±7.3 h training hrs/week).

Both sedentary and athletic HCM patients showed higher LVEF, lower LVEDVi and LVESVi and higher EDWT compared to the healthy

athletes. LVMi of both healthy athletes and athletic HCM patients was significantly higher than in sedentary HCM patients, respectively (98.9 ± 11.4 ; 94.5 ± 7.8 vs 78.1 ± 14.4 /m²). EDWT/LVEDVi ratio was higher in both sedentary and athletic HCM patients compared to healthy athletes, respectively (0.19 ± 0.04 ; 0.17 ± 0.04 vs 0.11 ± 0.02). LVM/LVEDV also showed significant difference between HCM patients and healthy athletes. GLS and GRS showed no significant difference between the three groups, GCS was higher in athletic HCM compared to healthy athletes (-20.7 ± 2.2 vs $-17.8 \pm 2.3\%$).

CMR characteristics of athletic and sedentary HCM may fundamentally alter. Our preliminary data suggest that besides conventional CMR parameters, derived parameters such as EDWT/LVEDVi and LVM/LVEDV ratios and deformation imaging may also help the differentiation between pathological and physiological hypertrophy.

Figure 1: Feature tracking analysis of a healthy athlete and a patient with HCM.



Comparison of efficacy of different anticoagulation strategies used during pulmonary vein isolation in left atrial blood samples

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Citation:

Introduction: Ablation of atrial fibrillation is based on the isolation of the pulmonary veins (PVI) from the left atrium. Cerebral thromboembolism is a rare but serious complication of PVI, which highlights the importance of peri-procedural anticoagulation.

Aim: Studying the coagulation and endothelium activation during PVI in case of using different anticoagulation protocols.

Method: 52 patients undergoing PVI with cryoballoon technique were involved and were grouped according to three different pre-procedural anticoagulation strategies: in the first group patients received no anticoagulation before the procedure (non anticoag., 24 patients), in the second group patients received uninterrupted vitamin K antagonist therapy, and their INR value was in therapeutic range on the day of the procedure (VKA group, 11 patients) and in the third group patients were on uninterrupted dabigatran therapy (dabigatran group, 17 patients).

Two blood samples were taken during PVI from the left atrium, the first one before ablation or iv. heparin administration, the second one directly after the last application at the end of the procedure. The samples were used to measure D-dimer, plasmin antiplasmin (PAP) complex, a2 plasmin inhibitor (a2PI), plasminogen, FVIII activity, von Willebrand factor (VWF) antigen levels.

Results: D-dimer levels increased in all three groups after ablation, but in the samples of patients on dabigatran therapy we detected significantly lower D-dimer levels in the pre- and post-procedural samples compared to patients on other therapeutic strategies (median values before or after PVI: non anticoag.: 0.48 and 1.09 mgFEU/L; VKA: 0.33 and 0.72 mgFEU/L, dabigatran: 0.12 and 0.30 mgFEU/L, $p < 0.001$ non anticoag. vs. dabigatran, $p < 0.01$ VKA vs. dabigatran). PAP complex values were increasing parallel with D-dimer levels and only in the dabigatran group did not increase significantly. VWF antigen and FVIII activity increased significantly in all three groups after ablation, but there was no significant difference between the groups.

Conclusions: the safest anticoagulation strategy for patients undergoing PVI was uninterrupted dabigatran therapy. The extend of endothelial damage was not affected by anticoagulation.

The impact of epicardial collateral use on the outcomes of retrograde chronic total occlusion percutaneous coronary intervention

Authors:

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On behalf: PROGRESS CTO Investigators

Citation:

Background: The impact of the type of collateral vessel used on the outcomes of retrograde chronic total occlusion (CTO) percutaneous coronary intervention (PCI) has received limited study.

Methods: We reviewed the baseline clinical and angiographic characteristics and procedural outcomes of 1,501 retrograde CTO PCIs performed in 1494 patients between 2012 and 2019 at 26 centres.

Purpose: We sought to examine the impact of the type of collateral vessel used on the outcomes of retrograde CTO PCI.

Results: Mean patient age was 65.0 ± 10 years and 86% were men. Septal collaterals or bypass grafts were used in 66%, epicardial collaterals in 34% of lesions. Compared with cases in which only septal collaterals and bypass grafts were used, use of epicardial collaterals were associated with larger vessel diameter ($3.0 [2.5; 3.0]$ vs. $3.0 [2.5, 3.2]$ mm, $p=0.005$), more moderate/severe tortuosity (55% vs. 42%, $p<0.0001$), more moderate/severe calcification (73% vs. 65%, $p=0.002$), and higher Japan chronic total occlusion score (3.34 ± 1.02 vs. 3.11 ± 1.07 , $p<0.0001$). Epicardial collateral use was associated with lower technical (76.3% vs. 80.6%, $p=0.053$) and procedural (71.9% vs. 77.8%, $p=0.011$) success rates, but similar incidence of major cardiac adverse events (4.72% vs. 4.56%, $p=0.889$). Epicardial collaterals were associated with more perforations (10.63% vs. 7.30%, $p=0.028$). Epicardial collateral use was associated with longer fluoroscopy time (82 [64, 104] vs. 76 [55, 102] p=0.0003) and higher contrast volume (300 [221; 414] ml vs. 270 [200; 370] ml, $p<0.0001$).

Conclusion: In a contemporary, multicenter registry epicardial collaterals were used in approximately one-third of retrograde CTO PCIs. Use of epicardial collaterals was associated with lower success but similar major complication rates.

Figure 1. Procedural outcomes

Figure 1A. Technical, procedural success and major cardiac adverse events (MACE) according to the used collateral type

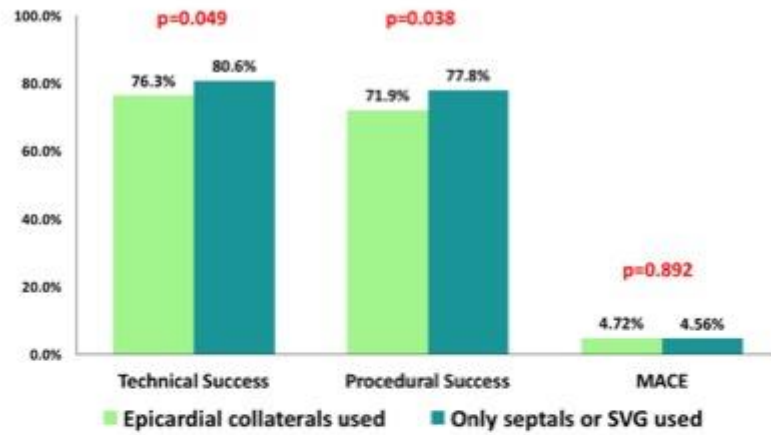
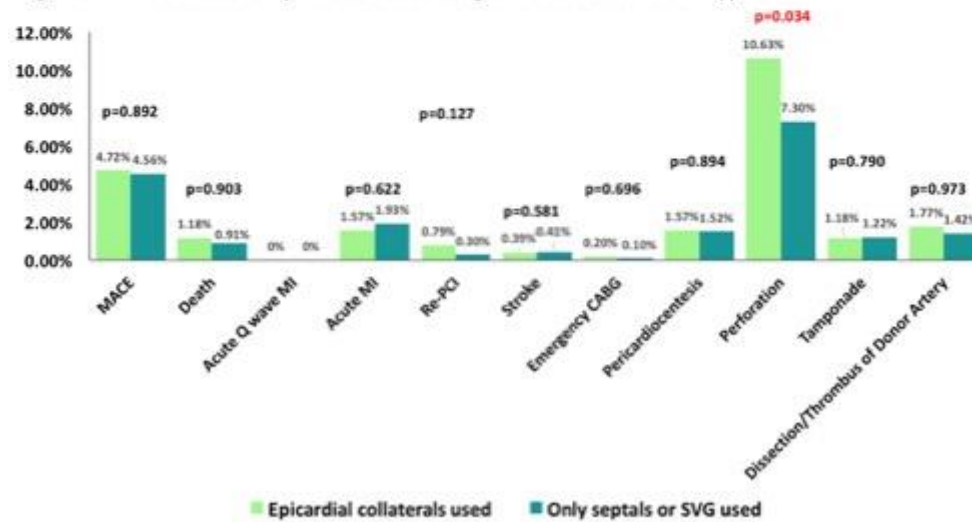


Figure 1B. Procedural complications according to the used collateral type



MACE: major cardiac adverse events; MI: myocardial infarction; CABG: coronary artery bypass grafting; Re-PCI: repeated percutaneous coronary intervention;

Pregnancy in congenital heart disease - risk stratification

Authors:

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Citation:

Introduction: Maternal congenital heart disease is a leading cause of peripartum maternal mortality, which is also associated with increased risk of fetal morbidity and mortality. We aimed to provide risk stratification for congenital heart disease patients using the recently introduced CARPREG (Cardiac Disease in Pregnancy) II score at our Institute. Patients and methods: We enrolled 191 pregnant women with congenital heart disease (mean age at pregnancy $29.2 \pm 5,7$ years). We recorded all foetal (premature birth, abortion, congenital heart abnormalities) and maternal (postpartum heart failure, stroke, hypertension) events in 276 pregnancies. High-risk pregnancy was defined as a CARPREG II score of ≥ 4 .

Results: High-risk pregnancy was detected in 14.1%. We found fetal and maternal events in 13.8 % and 14.5 % of all pregnancies, respectively, which both were more prevalent in the high-risk group ($p < 0.001$). No maternal death occurred, whereas premature birth and abortion was detected in 7.6 and 2.9 %, respectively, both complications were more frequent in the high-risk patient population as compared to the lower risk patients (30.8 vs. 7.2 %, $p < 0.001$). In univariate analysis, CARPREG II of ≥ 4 was significantly associated with fetal ($p < 0.001$, OR: 4.2) and maternal ($p < 0.001$, OR: 5.3) events. Risk factors of the CARPREG II were further analyzed using multivariate logistic regression analysis: prior cardiac events or arrhythmias ($p = 0.027$) and cyanosis ($p = 0.026$) were independent predictors of fetal complications. Left ventricular outflow tract obstruction ($p < 0.001$), cardiac interventions ($p = 0.024$) and prior cardiac events or arrhythmias ($p = 0.001$) demonstrated significant association with maternal events.

Conclusion: The CARPREG II could help in the identification of high-risk pregnancies and thus aids the selection of patients for strict monitoring and special therapies. In line with previous studies we detected higher rates of fetal and maternal events among patients with CARPREG II of ≥ 4 score.

Associations between atmospheric parameters and haemostatic factors: a case control study

Authors:

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Citation:

Background

One of the biggest health challenges in the 21st century is global climate change. The health effect of climate change is partly mediated through atmospheric parameters. There is a growing concern that atmospheric parameters might increase cardiovascular (CV) morbidity. Increased levels of haemostatic factors are predictors of CV events. The associations between CV diseases and atmospheric parameters have been widely reported, however there are few studies of atmospheric parameters' effects on markers of haemostasis.

Purpose

We examined the possible association between atmospheric parameters and several haemostatic markers.

Methods

The study consisted of 3800 hospitalized patients with acute CV diseases (ACVDs) and 260 healthy blood donors. We examined the relationship of haemoglobin (Hgb), white blood cells (WBC), thrombocytes (THR) and local atmospheric parameter conditions (temperature, atmospheric pressure, humidity, wind speed, atmospheric front) on a day-to-day basis in a 5-year period (2009-2013) using a General Additive Model with cubic splines of covariates, regularized by a ridge penalty, and employing generalized cross validation. Atmospheric parameters were allowed to have a lagged effect by up to 21 days.

Results

Among blood donors, the average of daily temperature lagged by 8-14 days had a significant effect on Hgb, exhibiting a U-shaped relationship, where higher Hgb values were associated with extremities of the observed temperature interval. For ACVD patients, all examined blood test variables has a significant association with at least some of the atmospheric parameters. Hgb was shown to have a negative linear relationship with mean daily humidity, and the average of daily temperature lagged by 15-21 days, while the average of daily temperature variation lagged by 2-7 days had highly non-linear effect. The relative strength of the association with Hgb was largest for daily temperature variation. WBC values had a slightly non-linear positive relationship with atmospheric pressure lagged by 1 day, with WBC being significantly increased above 1030 hPa. THR values decreased linearly with an increase in mean daily temperature averaged for days lagged 15-21. Atmospheric pressure lagged by 1 day also had a significant effect on THR, with a positive linear effect under 1010 and over 1020 hPa but no effect between. The relative effect of atmospheric pressure on THR was twice as large compared to temperature.

Conclusions

Our study showed that exposure to certain atmospheric parameters is associated with significant changes in haemostatic marker levels. In the

context of global climate change, the importance of focusing on atmospheric parameters as minor CV risk factor is substantially growing. A better understanding of the fluctuation of the examined markers, in light of atmospheric parameters, appears to be of particular importance for future studies and could help establish new CV prevention strategies.

Diagnostic performance of coronary computed tomography angiography-derived fractional flow reserve in patients with acute myocardial infarction and moderate non-culprit coronary stenosis

Authors:

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Citation:

Background:

Revascularisation of significant non-culprit coronary lesions (NCL) may improve clinical outcome in patients with myocardial infarction and multi vessel disease, however management of moderate NCLs is still controversial. Dobutamine stress echocardiography (DSE) and invasive fractional flow reserve (FFR) are accepted methods to detect myocardial ischemia, nevertheless coronary CT angiography-derived fractional flow reserve (CT-FFR) is a new modality, which has not been widely investigated to date in patients with NCLs.

Purpose:

Our aim was to determine the diagnostic performance of CT-FFR compared to DSE and invasive FFR.

Methods:

In this prospective trial, DSE, FFR and CT-FFR were performed in every patient with MI and at least one moderate NCL (30-70% diameter stenosis by visual assessment). New or worsening wall motion abnormality in at least two contiguous myocardial segments on DSE, and FFR value <0.8 in invasive FFR and CT-FFR as well were determined as abnormal. In comparison, DSE and FFR were regarded as reference standard methods.

Results:

Between March of 2017 and December of 2018, 51 patients (58.2±10.4 years, 74.5% male) were enrolled and 71 NCLs (40 LAD, 13 LCx, 18 RCA) were investigated. Dobutamine stress echocardiography, FFR and CT-FFR were positive in 30.9%, 32.3% and 22.5% of all lesions, respectively. FFR values were higher with CT-FFR compared to invasive FFR (0.85±0.11 vs. 0.83±0.08, p<0.05). Compared to DSE, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of CT-FFR were 40.9%, 85.7%, 56.2%, 76.3% and 71.8%, respectively. The same values were 39.1%, 85.4%, 56.2%, 74.5% and 70.4% compared to invasive FFR, respectively.

Correspondence of CT-FFR with DSE ($k=0.29$) and with FFR ($k=0.27$) was weak.

Conclusion:

This is the first study that compares the three modalities in the evaluation of moderate NCLs. Our results demonstrated moderate diagnostic accuracy, excellent specificity, poor sensitivity and PPV and acceptable NPV of CT-FFR compared to DSE and FFR. At this stage, CT-FFR is probably not accurate enough to determine revascularisation strategy of moderate NCLs as a single non-invasive method.

Subclinical myocardial dysfunction in pediatric kidney transplant recipients: a two-dimensional speckle-tracking echocardiography study

Authors:

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Citation:

Chronic kidney disease is associated with increased risk of cardiovascular mortality and morbidity in pediatric patients as well. Renal transplantation results in improved survival, however, several factors contribute to markedly elevated cardiovascular complication rate compared to the healthy population. While major cardiac events occur rarely in pediatric population, detection of subclinical changes in cardiac morphology and function may be of high interest to effectively identify high-risk patients.

Accordingly, our aim was to investigate left (LV)- and right ventricular (RV) morphology and function using conventional and two-dimensional (2D) speckle-tracking echocardiography (STE) in pediatric renal transplant recipients.

Our study group consisted of 41 kidney transplanted children (RTX; mean age: 14±3 years, m/f: 25/16) and 39 age- and gender matched healthy controls. Using 2D echocardiography, LV and RV focused apical loops were obtained and LV end-diastolic volume index (EDVi), ejection fraction (EF), mass index (Mi), RV end-diastolic area index (EDAi) and fractional area change (FAC) were measured. Using STE, we have determined LV global longitudinal (GLS) and circumferential strain (GCS), RV GLS, and LV and RV early diastolic longitudinal strain rate (LSrE).

LV EDVi did not differ between RTX and controls (51±13 vs. 52±10 mL/m², p=NS), while LVMI was markedly higher in RTX patients (36±8 vs. 28±6 g/m², p<0.0001). LVEF was comparable between the two groups (62±5 vs. 62±3%; p=NS), while LV GLS was significantly lower in RTX (-20.6±2.1 vs. -21.8±2.1%, p=0.01) along with a tendential increase in LV GCS (-31.6±4.3 vs. -29.7±4.6%, p=0.06). LV LSrE was significantly lower in RTX patients (1.29±0.29 vs. 1.45±0.27 1/s, p<0.05). RV EDAi did not differ between the two groups (11.2±2.3 vs. 11.6±2.0 cm²/m², p=NS). Interestingly however, RTX patients had significantly higher RV FAC and RV GLS (FAC: 46±7 vs. 42±4%, GLS: -24.6±3.7 vs. -22.4±2.6%, both p<0.01) along with lower RV LSrE (1.32±0.57 vs. 1.60±0.43, p<0.05).

Cardiac morphology and function shows distinct changes after RTX. Along with comparable ventricular dimensions, LV hypertrophy and subclinical systolic and diastolic dysfunction is present. RV systolic function is relatively increased accompanied by subclinical diastolic dysfunction of the chamber, which may refer to previous RV overload. STE may be a useful tool to reveal early myocardial dysfunction in pediatric kidney transplant recipients.

Cardiac magnetic resonance based feature-tracking myocardial strain analysis in MINOCA patients

Authors:

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Citation:

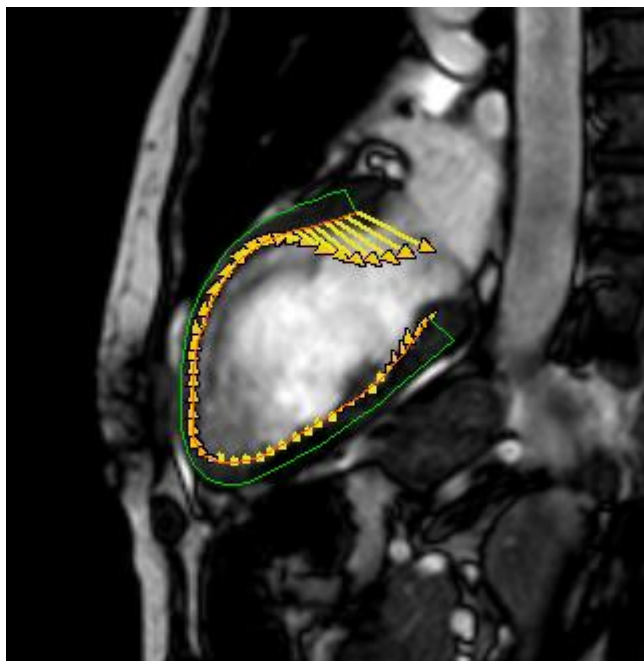
The diagnostic performance of cardiac magnetic resonance (CMR) based deformation imaging (feature tracking - FT) has been demonstrated in various groups of patients including acute myocardial infarction and acute myocarditis. However, the capability of this method to distinguish between patients with the working diagnosis of MINOCA is yet to be tested.

We aimed to compare standard CMR parameters and investigate the differential diagnostic value of CMR-FT myocardial strain in pts with the working diagnosis of MINOCA.

From our consecutive register of pts with troponin positive acute coronary syndrome (n=234 pts) we enrolled 100 pts (47.7±14 y;51 male) in this study. Twenty-five pts were selected randomly from each group of acute myocardial infarction (MI), acute myocarditis, Tako-Tsubo cardiomyopathy (TTC) and pts without structural alteration on CMR, and an additional group of healthy control (n=20, 46±8.2 y;12 male). Standard CMR parameters such as left ventricular ejection fraction (LVEF), end-diastolic (LVEDVi) and end-systolic (LVESVi) volumes, myocardial mass were assessed and compared between the groups. We performed CMR-FT analysis of the left ventricle, including: global longitudinal (GLS), circumferential (GCS), standard deviation (SD) of the peak circumferential (CS) strain furthermore mechanical dispersion (MD), defined as the SD of the time-to-peak circumferential (MDC) strain of the LV segments expressed as percent of the cardiac cycle.

LVEF was lower (44±9.1%) and LVESVi (52.5±12.9ml/m²) was higher in TTC pts compared to all other groups (p<0.001). The LVEF, LVEDVi and LVESVi parameters did not show significant difference between MI and myocarditis pts (LVEF 56.5±7% vs 55±6.6%; LVEDVi 85.4± 14.8 vs 92.7±10.7ml/m²; LVESVi 37.7±11.4 vs 41.5±9.1ml/m²). GLS and GRS were significantly reduced in TTC pts (-11.4±4.8%; 43.09±12.5%) compared to all other groups (p<0.001). GCS was impaired in pts with TTC, acute myocarditis and MI compared to healthy controls (-14±3.7 vs -18.7±3.7 vs -19.1±3.8 vs -23.2±3.1%, p<0.001), however there was no significant difference between myocarditis and MI pts. SD of the peak CS was lower in myocarditis compared to other groups (p<0.001). MDC was elevated in TTC and MI compared to myocarditis and healthy controls (16.3±5 vs 13.3±3.4 vs 8.1±3.3 vs 9.46±3.5% p<0.05). There was no significant difference between healthy controls and patients without structural alterations in any strain parameter.

Feature tracking analysis may enable differentiation between patients with MINOCA. TTC reduces global myocardial strain of the left ventricle and causes regional heterogeneity of the left ventricular contraction. Although standard volumetric CMR parameters and CMR based global strain values have limited capability to distinguish between MI and myocarditis with preserved ejection fraction, regional heterogeneity, expressible in MDC is significantly elevated in MI compared to myocarditis and healthy controls.



The effect of extracorporeal photopheresis on cardiac allograft rejection and on lymphocyte subclasses

Authors:

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Citation:

Background: Cardiac allograft rejection is known to have a profound impact on graft survival and mortality after heart transplant. Previous data on the efficacy of extracorporeal photopheresis (ECP) in the management of cardiac allograft rejection is encouraging. Though, clear evidence on the exact indication and data regarding its effect on distinct lymphocyte subtypes are still lacking. Based on their cytokine production, both helper and cytotoxic T cells can differentiate into either regulatory cells participating in the suppression of rejection or into effector cells responsible for its maintenance. Regulatory T cells are essential for the termination of rejection, while B lymphocytes and natural killer (NK) cells contribute to it.

Purpose: We aimed to investigate the anti-rejection efficacy and the impact of ECP on peripheral blood lymphocyte subclasses in adult heart transplant recipients.

Methods: In a retrospective analysis of 12 consecutive patients treated with ECP for cardiac allograft rejection between 2013 and 2019, we examined the grade of rejection in endomyocardial biopsies (EMB) based on the International Society for Heart and Lung Transplantation classification. We analysed the absolute counts and the percentages of helper, cytotoxic and regulatory T cells, B lymphocytes and NK cells with fluorescence activated cell sorting. Measurements were performed both before and after the ECP treatment period. Data values were given as either mean±standard deviation or median[*min-max*].

Results: The patients underwent 26[2-39] ECP treatments in addition to standard immunosuppressant therapy. Whereas grade 2R cellular rejection was detected in 83% of the cases prior to initiating ECP, none of the examined EMB specimen revealed rejection greater than grade 1R cellular rejection post ECP therapy. The average grade of cellular rejection improved significantly (1.25 ± 0.45 vs. 0.50 ± 0.53 ; $p=0.022$). The absolute count and the percentage of helper T cells increased significantly post ECP therapy ($0.34\text{ G/l}\pm 0.26\text{ G/l}$ vs. $0.51\text{ G/l}\pm 0.39\text{ G/l}$; $p=0.018$ and $3.43\%\pm 2.24\%$ vs. $5.98\%\pm 3.64\%$; $p=0.017$, respectively). There was also a significant rise in the percentage of cytotoxic T cells ($2.33\%\pm 1.46\%$ vs. $4.16\%\pm 2.98\%$; $p=0.027$). We noticed an almost significant twofold increase in the percentage of regulatory T cells on completion of the ECP therapy ($0.20\%\pm 0.22\%$ vs. $0.37\%\pm 0.20\%$; $p=0.060$). Neither B lymphocyte nor NK cell counts revealed any significant changes.

Conclusion: ECP was effective in reducing the severity of cardiac allograft rejection episodes. The significant decrease in rejection rates might be indicative of the predominance of anti-inflammatory helper and cytotoxic T cell subpopulations and the increase of regulatory T cell count post ECP therapy. However, discussion of the results are limited by small sample size and the effect of medical therapy on the lymphocytes.

Myocardial reverse remodeling occurs to a comparable extent in male and female aortic-banded rats following pressure unloading

Authors:

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Citation:

Background: Sex differences have been intensely investigated during the development of pressure overload (PO; e.g. aortic stenosis, arterial hypertension)-induced left ventricular (LV) myocardial hypertrophy (LVH). However, it is less clear whether sex-related differences also affect the regression of pathological LVH after pressure unloading.

Purpose: Therefore, we investigated the potential influential effect of sex on myocardial reverse remodeling in a relevant rat model of banding and debanding of the abdominal aorta.

Methods: PO of the left ventricle was induced in male (M) and female (F) rats by abdominal aortic banding (AB) for 6 or 12 weeks. Sham operated animals served as controls. Pressure unloading was evoked by removing the aortic constriction at week 6 (debanding). Serial echocardiography was performed to detect temporal alterations in LV morphology and geometry. Furthermore, distinct aspects of LV systolic and diastolic function were assessed by pressure-volume analysis. Structural changes, such as cardiomyocyte hypertrophy and interstitial fibrosis were measured on histological sections. Fetal gene expression (a molecular marker of pathological LVH) was analyzed by quantitative real-time PCR.

Results: In both male and female AB rats, PO induced the development of marked LVH as confirmed by increased LV mass, heart weight-to-tibial length ratio (HW/TL [g/cm]: 0.47±0.01 AB-M vs. 0.36±0.01 Sham-M, p<0.05; 0.36±0.02 AB-F vs. 0.26±0.01 Sham-F, p<0.05) and cardiomyocyte diameter. Similarly, reactivation of fetal gene expression (indicated by increased atrial natriuretic peptide [ANP]) and enhanced interstitial collagen accumulation was also observed in male and female AB groups as well. The extent of myocardial hypertrophy was greater among female AB animals, while fibrosis was more severe in male AB rats. In both genders, LVH was associated with prolonged ventricular relaxation (active relaxation time constant, Tau [ms]: 19.6±0.8 AB-M vs. 13.1±0.4 Sham-M, p<0.05; 15.2±1.3 AB-F vs. 12.2±0.3 Sham-F, p<0.05). However, systolic function was impaired only in males (ejection fraction, [%]: 44.4±2.3 AB-M vs. 57.5±2.1 Sham-M, p<0.05; 49.7±2.2 AB-F vs. 53.4±1.7 Sham-F, n.s.). Contrary to the sex-dependent differences during the development of LVH, removing the aortic constriction resulted in a comparable degree of reverse remodeling on the morphological (decreased LV mass, HW/TL), histological (decreased CD and interstitial fibrosis), molecular (reduced ANP expression) and functional (recovered ejection fraction and Tau) levels in both male and female rats.

Conclusion: Pressure unloading at a relatively early time point leads to myocardial reverse remodeling to a comparable degree in male and female rats.

The impact of meteorological parameters on the incidence of myocardial infarction

Authors:

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Citation:

Introduction: The changing of some meteorological parameters have major burden on the human body. That's why it became necessary to adopt to the altering conditions. The air temperature, atmospheric pressure have a significant influence on the patient's physical shape, blood pressure and response to stress.

The aim of our study was to assess the impact of the fronts and all the factors forming the weather at the same time on the incidence of myocardial infarction and its prognosis.

Methods: We performed a retrospective analysis on the data of 11820 consecutive patients surviving acute myocardial infarction between 2005 and 2014. We used to scales applied in meteorology to characterise the days (Péczy Scale, Front Scale). We studied the incidence of the values of the different scales 2 days before and after the infarction.

Results: We had a database of 11820 patients, STEMI (n=5183) and NSTEMI (n=6004). We created different subgroups (age, 30-day mortality, occurrence of primary ventricle fibrillation) to make our estimation. Considering non VF patients the effect of Front 3 whereas among VF positive patients Front 5 is more significant. The incidence rates of Front 3 one day before and on the day of the infarction in the non-VF and NSTEMI group is 0.2041 and 0.1735, in the non-VF and STEMI group it is 0.1939 two days before the event. The incidence rate of Front 5 on the -2nd day in the NSTEMI and VF positive group is 0.0357, it is 0.0714 among STEMI and VF positive patients on the day of the event. The influence of the approaching warm front is significant ($p < 0.05$).

Conclusion: The influence of the weather is not irrelevant in the occurrence of MI. The mortality rates are higher in several subgroups on days having a Péczy Scale 3. The different fronts have a major impact on the severity of the infarction. The Front 5 causes higher incidence of VF due to MI. We proved that warm fronts have a significant effect on patients dying within 30 days.

Perioperative shift in right ventricular mechanical pattern in patients undergoing mitral valve surgery: a predictor of right ventricular failure?

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Citation:

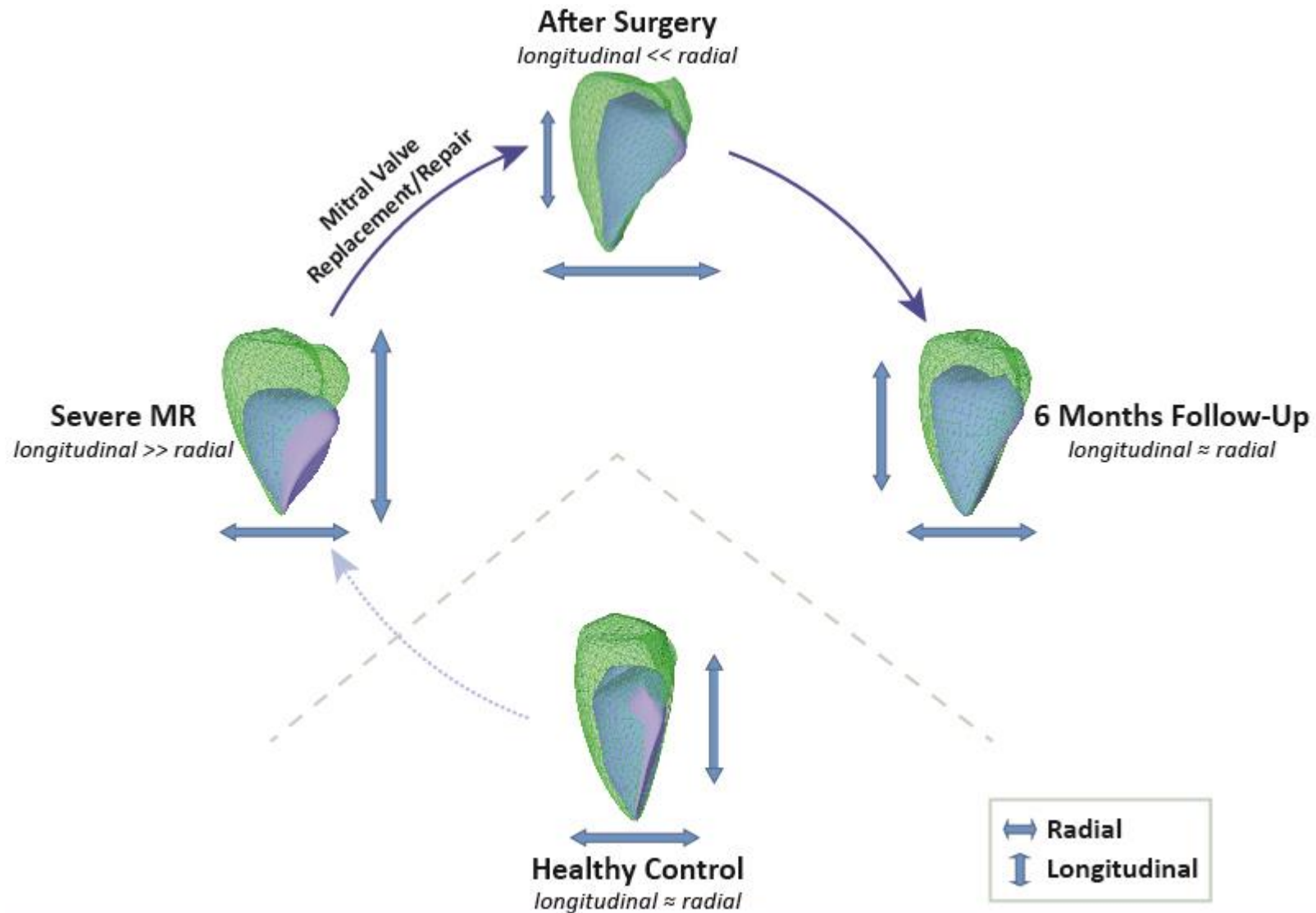
Background: Severe mitral regurgitation (MR) induces significant changes not only in the left, but also in the right ventricular (RV) morphology and function. Early treatment of MR is recommended, however, surgical procedure disrupts the native RV contractile pattern and predisposes the at-risk ventricle to develop postoperative RV failure (RVF) which is associated with poor outcomes.

Purpose: Accordingly, the PREPARE-MVR study (PREdiction of Early PostoperAtive Right vEntricular failure in Mitral Valve Replacement/Repair patients) aims to explore the alterations of RV contraction pattern in patients undergoing MVR and to investigate the association of preoperative echocardiographic findings with early postoperative RVF.

Methods: We prospectively enrolled 70 patients (62±12 years, 67% males) undergoing open heart MVR. Thirty age and gender matched healthy volunteers served as control group. Transthoracic 3D echocardiography was performed preoperatively and at intensive care unit discharge. Furthermore, focused 2D echocardiogram was also obtained during the ICU stay. Forty-three patients also completed 6 months follow-up. 3D model of the RV was reconstructed and end-diastolic volume index (EDVi) along with RV ejection fraction (RVEF) were calculated. For in-depth analysis of RV mechanics, we decomposed the motion of the RV to compute longitudinal (LEF) and radial ejection fraction (REF). Right heart catheterization was performed to monitor RV stroke work index (RVSWi).

Results: RV morphology as assessed by EDVi was unaffected by surgery (preoperative vs postoperative; 73±17 vs 71±16 mL/m², p=NS). RVEF was slightly decreased after MVR (52±6 vs 48±7 %, p<0.05), whereas RV contraction pattern has changed notably. Before MVR, the longitudinal shortening was the main contributor to global systolic function (LEF/RVEF vs REF/RVEF; 0.53±0.10 vs 0.43±0.12; p<0.001), whereas in controls the longitudinal and radial shortening contributed equally to RVEF (0.47±0.07 vs 0.43±0.09; p=NS). Postoperatively, the radial motion became dominant (0.35±0.08 vs 0.47±0.09; p<0.001). However, this shift was only temporary as 6 months later the contraction pattern became similar to controls showing equal contribution of the two components (0.44±0.10 vs 0.42±0.11; p=NS). Postoperative RVF (defined as RVSWi < 300 mmHg*mL/m² or ICU TAPSE < 10 mm) was detected in 14 [20%] patients. Preoperative LEF was associated with postoperative RVSWi (r=-0.61, p<0.001) and it was an independent predictor of postoperative RVF (OR=1.16 [1.03-1.35], p<0.05).

Conclusion: Severe MR induces a significant shift in the RV mechanical pattern which may influence the development of postoperative RV dysfunction and failure after MVR. Advanced indices of RV mechanics are associated with invasively measured parameters of RV contractility and may predict postoperative RVF.



Right ventricular mechanics in healthy controls and patients undergoing surgical treatment of severe organic mitral regurgitation (MR)

Uninterrupted and minimally-interrupted direct oral anticoagulant therapy in patients undergoing catheter ablation for atrial fibrillation. An updated meta-analysis

Authors:

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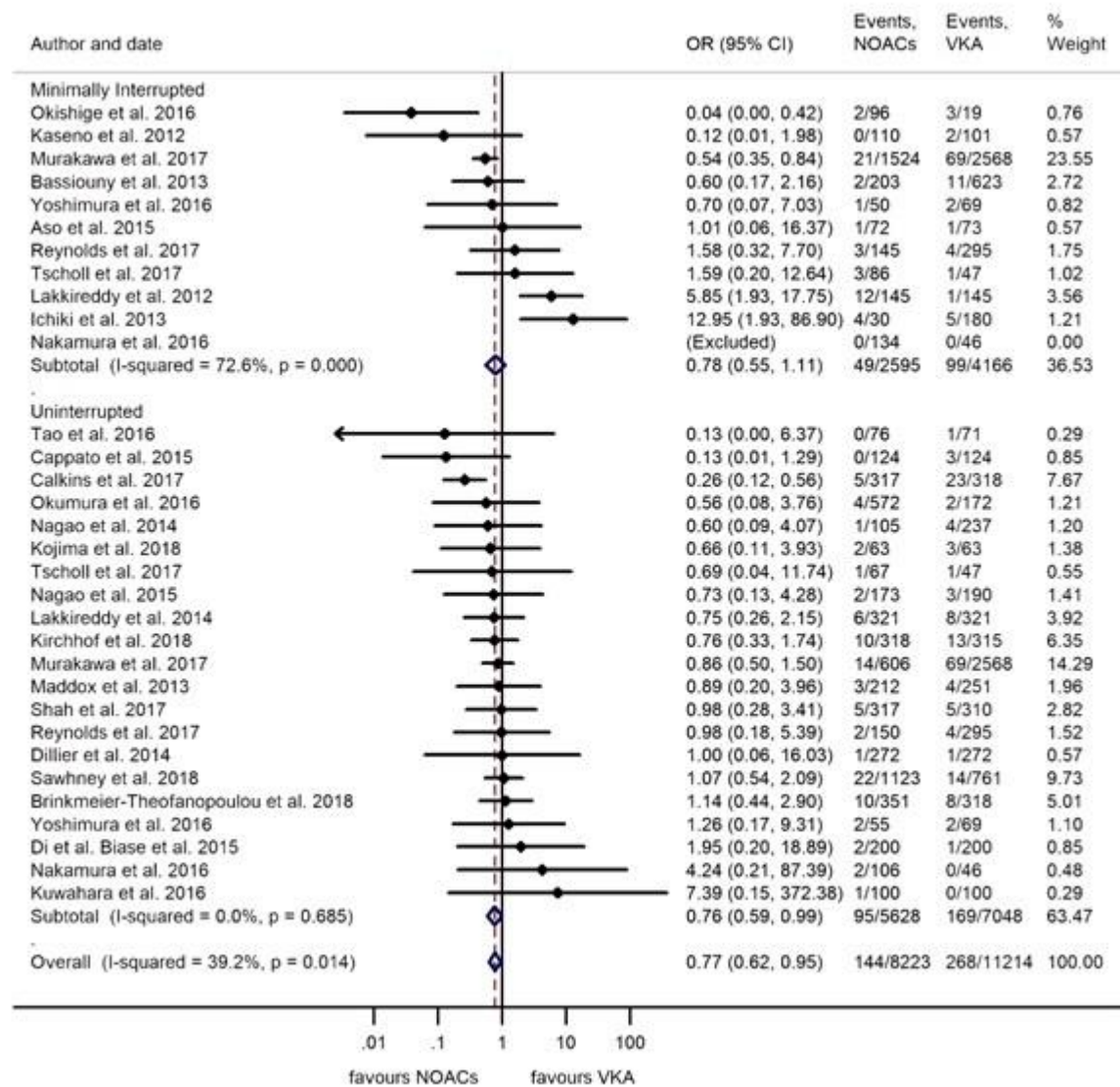
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Background: Adequate anticoagulation in catheter ablation of atrial fibrillation (AF) is crucial in preventing both thromboembolic events and life-threatening bleeding. As clinicians gain more experience and reassurance with data from clinical trials, the usage of Direct Oral Anticoagulants (DOAC) in patients undergoing catheter ablation of AF has rapidly increased over the last years. The purpose of this updated meta-analysis was to assess the latest evidence and compare the safety and efficacy of uninterrupted and minimally interrupted periprocedural DOAC anticoagulation protocols with uninterrupted Vitamin K Antagonists (VKA) in this setting.

Methods: Randomized or prospective controlled observational studies comparing DOACs to VKAs were identified with multiple databases (Embase, PubMed, Cochrane, and Scopus). Uninterrupted and minimally interrupted DOAC (single dose of dabigatran or apixaban withheld) were distinguished, VKA therapy was always uninterrupted. The primary outcomes were stroke or transient ischemic attack (TIA), major bleeding, and net clinical benefit.

Results: 32 studies were included in the final analysis, encompassing a total of 19.437 patients. The incidence of thromboembolic events was rare (less than 0.2%), with no significant difference between groups. Occurrence of major bleeding and net clinical benefit were significantly improved in patients assigned to uninterrupted DOAC treatment compared to VKAs (1.5% vs 2.2%, POR: 0.74, CI: 0.56-0.98, I²=0,0% and 1.7% vs 2.4%, POR: 0.76; CI: 0.59-0.99, I²=0,0%, respectively).

Conclusion: This updated meta-analysis, based on a large database, showed that DOAC therapy is equally effective as VKA in preventing stroke and TIA. Minimally-interrupted DOAC therapy is a non-inferior peri-procedural anticoagulation strategy, however, uninterrupted DOAC therapy showed superiority when compared to VKA regarding major, life-threatening bleeding. Our findings showed that uninterrupted periprocedural DOAC therapy is a safe and preferable alternative to VKAs in patients undergoing catheter ablation for atrial fibrillation.



Role of BGP-15 treatment in hypertensive heart failure progression and mitochondrial protection

Authors:

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Citation:

Introduction: The deterioration of mitochondrial quality control greatly contributes to the hypertension induced cardiac remodeling and progression of heart failure. Our previous in vitro results demonstrated the mitochondrial protective effect of antioxidant BGP-15 compound in the presence of cellular stress.

Purpose: In our recent study we investigated the effect of BGP-15 on cardiac remodeling in spontaneously hypertensive rats (SHR) with manifested heart failure and on mitochondrial dynamics and function in cell culture model.

Methods: 15-month-old male SHR received 25 mg/kg/day BGP-15 (SHR-B) or placebo (SHR-C) for 18 weeks. Age matched Wistar rats (WKY) were used as normotensive control. The heart function was monitored by echocardiography. Histological preparations were made from cardiac tissue. Neonatal rat cardiomyocytes (NRCMs) were used as in vitro model. 150 μ M H₂O₂ stress and 50 μ M BGP-15 treatment was applied. Mitochondrial network was stained with MitoTracker Red. Mitochondrial membrane potential was detected using JC-1 dye, while mitochondrial function was monitored by the Agilent Seahorse XFp, Cell Mito Stress Test. In both model the cellular levels of mitochondrial dynamics proteins were measured in Western blot. To study the ultrastructure we used electron microscopy in our in vivo and in vitro model.

Results: Left ventricular (LV) mass and LV wall thickness were increased significantly in SHR-C group compared to the initial values ($p < 0.05$). These parameters were decreased considerably in the SHR-B group. Ejection fraction (EF%) decreased in both SHR group although this downturn was minimal because of the treatment. Chronic high blood pressure caused higher collagen deposition in SHR-C rats that was significantly diminished in the SHR-B group. Regarding the mitochondrial function decrease in the levels of fusion proteins OPA1 and MFN2 was observed in the SHR-C group. These differences were significantly reduced by BGP-15 treatment ($p < 0.05$). Mitigation of the level of fission protein DRP1 was however reduced by BGP-15 ($p < 0.05$). In our cellular model, we observed that the H₂O₂-induced mitochondrial fragmentation was decreased by BGP-15 treatment ($p < 0.05$). BGP-15 treatment prevented mitochondrial membrane potential fall in H₂O₂ stress ($p < 0.05$). There was no significant difference in basal respiration among groups by monitoring the mitochondrial function. The maximal respiration capacity and ATP production were significantly higher in the BGP-15 treated group in comparison to the stressed group ($p < 0.05$).

Conclusion: BGP-15 treatment has beneficial effects on mitochondrial dynamics and structure by promoting fusion processes. It also supports the maintenance of mitochondrial function through the preservation of the mitochondrial structure. The mitigation of remodeling processes and the preserved EF in the treated group are results at least partly of the comprehensible effects of BGP-15 on mitochondrial structure and function.

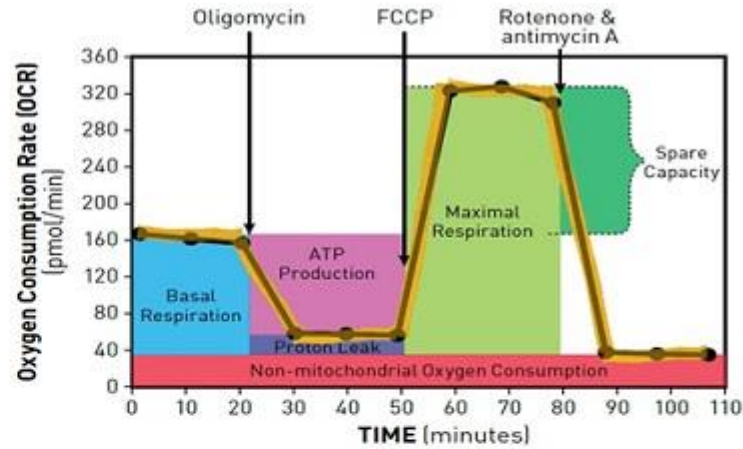
ECHOCARDIOGRAPHIC PARAMETERS

	SHR Control group (n=15)		SHR BGP-15 treated group (n=15)	
	Start	End	Start	End
	Mean ± SEM	Mean ± SEM	Mean ± SEM	Mean ± SEM
Septum	2,31 ± 0,137	2,32 ± 0,073	2,32 ± 0,084	2,087 ± 0,078 * ¥
Post wall	2,088 ± 0,121	1,9675 ± 0,08	2,027 ± 0,061	1,811 ± 0,072
LVIDd (mm)	7,625 ± 0,314	8,55 ± 0,234	7,857 ± 0,104	8,314 ± 0,175
LVIDs (mm)	4,345 ± 0,455	5,865 ± 0,311	4,81 ± 0,186	5,194 ± 0,323
LVEDV (µl)	313,081 ± 30,593	402,40 ± 24,767	331,63 ± 9,778	377,187 ± 17,369
LVESV (µl)	92,12 ± 24,952	175,52 ± 22,469	109,549 ± 9,557	137,229 ± 16,466
LV mass (mg)	1359,88 ± 60,845	1587,375 ± 106,361 ¥	1405,45 ± 57,840	1321,442 ± 75,584 * ¥
EF%	72,56 ± 4,18	57,206 ± 3,021 ¥	67,038 ± 2,660	64,298 ± 2,879 ¥
E/A	1,643 ± 0,085	2,015 ± 0,258	1,885 ± 0,435	1,27 ± 0,08
E'/A'	1,46 ± 0,111	1,113 ± 0,128	1,4942 ± 0,237	1,892 ± 0,298
E/E'	25,425 ± 1,733	40,409 ± 2,939 ¥	34,514 ± 4,959	25,708 ± 3,025 * ¥

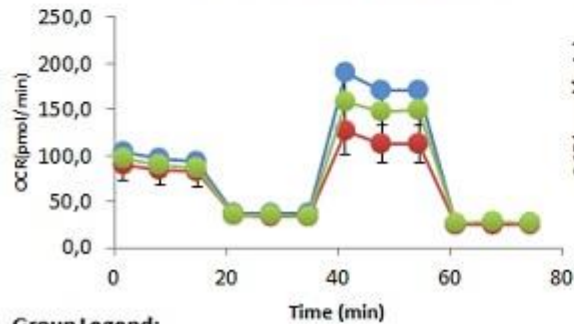
p<0.05 vs SHR Control group Start
 * p<0.05 vs SHR BGP-15 treated group Start
 ¥ p<0.05 vs SHR Control group End

Seahorse XF Cell Mito Stress Test Profile

Mitochondrial Respiration

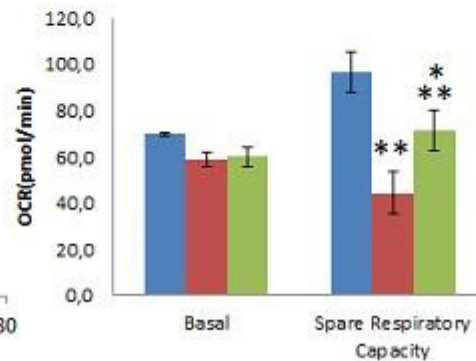


Mitochondrial Respiration

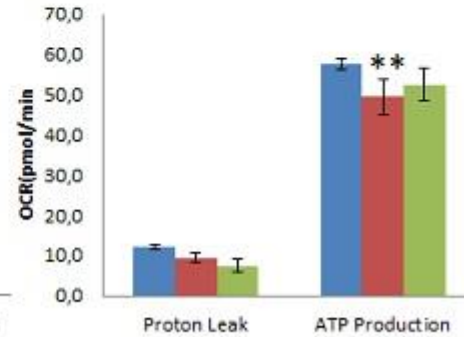


Group Legend:

■ Control ■ 150 µM H₂O₂ ■ 150 µM H₂O₂ + 50 µM DGP15



* p<0.05 vs H₂O₂ group
 ** p<0.05 vs Control group (n=5)



** p<0.05 vs Control group (n=5)

The specific characteristics and independent predictors of no-reflow phenomenon, development of a clinically-adaptable risk estimation system

Authors:

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Citation:

Introduction: No-reflow (NR) phenomenon occurs, when myocardial perfusion is not re-established despite opening the coronary artery during percutaneous coronary intervention (PCI).

Purpose: Our aim was to identify no-reflow specific characteristics, its independent predictors, and to develop a clinically-adaptable risk score.

Methods: We have analysed 4085 patient data from two Hungarian cardiovascular centres. We included all STEMI/NSTEMI patients underwent PCI (n=3187). 158 patients treated with papaverine/adenosine formed NR group, while 3029 patients were in control (C) group. Anamnestic parameters, laboratory and operation data were compared. Statistical analysis was carried out with Mann-Whitney-, Fisher test, binary logistic regression and Kaplan Meier survival curve. Based on our results, we designed a risk estimation system, checking its applicability with ROC analysis.

Results: As for NR-specific characteristics, malignant ventricular arrhythmias (11% vs. 4%, p=0,0031; NR-C consequently) and complications (21% vs. 11%, p=0,064) showed their vulnerability. The increment of glucose (8,1 vs. 7,1 mmol/l, p=0,004), WBC (12,08 vs. 10,5 G/l, p=0,001), CRP (12,46 vs. 7,67 mg/l, p=0,051) and LDL levels (3,34 vs. 3,13 mmol/l, p=0,059) supported the pathomechanism of NR. Higher biomarker levels (troponinT: 2040 vs. 510,5 ng/ml; CK-MB: 100,4 vs. 63,65 U/l, p<0,0001) indicated severe perfusion disturbance. Tendency was seen in higher BMI (28,65 vs. 28,03 kg/m², p=0,12). STEMI dominated in NR (83 vs. 59%, p<0,0001). Lower platelet level (213,3 vs. 228 G/l, p=0,107) and single vessel disease (46 vs. 25%, p=0,0042) characterized NR.

30-day survival was significantly different (85,1 vs. 93,54%, p<0,0001). The mortality rate of NR in STEMI was 69,7% (69,7% vs. 7,94%, p<0,0001) and in NSTEMI 3,7% (3,7% vs. 4,32%).

From the significant differences, CRP was the independent predictor of NR (OR:1,011, p=0,004; pro 1 mg/l change). Examining STEMI/NSTEMI separately, in STEMI CRP was the independent predictor (OR:1,0092, p=0,036). In NSTEMI LDL (OR:4,23, p=0,021) was the independent factor.

In the risk score, the following 8 parameters were included: BMI>28 kg/m², glucose>8 mmol/l, WBC>12 G/l, CK-MB>100 U/l, hs troponin T>2000 ng/ml, CRP>12 mg/l, LDL>3,3 mmol/l, STEMI (yes/no), thus maximum 8 points could be reached. Low (0-1 points, 5-20%), moderate (2-5 points, 55-70%) and high risk groups (6-8 points, 41-11%) were formed. Supervising the model with ROC analysis: AUC=0,69, p=0,0026, which indicates its ability to discriminate effectively between different risk levels of NR.

Conclusions: The specific characteristics of NR group were identified, from which CRP was the independent predictor - as well as in STEMI, while in NR-NSTEMI LDL was the independent factor. With the elaborated risk estimation system –using anamnestic and routine laboratory parameters– NR could be predicted and unsuccessful PCI could be reduced, resulting in positive therapeutic consequences.

Atmospheric front patterns and acute cardiovascular diseases, a new perspective in the cardiovascular threat of global climate change

Authors:

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Citation:

Background:

There is substantial evidence that the health threat of global climate change is real and it could be a medical emergency. The impact of climate change on health is mediated through atmospheric parameters which are direct environmental stressors on the human body and have a potential cardiovascular (CV) morbidity and mortality effect. Acute cardiovascular diseases (ACVDs) are already major public health issues and in the future unfavourable atmospheric situations, such as increasingly volatile fronts and their negative effects can further increase this problem. Despite evidence about the importance of different atmospheric parameters on health outcomes, there have been few results for atmospheric front patterns' CV effects. Weather fronts are the most complex atmospheric phenomena therefore these atmospheric parameters might have the greatest influence on ACVDs.

Purpose:

We aimed to explore the effects of atmospheric front patterns on ACVDs.

Methods:

A time series Poisson-regression analysis was used to analyse 6499 ACVD hospital admissions, during a five-year period (2009-2013), in light of front patterns. Covariates were three-day (target day and the two previous days) front sequence patterns comprised of the five major front types (no front, warm front, occluded front, cold front, stationary front). Relative risk (RR) estimates for front effects were adjusted for seasonality. The relationship on all ACVDs combined and separately on patient groups by major CV risk factors (hypertension, hyperlipidaemia, diabetes, previous CV diseases) was examined.

Results:

We found that in general, front patterns containing warm front days had a detrimental effect. A warm front, when followed by two days with no fronts present, increased RR by 46% (CI: 4-89%, $p=0,015$). Cold fronts however were protective. A no front – cold front – occluded front pattern corresponded to a 28% (CI: 8-49%, $p=0,037$) decrease in RR, with this pattern being present in 1.1% of all days of the study period. Out of the group specific results an occluded front, following days with no fronts present, showed to have the largest effect on hyperlipidaemic patients, increasing RR by 144% (CI: 51-295%, $p<0.001$).

Conclusions:

This work provides both independent evidence of front patterns' CV effects and a novel tool to investigate and help the understanding of complex associations between atmospheric fronts and ACVDs. The importance of our findings is growing in the context that extreme atmospheric conditions and changes are likely to become more common in the future as a result of climate change. Medical meteorology may open up a new horizon and become an important field of preventive cardiology in the future. In conclusion, a better understanding of atmospheric front effects is of particular importance in order to help identify possible targets for future prevention strategies.

CTEPH patients long term follow-up: results from a single center

Authors:

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Citation:

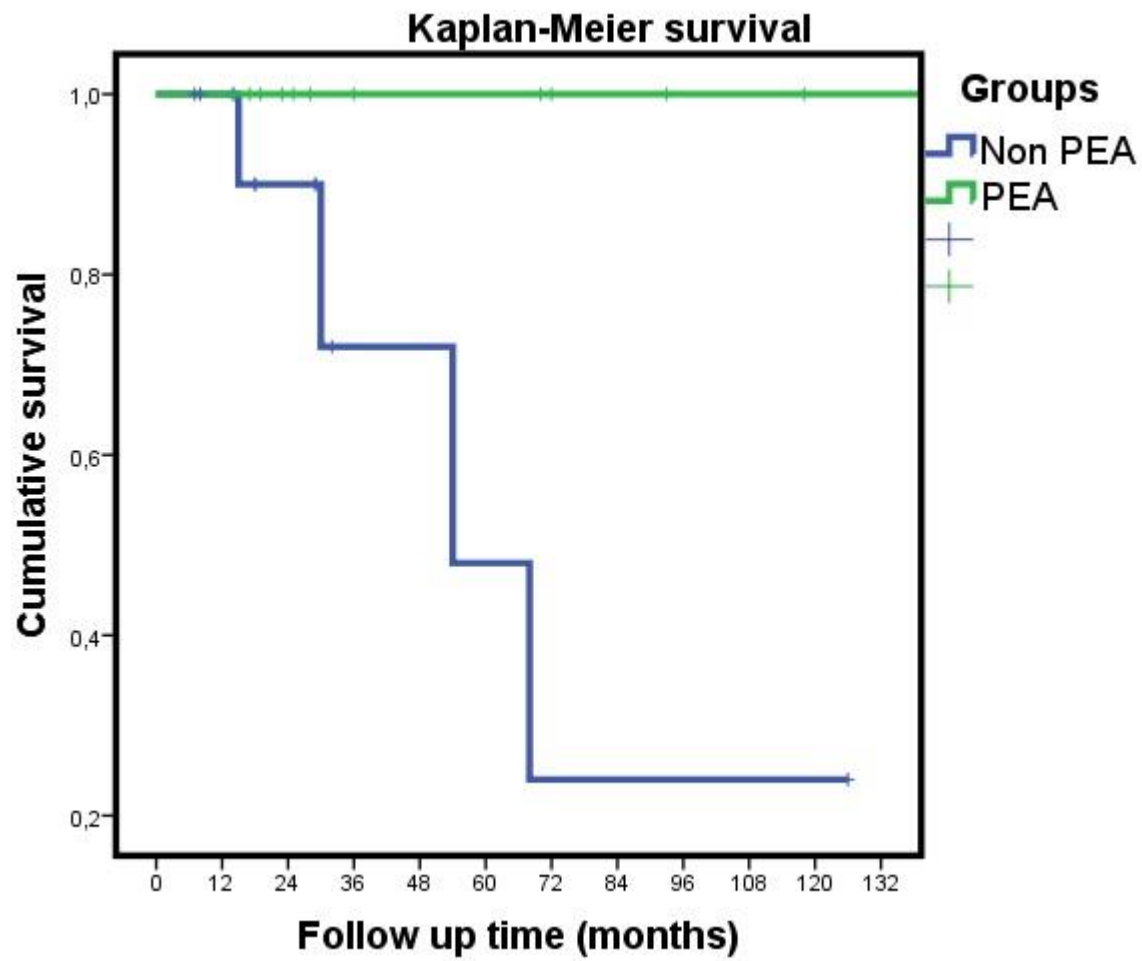
Background: Chronic thromboembolic pulmonary hypertension (CTEPH) is a thrombotic pulmonary disease associated with pulmonary vasculopathy. Pulmonary endarterectomy (opus, PEA) is the first treatment choice in CTEPH, and specific PAH medication when there is a contraindication for surgery or residual pulmonary arterial hypertension (rPAH) occurs. In the presence of PAH balloon pulmonary angioplasty (BPA) might be also recommended if available.

Objective: We investigated the long term outcome of our CTEPH patients.

Methods: CTEPH from our institution retrospectively analyzed (data between 2003 and 2018). Baseline, treatment and outcome data were documented. We compared the outcome, together with mortality in those with and without surgery (PEA vs. non PEA group). NYHA class, 6 minutes walking distance (6MWD) and NT-proBNP were also reported during follow-up.

Results: Of 29 CTEPH patients (mean age was 62±19 years, 52% male) 16 (55%) were accepted for PEA, and further 12 of them had a long term follow-up post surgery (n=3 periop exit, n=1 waiting for surgery). Half of the PEA patients were cured (n=6) and the other half (n=6) required specific PAH treatment (n=1, in combination with BPA) for rPAH. All patients from the non-PEA group (n=13) were started on specific PAH treatment (n=1 in combination with BPA). Patients with or without PEA did not differ hemodynamically. At the late follow-up there was a significant improvement in PEA group for NYHA class and NT-proBNP (p<0,001, and p=0,046), and in non PEA group for NYHA class and the 6MWD (p=0,012, and 0,006). We found significant difference in mortality at 1,3,5 year (Kaplan-Meier survival analysis) follow-up, for PEA group 100%-100%-100% and non PEA group 100%-85%-78% (p=0,013), respectively.

Conclusions: 55% of CTEPH patients were suitable for PEA, and those who survived the surgery 50% were cured. Non PEA patients improved functionally on the long term, but had worse survival.



Survival prediction in patients undergoing cardiac resynchronization therapy: a machine learning based risk stratification system

Authors:

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Citation:

Background: Cardiac Resynchronization Therapy (CRT) has well-known beneficial effects in patients with advanced heart failure, reduced ejection fraction and wide QRS complex. However, mortality rates still remain high in this patient population. Therefore, precise risk stratification would be essential, nonetheless, the currently available risk scores have several shortcomings which hamper their utilization in the everyday clinical practice.

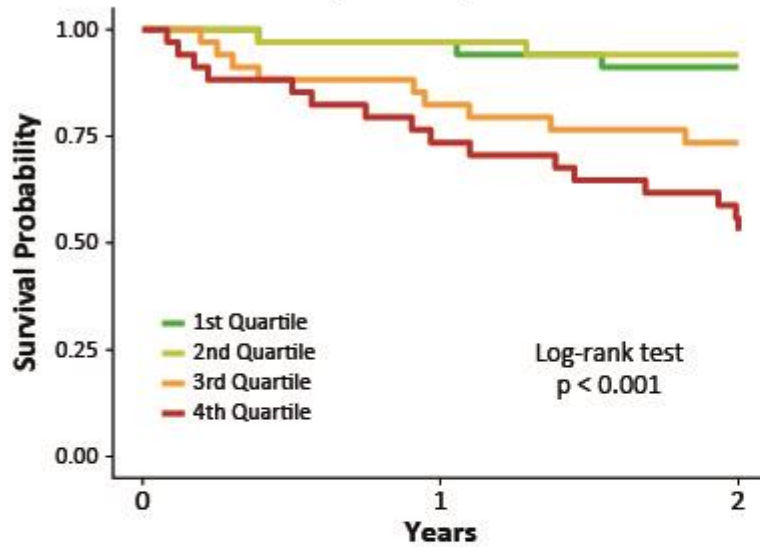
Purpose: Accordingly, our objective was to design and validate a machine learning based risk stratification system to predict 2-year and 5-year mortality from pre-implant parameters of patients undergoing CRT implantation.

Methods: We trained two models separately to predict 2-year (model 1) and 5-year mortality (model 2). As training cohort of model 1 we used 1678 patients (67±10 years, 1251 [75%] males) undergoing CRT implantation. From this population, 1320 patients (66±10 years, 1005 [76%] males) also completed 5-year follow-up and they served as the training cohort for model 2. Forty-seven pre-implant parameters (demographics, cardiovascular risk factors and clinical characteristics) were used to train the models. Our models were designed in a way to tolerate missing values. Among non-linear classifiers, random forest demonstrated the best performance. We validated our models, along with the Seattle Heart Failure Model (SHFM), VALID-CRT risk score and EAARN score on an independent cohort of 136 patients (66±10 years, 110 [81%] males). Based on the predicted probability of survival, patients were split into quartiles and survival was plotted via Kaplan-Meier (KM) curves.

Results: There were 358 (21%) deaths in the 2-year, 697 (53%) deaths in the 5-year training cohort. In the validation cohort, there were 30 (22%) deaths at 2 years and 58 (43%) deaths at 5 years after CRT implantation. For the prediction of 2-year mortality, the Area Under the Receiver-Operating Characteristic Curve (AUC) for model 1 was 0.77 (95% CI: 0.67-0.87; p=0.002), for SHFM was 0.54 (95% CI: 0.39-0.69; p=0.006), for EAARN was 0.57 (95% CI: 0.46-0.68, p=0.002), and for VALID-CRT was 0.62 (95% CI: 0.52-0.71; p=0.002). To predict 5-year mortality, the AUC for model 2 was 0.85 (95% CI: 0.78-0.91; p=0.001), for SHFM was 0.62 (95% CI: 0.51-0.74; p=0.003), for EAARN was 0.61 (95% CI: 0.51-0.70, p=0.002), for VALID-CRT was 0.65 (95% CI: 0.56-0.74; p=0.002). The AUCs of the machine learning based models were significantly higher than the AUCs of the pre-existing scores (DeLong test, all p<0.05). The KM curves of the quartiles were significantly separating in both models (Log-rank test, both p<0.001).

Conclusion: Our results indicate that machine learning algorithms can outperform the already existing linear model based scores. By capturing the non-linear association of predictors, the utilization of these state-of-the-art approaches may facilitate optimal candidate selection and prognostication of patients undergoing CRT implantation.

Quartiles based on probabilities
predicted by the 2-year Random Forest model
/Model 1/

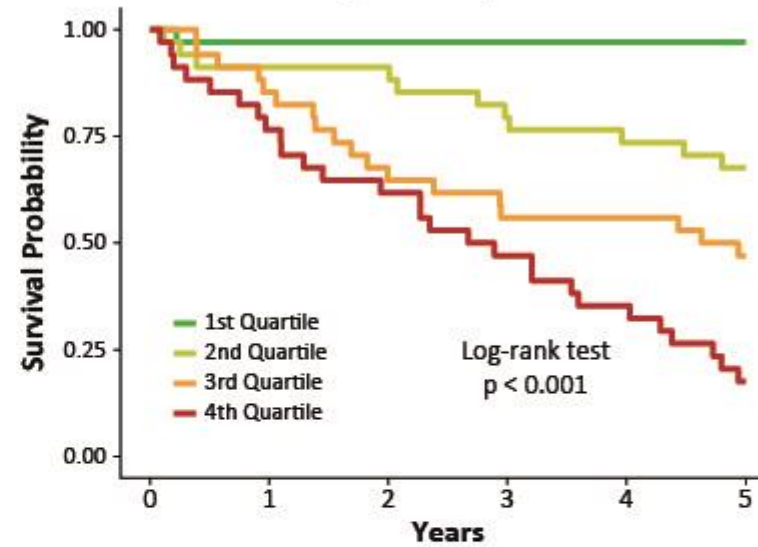


Number of patients at risk			
	0	1	2
1st Quartile	34	33	31
2nd Quartile	34	33	32
3rd Quartile	34	28	25
4th Quartile	34	25	19

Years

	Hazard Ratio	95% Confidence Interval	p
2nd vs. 1st Quartile	0.67	0.11 – 3.99	NS
3rd vs. 1st Quartile	3.36	0.91 – 12.42	NS
4th vs. 1st Quartile	6.74	1.96 – 23.16	<0.01

Quartiles based on probabilities
predicted by the 5-year Random Forest model
/Model 2/



Number of patients at risk						
	0	1	2	3	4	5
1st Quartile	34	33	33	33	33	33
2nd Quartile	34	31	31	27	25	23
3rd Quartile	34	29	22	19	19	16
4th Quartile	34	26	21	16	12	6

Years

	Hazard Ratio	95% Confidence Interval	p
2nd vs. 1st Quartile	12.57	1.62 – 97.47	<0.05
3rd vs. 1st Quartile	23.94	3.19 – 179.80	<0.01
4th vs. 1st Quartile	53.83	7.26 – 398.90	<0.001

The added value of cardiac magnetic resonance to the diagnosis of patients after aborted sudden cardiac death

Authors:

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Citation:

Introduction: An estimated 25% of all cardiovascular deaths are due to sudden cardiac death (SCD). The primary cause of SCD is coronary artery disease, however cardiac diseases accounted for SCD differ in young vs. older individuals. In patients with normal coronary angiography (NCA) the differential diagnosis is still challenging, due to the broad spectrum of underlying cardiovascular abnormalities. Cardiac magnetic resonance (CMR) provides accurate tissue specific and functional information of the heart.

Purpose: We aimed to investigate patients after aborted sudden cardiac death but NCA using cardiac magnetic resonance imaging (CMR). Our goal was to evaluate left and right ventricular parameters, presence of late gadolinium enhancement (LGE) and to assess the diagnostic value of CMR.

Methods: We enrolled 84 consecutive patients (39±13 y; 51% male) after aborted SCD with NCA and without CMR contraindication. CMR examination including long- and short-axis cine, T2-weighted and LGE images were performed. Left and right ventricular parameters were evaluated. Presence and pattern of the oedema and LGE were also assessed.

Results: Structural myocardial abnormality was present in 57% of pts: dilated (n=13), arrhythmogenic right ventricular (n=6) and hypertrophic (n=4) cardiomyopathy (CMP), moreover acute (n=2) and chronic (n=3) myocardial infarction, acute (n=2) and chronic (n=2) myocarditis, Tako-Tsubo CMP (n=1), noncompaction CMP (n=1), endomyocardial fibrosis (n=1). In 13 cases aspecific structural alterations were detected with (n=7) and without (n=6) LGE. Only 13% of the patients showed ejection fraction lower than 35% (LVEF=52±9%), 54% showed LV dilation (LVEDVi>100 ml/m² in males and >90 ml/m² in females; LVEDVi=104±22 ml/m²). LGE was present in 36%, showing ischemic pattern in five cases and nonischaemic pattern in 25 cases. Eleven patients were elite athletes (28±10y, 91% male, training hours: >10 hours/week). Three of them showed ARVC based on the current Task Force criteria, another three athletes showed aspecific structural alteration with nonischaemic LGE.

The CMR examination confirmed the referral diagnosis in 22%, excluded the presence of structural myocardial alteration in 43% and changed the clinical diagnosis in 35% of the patients.

Conclusion: CMR has an important diagnostic value in patients after reanimation but NCA. More than half of these patients showed structural alteration and CMR provided a diagnosis in 42%.

Differentiation between arrhythmogenic right ventricular cardiomyopathy and athlete's heart using cardiac magnetic resonance based derived parameters and strain analysis

Authors:

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Citation:

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a major cause of sudden cardiac death in young athletes. However diagnosing ARVC in highly trained athletes may be complicated because of overlapping features such as elevated right ventricular (RV) end-diastolic volume index or T-wave inversion in precordial leads. The revised Task Force criteria contain no specific cut-off value for professional athletes. Additional CMR parameters and CMR deformation imaging may have an added diagnostic value in this special patient population.

Our goal was to determine novel CMR parameters which can help to distinguish between ARVC and athlete's heart. CMR examination of ARVC patients with definite diagnosis based on the revised Task Force criteria (n=34; 41±13 y, 22 male) and healthy professional athletes (members of the Hungarian national water polo, canoing or rowing team performing minimum of 15 hours of training per week, n=34, 32±6 y, 22 male) was performed. We evaluated left and right ventricular end-systolic, end-diastolic (EDVi) and stroke volume index, ejection fraction (EF) and mass. We established derived parameters such as ejection fraction ratio (LVEF/RVEF) and end-diastolic volume ratio (LVEDV/RVEDV). Global and regional strain analysis for the right ventricle was performed using feature tracking technique. Area under the ROC curves (AUC) of conventional and derived CMR parameters and CMR based strain values were analysed.

There was no significant difference between RVEDVi of ARVC patients and athletes (124 ± 17 vs 142 ± 47), RVEF was lower in ARVC patients compared to athletes (56±5 vs 41±14%; p<0.001). Significant differences were found between athletes and ARVC patients in LVEDV/RVEDV (0.96±0.08 vs 0.82±0.23), LVEF/RVEF (1.04±0.06 vs 1.41±0.56), global circumferential strain (-34.8±5.9 vs -25.2±12.2) and regional strain values such as midventricular RV strain (-31.5 ± 10.2 vs -20.0 ± 13.4) or midventricular RV strain rate (-1.37 ± 0.56 vs -1.04 ± 0.68), respectively.

RVEF and LVEF/RVEF showed excellent (AUC of 0.9-1.0), RV global strain and RV midventricular strain values showed good diagnostic accuracy (AUC of 0.8-0.9), while RVEDVi showed poor diagnostic accuracy (AUC of 0.59).

Consequently, in highly trained healthy athletes RVEDVi is in the range of major Task Force criteria, while CMR based derived parameters such as LVEDV/RVEDV or LVEF/RVEF and both global and regional RV strain parameters can be useful parameters in the differential diagnosis.

Radiomics-based machine learning versus histogram analysis and visual assessment to identify advanced atherosclerotic lesions on coronary computed tomography angiography

Authors:

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Citation:

Background:

Currently used coronary CT angiography (CTA) plaque classification and histogram-based methods have limited accuracy to identify advanced atherosclerotic lesions. Radiomics-based machine learning (ML) could provide a more robust tool to identify high-risk plaques.

Purpose:

Our objective was to compare the diagnostic performance of radiomics-based ML against histogram-based methods and visual assessment of ex-vivo coronary CTA cross-sections to identify advanced atherosclerotic lesions as defined by histology.

Methods:

Overall, 21 coronaries of seven hearts were imaged ex vivo with coronary CTA. From 95 coronary plaques 611 histological cross-sections were obtained and classified based-on the modified American Heart Association scheme. Histology cross-sections were considered advanced atherosclerotic lesions if early, late fibroatheroma or thin-cap atheroma was present. Corresponding coronary CTA cross-section were co-registered and classified into homogenous, heterogeneous, napkin-ring sign plaques based on plaque attenuation pattern. Area of low attenuation (< 30HU) and average CT number was quantified. In total, 1919 radiomic parameters describing the spatial complexity and heterogeneity of the lesions were calculated in each coronary CTA cross-section. Eight different radiomics-based ML models were trained on randomly selected

cross-sections (training set: 75% of the cross-sections) to identify advanced atherosclerotic lesions. Plaque attenuation pattern, histogram-based methods and the best ML model were compared on the remaining 25% of the data (test-set) using area under the receiver operating characteristic curves (AUC) to identify advanced atherosclerotic lesions using histology as a reference.

Results:

After excluding sections with heavy calcium (n=32) and no visible atherosclerotic plaque on CTA (n=134), we analyzed 445 cross-sections. Based on visual assessment, 46.5% of the cross-sections were homogeneous (207/445), 44.9% heterogeneous (200/445) and 8.6% were with napkin-ring sign (38/445). Radiomics-based ML model incorporating 13 parameters significantly outperformed visual assessment, area of low attenuation and average CT number to identify advanced lesions (AUC: 0.73 vs. 0.65 vs. 0.55 vs. 0.53; respectively; p<0.05 for all).

Conclusions:

Radiomics-based ML analysis may be able to improve the discriminatory power of CTA to identify high-risk atherosclerotic lesions.

Maternal and fetal outcomes in pregnancies with corrected Tetralogy of Fallot.

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Background:

Patients with corrected Tetralogy of Fallot (cTOF) are at risk for cardiac complications (mostly arrhythmia) at a childbearing age, which might be even more severe during a pregnancy.

Objective:

Our objective was to examine the maternal and fetal events in pregnancies with cToF.

Method:

We selected pregnancies in women with congenital heart disease from our prospective registry (n=276). Demographic data and previous cardiac events, and complication during pregnancy (maternal cardiac, fetal and obstetric) were documented.

Results:

We identified 36 index pregnancies with cTOF (mean maternal age 28±6 years). At the baseline evaluation 17% (n=6) had a previous cardiac event (arrhythmias), 44 % (n=16) had a dilated right ventricle with moderate to severe pulmonary regurgitation, and 14% (n=5) were in NYHA functional

class at least gr. II. Two pregnancies ended with spontaneous abortion (6%). In 34 index cases followed, during pregnancy we found 18% rate of maternal cardiac event (NYHA progression n=2, arrhythmia n=4), 9% rate of fetal event (congenital heart disease n=2, low birth weight n=1) and 6% rate of obstetric events (emergent caesarean section n=2). In univariate analysis, previous cardiac events ($p=0.001$; OR 15,9) and right ventricular dilatation with severe pulmonary regurgitation ($p=0,03$; OR 1,6) were significantly associated with a maternal cardiac event. Risk factors of the maternal cardiac event were further analyzed using multivariate logistic regression analysis, the only independent predictor was the previous cardiac event ($p=0.001$). None of the analyzed parameters were predictors of fetal or obstetric outcome.

Conclusions:

Women with cTOF and an arrhythmia before pregnancy are prone to develop arrhythmia complications (not fatal) during pregnancy as well. Mothers with severe pulmonary regurgitation associated with dilated right ventricle may be at risk for functional class deterioration at the time of pregnancy. In our population, congenital heart disease in offspring was not rare, 6%.

