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Quantification of longitudinal and radial motion of the right ventricle using 3D echocardiography: technical aspects and clinical relevance in heart transplant patients

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Longitudinal shortening is considered to be the most important motion determining right ventricular (RV) function. However, the radial direction ("bellows" effect) can gain particular importance in certain conditions. Our aim was to quantify the longitudinal and the radial components of RV performance using three-dimensional (3D) echocardiography and assess their relative contribution in normal subjects versus patients after heart transplantation (HTX).

Thirty HTX patients and 30 healthy volunteers were enrolled. Using dedicated software for RV 3D and speckle tracking analysis (4D RV-Function 2), beutel model was created and exported volume-by-volume throughout the cardiac cycle. Beside end-diastolic (EDV) volume and total ejection fraction (TEF), we quantified longitudinal (LEF) and radial ejection fraction (REF) by decomposing the motion of each vertex of the reconstructed 3D beutel model along three orthogonal axes and omitting the other two directions.

EDV did not differ between the groups (HTX vs control; 87±22 vs 80±26mL). In HTX patients TEF was lower, but tricuspid annular plane systolic excursion (TAPSE) was decreased to a greater extent (TEF: 45±7 vs 51±4% [−12%], TAPSE: 15±4 vs 22±3mm [−32%], p<0.01). LEF correlated robustly with TAPSE (r=0.75) and free wall longitudinal strain (r=−0.69, p<0.001). In healthy subjects, TEF correlated with LEF (r=0.50) and REF (r=0.37, p<0.05). In HTX patients, TEF correlated with REF (r=0.80, p<0.001), but not with LEF. REF/TEF ratio was significantly higher in HTX patients (56±12 vs 46±9%, p<0.001).

Our software allows to quantify longitudinal and radial motion of the RV separately using 3D analysis. Current results confirm the empirical phenomenon on the superiority of radial motion in determining RV function in HTX patients.
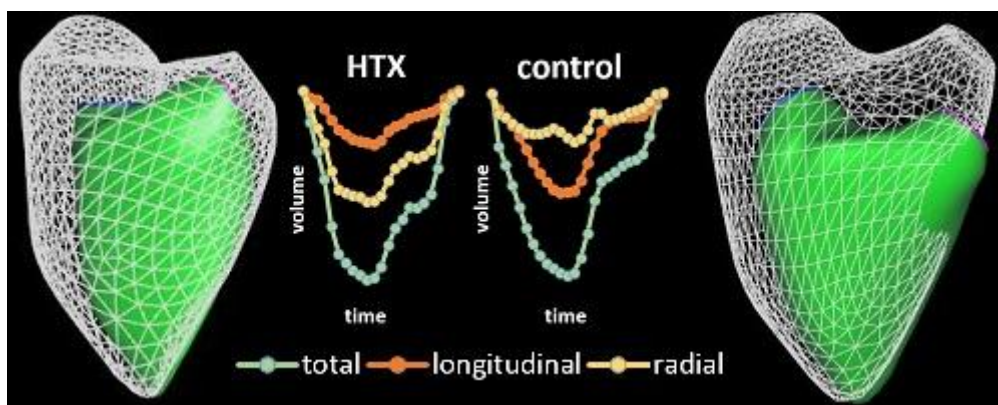
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Inheritance of left ventricular deformation: the BUDAPEST Twins study

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Although diagnostic and prognostic value of left ventricular (LV) deformation is widely recognized, data on its determinant factors are still scarce. The BUDAPEST Twins study was established to assess the genetic and environmental effects on different cardiovascular phenotypes. The aim of our present study was to estimate the heritability of LV mechanical function by quantifying myocardial strains in twin pairs.

Two hundred and twelve twin siblings were recruited (65 monozygotic and 41 same-sex dizygotic twin pairs, mean age 57±9 years). Siblings with coronary artery disease, any cardiomyopathy or severe valvular disease were excluded. Beyond the standard echocardiographic protocol, parasternal short axis- and apical views were obtained, optimized for speckle tracking analysis. Using dedicated software, global circumferential (GCS), longitudinal (GLS) and radial (GRS) strains were calculated by averaging the corresponding values of the 16 LV segments. Apical counter-clockwise, basal clockwise rotation and their net difference, the LV twist were also measured.

After adjusting for age and sex, the univariate additive genetic (A), dominant genetic (D) and unique environmental (E) effects model showed 75% additive genetic component in the variance of GCS, while 46% for twist. Similarly high, but dominant genetic effects (D) were

found regarding GLS, GRS, apical rotation and basal rotation (D: 77%, 70%, 74% and 62%, respectively). Unique environmental effects were responsible for the rest of the variance (E: 23% to 54%).

Our study demonstrated high heritability of LV deformation. Role of unique environmental factors is less prominent. These results urge to search for the responsible genes determining LV deformation, whilst also highlight the importance of advanced echocardiographic screening.

Cardiac resynchronisation alleviates chest pain due to exercise-induced left bundle branch block

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Topic(s):
Resynchronisation therapy

Introduction: Cardiac resynchronisation therapy (CRT) is indicated in symptomatic heart failure with left bundle branch block (LBBB) when the QRS duration is greater than 120ms. LBBB in some reports is associated with perfusion abnormalities in the septum and this is thought to be a mechanism for angina. Patients who had CRT often report angina relief. We therefore hypothesise that patients with LBBB and severe angina but without heart failure would also benefit from CRT.

Procedures: We describe here the use of CRT in a 54-year-old woman with disabling and intractable angina referred for a second opinion. During her exercise tolerance test, she developed LBBB within 42s when her heart rate exceeded 97/min and this reproduced her angina. Her symptoms were relieved during recovery when she reverted back to her usual narrow complex sinus rhythm. She underwent left heart catheterisation which found no significant coronary artery stenoses. During right atrial (RA) pacing, she developed angina with LBBB when the heart rate exceeded 110/min. Her angina disappeared when she had synchronised and sequential RA-left ventricular (LV) pacing up to 140/min. Withdrawal of LV pacing was associated with recurrent angina with a blood pressure fall. She was offered CRT following counselling and the upper tracking rate was set to 140/min to stop breakthrough of heart rate related LBBB during the course of her daily life activities. This appeared to have relieved her angina allowing improved quality of life and return to work.

Question: What differential diagnoses and potential pathophysiology in this patient should be considered?

Answer and discussion: Exercise-induced left bundle branch block (EI-LBBB) is an uncommon condition associated with angina. It carries adverse prognosis with higher mortality and major cardiovascular events. The aetiology of EI-LBBB is unclear, but its development could be due to microvascular ischaemia or conduction abnormality in response to the increasing heart rate. LV dyssynchrony during LBBB may contribute not only to a

decreased cardiac output, but also to high LV filling pressures and subendocardial ischaemia. The findings of our pacing study indicated that LV dyssynchrony was a major cause of our patient's symptoms, and she responded to CRT.

Conclusion: We present here a unique case of a patient with EI-LBBB with severe angina, who was successfully managed with CRT.

Diagnostic value of long non-coding RNA (LIPCAR) in patients with acute coronary syndrome and stable coronary artery disease

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Topic(s):
Infarction acute phase non STEMI

Background: Long non-coding RNAs (lncRNA) belong to the non-protein coding transcriptom family and characterized by consisting of >200 nucleotids. Their role as circulating biomarker has been investigated in cancer and cardiovascular system. It has recently been shown that the circulating level of the mitochondrial lncRNA uc022bqs.1 (Long Intergenic non-coding RNA predicting cardiac remodeling, LIPCAR) was associated with development of cardiac remodeling and cardiovascular death.

Purpose: The aim of our study was to compare the diagnostic value of LIPCAR in patients with STEMI, NSTEMI and stable coronary artery disease (CAD) and to associate with clinical outcome at 1-year follow-up.

Methods: Sixty-one patients with either stable coronary artery disease with previous coronary intervention (group CAD, n=30), or STEMI with primary PCI (group STEMI, n=15) or NSTEMI with coronary intervention (group NSTEMI, n=16) were prospectively included into the study. Clinical characteristics (age, gender, atherosclerotic risk factors, presence of peripheral artery disease or chronic renal insufficiency), and routine laboratory parameter (creatine kinase (CK), troponin T) were measured. Cardiac adverse events (coronary revascularization, implantation of pacemaker or implantable defibrillator, hospitalization due to angina pectoris) were recorded at the 1-year clinical follow-up. LncRNAs were isolated from the plasma samples using miRNeasy kit, and the LIPCAR level was measured by quantitative real-time PCR and normalized to controls, and expressed on arbitrary scale.

Results: Group STEMI patients were younger than the patients in CAD and NSTEMI groups, and had significantly higher troponin T and CK. LIPCAR value was found significantly down-regulated in group STEMI (0.45±0.08) (mean±SE) as compared to

groups NSTEMI (0.68±0.21) or CAD (0.79±0.14). Time of plasma sampling was significantly negatively correlated with LIPCAR levels in groups STEMI and NSTEMI (p=0.018, r=0.44), suggesting an early massive down-regulation of LIPCAR in the acute phase of STEMI and NSTEMI. Patients with stable CAD having cardiac adverse events at the follow-up had significantly higher levels of LIPCAR (1.12±0.11 vs 0.73±0.19). Our results indicate biphasic response of LIPCAR regulation: down-regulation in acute phase of STEMI and NSTEMI, and up-regulation in chronic CAD.

Conclusions: In a consecutive patient cohort, LIPCAR proved to be an early discriminative diagnostic marker of STEMI and NSTEMI, and might be a valuable additional parameter for diagnosis and prognosis of acute or chronic CAD.

Differentiation of physiological sport adaptation from pathological left ventricular hypertophy with the help of trabeculae quantification using cardiac magnetic resonance imaging

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Distinguishing hypertrophic cardiomyopathy (HCM) from athlete's heart is crucial because HCM is one of the most common causes of sudden cardiac death in young professional male athletes.

With a new software version it is now possible to analyze myocardial trabeculation quantitatively. This method has not been used in the differential diagnosis of athlete's heart and hypertrophic cardiomyopathy till now.

The aim of our study was to compare the left ventricular parameters of professional athletes and HCM patients with the help of the new quantification software.

We carried out CMR examinations on 76 professional male athletes free of complaint (24.5±5 years), 107 HCM male patients (40±2 years) and 41 healthy male volunteers (27±6 years). We determined several parameters using Medis QMass 7.6 software: left ventricular ejection fraction (EF), end-diastolic, end-systolic volume indices (LVEDVi, LVESVi), stroke volume index (LVSVi), mass index (LVMi) and trabecular mass (TrM). Derived parameters were calculated to evaluate the hypertrophic pattern [1. trabecular mass percent: TrM% (Trabecular mass (g)/LVM(g)*100), 2. left ventricular maximal diastolic wall thickness and end-diastolic volume index ratio (DWT_V), 3. left ventricular mass index and end-diastolic volume index ratio (M_V)].

The LVMi and TrM index were significantly higher in athletes and HCM patients compared to control group (athletes: 115.3 g/m^2, 21.3 g/m^2; HCM: 127.6 g/m^2, 27.5 g/m^2; control: 87.6 g/m^2, 18.2 g/m^2; p<0,001). The LVMi did not differ significantly in athletes and HCM patients, but TrM% was higher in HCM patients (22.4% vs 18.5%, p<0.05). The derived DWT_V and M_V parameters were significantly higher in the HCM group compared to athletes (0.35 mm·m^2·ml vs 0.14 mm·m^2·ml; 1.92 g/ml vs 1.13 g/ml).

Our results demonstrated that in professional athletes the hypertrophy of the compact myocardium was more pronounced compared to the hypertrophy of trabeculae. However, it was not typical of HCM patients. A quantitative analysis of the myocardial trabeculae and the derived CMR parameters seem to play an important role in distinguishing athlete's heart from pathological hypertrophy

Safety and efficacy of the direct factor Xa inhibitor rivaroxaban for peri-procedural anticoagulation in catheter ablation of atrial fibrillation: A systematic review and meta-analysis

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Topic(s):
Atrial fibrillation (AF)

Introduction: The novel oral anticoagulant rivaroxaban is being used more frequently in patients (pts) undergoing catheter ablation of atrial fibrillation (AF). For rare outcomes such as procedure-related thromboembolic or bleeding events, a meta-analysis of the literature may be the best way to obtain reliable evidence on peri-procedural safety and efficacy of rivaroxaban until proper randomized clinical trials become available.

Purpose: To provide detailed analysis of the currently available study reports on the safety and efficacy of peri-procedural rivaroxaban in pts undergoing AF ablation.

Methods: We performed a systematic search (2004–2014) of the English literature for studies comparing peri-procedural rivaroxaban therapy with vitamin K antagonists (VKAs) reporting detailed data on bleeding and/or thromboembolic complications. The Peto Odds Ratio (POR) was used to pool data into a fixed-effect meta-analysis.

Results: A total of 6,234 pts undergoing catheter ablation were included in 12 observational studies of whom 1,487 were receiving rivaroxaban and 4,747 VKAs. A total of 59 minor bleeding events were reported in 1,233 pts (4.79%) in the rivaroxaban group and in 133 of 3,330 pts (3.99%) in the VKA group (POR 0.77, 95% confidence interval (CI), 0.55 to 1.07, p=0.12, I^2=0%). Major bleeding events occurred in 22 of

1,487 cases (1.48%) in the rivaroxaban and 87 of 4,747 (1.83%) in the VKA group (POR 0.77, 95% CI, 0.47 to 1.28, p=0.31, I^2=0%) The risk of thrombo-embolic events trended to be lower in the rivaroxaban group (3 vs. 17, POR 0.40, 95% CI, 0.15 to 1.10, p=0.08, I^2=0%).

Conclusion: The risk of rivaroxaban-associated bleeds and thromboembolism is similar to that of VKA in pts undergoing AF ablation. Hence, rivaroxaban may be an alternative to VKA in this clinical scenario.

Troponin T or I levels following ICD implantation with and without defibrillation testing and their predictive value for outcomes: Insights from the SIMPLE trial

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On behalf: SIMPLE trial investigators

Topic(s):
Sudden death / resuscitation

SIMPLE randomized 2,500 patients receiving a first ICD to defibrillation testing (DT) or not. It demonstrated that DT did not improve shock efficacy or reduce mortality. This prospective sub-study sought to evaluate postoperative troponin (Trop) concentrations and their predictive value for total and arrhythmic mortality.

Methods and results: A Trop measurement was taken between 6 and 24 hours following ICD implantation in 2201/2500 patients. A postoperative Trop above the upper limit of normal (ULN) was more common in patients undergoing DT (N=509, 46%) than in those not having DT (N=457, 41%; p=0.02). After excluding patients with known preoperative Trop > ULN, similar findings were observed (42% vs. 38%, p=0.04). During a mean follow-up of 3.1±1.0 years, the annual mortality rate was 7.3% in patients with a postoperative Trop > ULN compared to 4.2% in patients with Trop ≤ ULN (HR 1.73, 95% CI, 1.41–2.12; p<0.001). Similarly, patients with elevated Trop had a significantly higher risk of arrhythmic death (HR 2.20, 95% CI, 1.54–3.15; p<0.001). The rate of failed appropriate first shock (component of the primary outcome of the main trial) was similar in patients with or without Trop elevation (HR 1.13, 95% CI, 0.68–1.88; p=0.65).

Conclusion: DT at time of ICD implant is associated with increased Trop levels indicating some myocardial injury caused by the procedure. Trop appears to represent a valuable predictor of clinical outcomes in ICD recipients.

Release of interferon-gamma by activated CD8-positive T cells in human calcified aortic valves fosters formation of osteoclasts with impaired calcium resorptive potential

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Background: The valve calcium content in human calcific aortic valve disease (CAVD) correlates with clinical stenosis severity and independently predicts outcomes. Histologically, large numbers of activated T-lymphocytes, predominantly memory-effector CD8+ cells localize in close proximity to calcified regions. The role of CD8+ cells and their association with osteoclasts, the cells with specialized calcium resorptive potential, remains unknown in CAVD.

Purpose: To test the hypothesis that CD8+ T cells promote calcification in CAVD.

Methods: CAVD valves (n=46) from valve replacement surgeries were dissected into non-calcified and calcified parts followed by mRNA extraction and quantitative qPCR. Gene expression patterns were confirmed by immunohistochemistry and ELISA. To recapitulate a CAVD environment with high interferon (IFN)g expression, calcified parts were stimulated with phorbol 12-myristate 13-acetate and ionomycin. qPCR detected signature molecules of CD8+ cells activation and osteoclast differentiation. Valve calcium content was detected using ex vivo fluorescence reflectance molecular imaging with near-infrared calcium tracer. In addition, CD14+ cells isolated from healthy donors were treated with either recombinant human IFNg or IFNg from conditioned medium (CM) derived from stimulated organoid cultures with or without neutralizing anti-IFNg antibody.

Results: Calcified regions exhibited significantly elevated transcript levels for CD8: 2.8 ± 0.6-fold, p=0.03; IFNg: 2.2 ± 0.5-fold, p=0.01; CXCL9: 3.9 ± 0.9-fold, p=0.01; Perforin1: 4.3 ± 0.8-fold, p=0.003; Granzyme B: 6.1 ± 1.8-fold, p=0.003; Hsp60: 3.8 ± 1.2-fold, p=0.01. Further, mRNA levels for osteoclast markers, including RANKL: 6.4-±1.9-fold, p=0.01; and TRAP: 8.3 ± 2.9-fold, p=0.01 increased significantly, whereas Cathepsin K: 1.6-fold, p=0.8 did not change. In stimulated organoid culture, elevated levels of IFNg, confirmed by ELISA in CM (13.6 ± 6.5-fold, p=0.01) and qPCR (44.3 ± 24.8-fold, p<0.001) reduced mRNA levels of RANKL (0.03 ± 0.01, p=0.01) and Cathepsin K (0.013 ± 0.01, p<0.001), whereas TRAP did not change (0.4 ± 0.2, p=0.6) compared to unstimulated regions. In addition, calcium signal intensity was increased in stimulated vs. unstimulated calcified parts (p<0.001). Moreover, IFNg reduced transcripts for Cathepsin K, TRAP, RANK and TRAF6, whereas CD80 and CD86 increased in parallel with reduced osteoclast resorptive function, which was restored by neutralizing anti-IFNg antibody.

Conclusion: Our results indicate that CD8+ cells highly expressing IFNg in CAVD may mute osteoclastogenesis, and thus promote valvular calcification.

Altered torsion mechanics in patients with hypertrophic cardiomyopathy: blame it on the LVOT-obstruction?

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Topic(s):
Diastolic dysfunction

The 3-dimensional Myocardial Deformation Imaging (3D-MDI) is able to characterize complex events of myocardial function, however, changes of deformation mechanics has not been well defined in different forms of hypertrophic cardiomyopathy (HCM). We aimed to examine parameters of LV deformation in patients with HCM using 3D-MDI and to detect if there were any effects of outflow tract obstruction on deformation patterns.

Methods: 45 consecutive patients with HCM (age 43.8 ± 9.3yrs, 14 females,

20 with LVOT-obstruction>30mmHg, HOCM), including 18 from the MAGYAR-PATH HCM-Registry were compared with 25 gender and age-matched control subjects. Inclusion done by standard echocardiographic criteria, confirmed by T1-weighed cMRI findings. Systolic MDI indices: peak systolic strain (S), strain-rate (SR) in longitudinal, circumferential and radial directions. Twist was given as difference in apico-basal rotation angles, Torsion (Tor) as LV-twist normalized to ventricular length (°/cm), its rate as Tor-Rate measured (°/s). Diastolic indices: untwisting rate (UTR) at 25% of diastole, untwisting time (UTT) measured from aortic valve closure to peak untwist. Corrected recoil rate (REC) calculated as [(TwistES−TwistMVO/ TwistES) x 100]/IVRT as a relative load-independent diastolic index.

Results: Compared with controls, HCM patients had increased peak LV twist (12.3±4.0° vs 9.1±3.2°, p<0.01) with increased apical rotation of HOCM cases (obstructive, 15.7±3.4° vs non-obstructive, 10.7±1.8°, p=0.001). The Tor-R was quicker with obstruction (66.8±10.1 vs 53.6±3.3 °/s, p=ns) or that in controls (50.5±4.4°/s). HOCM cases had slower UTR (98.8±29.1 vs 110±28.2°/s, p=ns), longer UTT (195.8±20.3 vs 129.1±23.0ms, p=0.01), the onset of untwist occurred closer to aortic valve closure (90.9±3.1 vs 75.5±6.6%, p<0.001; as time normalized by length of systole). The REC diminished more in HOCM (31.0±5.9 vs 52.3±8.8°/s, p<0.01), and both were less than in controls (49.1±6.6°/s, p<0.001).

Conclusions: LV Torsion links systolic contraction with diastolic relaxation and plays a major role in cardiac physiology. HOCM patients had more increased systolic Torsion implying hyperdynamic contraction. Untwist and recoil started earlier, but remained slower to see just limited completion during early diastole leading to isolated impairment of early diastolic function, contributing to increased LV filling pressures. The 3D-MDI hence appears to be able to reflect the changes of Torsion behaviour, which might have a role in screening subclinical cases.

Comparison of conventional measures to estimate right ventricular function in patients after heart transplantation using 3D and speckle-tracking echocardiography

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Right ventricular (RV) dysfunction is a common finding in patients underwent heart transplantation (HTX). However, certain limitations may apply regarding the conventional echocardiographic measures of RV performance. We aimed to investigate RV function of HTX patients using three-dimensional (3D) and speckle tracking echocardiography and correlate them with standard parameters.

Thirty patients were enrolled (mean age 54±14 years, 15 patients within one year, 15 over one year after HTX) and compared to 30 age- and gender matched healthy volunteers. Beyond the measurement of tricuspid annular plane systolic excursion (TAPSE) and fractional area change (FAC), we acquired 3D datasets from apical view using multi-beat reconstruction from 4 or 6 cardiac cycles. Using a dedicated software for RV quantification (4D RV-Function 2), RV end-diastolic (EDV), end-systolic (EDV) volumes, ejection fraction (EF) were measured and furthermore, free wall longitudinal strain were quantified using speckle-tracking analysis.

EDV did not differ between the two groups (HTX vs. control; 87±22 vs 80±26mL). In HTX patients EF and FAC were lower, however, TAPSE was decreased to a greater extent (EF: 45±7 vs 51±4% [−12%], FAC: 43±7 vs 48±6% [−10%], TAPSE: 15±4 vs 22±3mm [−32%], all p<0.05). There was no correlation between TAPSE and EF in HTX patients, whereas free wall longitudinal strain correlated with it (r=0.39, p<0.05). Notably, FAC referred to EF robustly (r=0.74, p<0.001). Patients over one year after HTX had better TAPSE (17±4 vs 14±4 mm in patients within one year, p<0.05), whilst EF did not differ between the two groups (43±6 vs. 46±7%; p=NS). TAPSE correlated with the time elapsed after HTX (r=0.60, p<0.01). The widely used TAPSE is not a reliable measure of RV systolic function in patients underwent heart transplantation. Free wall strain describing longitudinal shortening provides a better estimate. If 3D echocardiography is not available, FAC is the method of choice to assess RV performance. Our data also suggest a relevant radial component in RV function. In time, longitudinal function can recover.

Evaluation of left ventricular myocardial mechanics and synchrony in heart transplant patients using three-dimensional echocardiography

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Topic(s):
Medical aspects of transplantation

Citation:

Speckle-tracking echocardiography gained particular interest as it allows to quantify sensitive and predictive parameters of myocardial function in numerous cardiac diseases. However, data on left ventricular (LV) deformation are scarce in patients after heart transplantation (HTX). Early identification of the pathological conditions associated with HTX would be of high importance.

We aimed to evaluate LV deformation of multiple directions in patients after HTX and compare them to healthy volunteers.

Twenty-four HTX patients (mean age 54±14 years, with a median of 366 days after HTX) were enrolled and compared to 17 age- and gender matched healthy volunteers. Patients with history of allograft rejection were excluded. Beyond standard echocardiographic protocol, we acquired 3D datasets from apical view using multi-beat reconstruction from 4 or 6 cardiac cycles. Using a dedicated software for LV quantification (4D LV-Function 3), LV end-diastolic (EDV), end-systolic (EDV) volumes, ejection fraction (EF) were measured. Furthermore, global longitudinal and circumferential strain were quantified by 3D speckle tracking analysis. Systolic dyssynchrony index (SDI) derived from 16 subvolumes of the LV was also assessed.

EDV of healthy subjects was higher, however, EF was similar in the two groups (HTX vs control; EDV: 123±34 vs 94±24mL, p<0.01, EF: 62±8 vs 64±4%). GCS did not differ either (GCS: −30±7 vs −31±4%). Interestingly, GLS was signficantly decreased in HTX patients compared to controls (−18±4 vs −21±1%, p<0.01). SDI referring to intraventricular dyssynchrony was higher in HTX patients (9±3 vs 4±2%, p<0.01).

Despite the lack of known pathology and maintained ejection fraction, 3D longitudinal strain may indicate subclinical LV dysfunction in HTX patients. Mild degree of intraventricular dyssynchrony is also suggested to be present. Further enrollment and follow-up may verify the importance of our results.

Persistence of fixed and free combination of ramipril and amlodipine in hypertension

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**Topic(s):**
Treatment of hypertension

Introduction: Adequate patient adherence is of outstanding importance during the management of chronic disorders including hypertension. In particular, target blood pressure and the reduction of cardiovascular risk can be reached only by prolonged, effective pharmacotherapy.

Purpose: Our aim was to evaluate the persistence on one-year treatment with the free or fixed combination of ramipril and amlodipine in hypertension.

Methods: Information from the National Health Insurance of Hungary prescriptions database, on pharmacy-claims between October 1, 2012 and September 30, 2013 was analyzed. We identified patients who filled prescriptions for free of fixed combinations of ramipril and amlodipine, prescribed for the first time. Using the Kaplan-Meier technique we constructed persistence curves. We used semi-parametric Cox's regression where antihypertensive therapy was the only (categorical) explanatory variable. Patients taking the fixed combination were regarded as the reference group.

Results: Combination antihypertensive therapy with ramipril and amlodipine was started with a free or a fixed combination of these agents in 20,096 and 10,449 patients, respectively. One-year persistence rate in patients taking ramipril and amlodipine as a free combination was 34%, whereas it was 54% in those on the fixed combination. Analyzing persistence on treatment with these combinations showed that the actual rate of discontinuation was approx. twice higher during treatment with the free, compared with the use of the fixed combination (HR=1.94, $p<0.001$).

Conclusions: Our study, which is unique even by international standards, demonstrated the clear benefit of initiating antihypertensive therapy with the fixed combination of ramipril and amlodipine over starting treatment with the free combination.
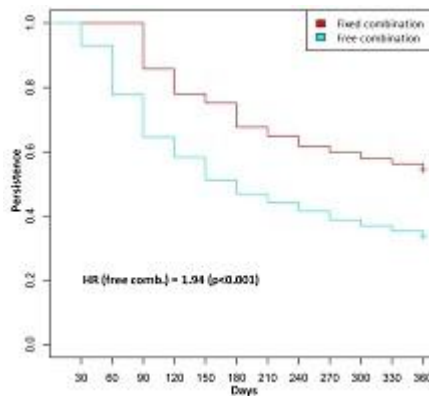
Persistence of therapy

Does coronary CTA provide sufficient image quality in heart transplant recipients with suboptimal heart rate during scan?

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Topic(s):
X-ray Computed Tomography (CT)

Aims and objectives: Cardiac allograft vasculopathy (CAV) is the leading cause of death after the first year of heart transplantation (HTX). According to the international guidelines the annual or biannual assessment of coronary status in HTX recipients is recommended with conventional invasive coronary angiography (ICA). However, the serial invasive examinations pose a great burden to the patients. Coronary CT angiography (CTA) was proposed as an alternative imaging test, however due to the higher heart rate (HR) of HTX patients and their challenging HR control precluded the widespread use of this technique. Therefore, our aim was to evaluate the image quality of coronary CTA in patients with HTX.

Methods and materials: In total 41 patients with HTX were investigated. Coronary CTA was performed with a 256-slice CT-

scanner, using prospectively ECG-triggered scan mode. For HR control ivabradin (83%) and/or beta blocker (21%) was used. The control group of 41 patients was selected from our clinical database of 2540 coronary CTA exams matched for HR, coronary dominance, age and BMI. The presence and degree of motion artifacts was evaluated per segment basis on a four point scale in the proximal and mid segments of the coronary arteries (0=no motion, 1=mild motion, 2= moderate motion, 3= severe motion, not evaluable). For the comparison of the two groups we used Mann-Whitney U and Fisher exact tests.

Results: The median HR was 70/min [IQR: 66–76] in HTX group and 70/min [IQR: 62–75] in the control group (p=0.265). We have analyzed 282 coronary segments in the HTX group and 281 segments in the control group. In the HTX group 98.6% (278/282) and in the control group 88.3% (248/281) of the segments were diagnostic (SMS<3), p<0.0001. Excellent image quality (SMS=0) was present in 83.0% (234/282) of HTX and 51.6% (145/281) of control group's coronary segments, p<0.0001.

Conclusion: The coronary CTA exams of HTX patients had a better image quality as compared to the control group with similar heart rate, coronary dominance, age and BMI. The loss of autonomous neural control results in a regular, steady HR in HTX patients, which seems to be beneficial for coronary CTA imaging. Coronary CTA provides diagnostic image quality in HTX recipients, therefore it might be utilized as a non-invasive alternative to ICA during the follow-up exams for CAV.

Genetic but not environmental factors have substantial influences on epicardial adipose tissue quantity: a classical twin study

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On behalf: MTA-SE Lendulet Cardiovascular Imaging Research Group

Topic(s):
Nutrition / obesity

Background and aims: It has been reported that epicardial adipose tissue might have an important role in the pathogenesis of coronary artery disease because of its metabolic activity and proximity to the epicardial coronary arteries. Whether the epicardial adipose tissue depends on environmental influences or determined by genetic factors is unclear. The aim of the study was to evaluate the genetic and environmental impacts on the epicardial adipose tissue quantity within a cohort of twin pairs.

Methods: We have enrolled 210 twin subjects without known cardiovascular disease of whom 63 were monozygotic (MZ) pairs (age: 55.7±9.7 years) and 42 were dizygotic (DZ) pairs (age: 58.1±8.7 years). All subjects were investigated with a 256-slice CT-scanner. For each twin subject epicardial fat volume (EFV), waist circumference (WC) and body mass index (BMI) were assessed. To quantify phenotypic similarity, intra-pair correlations were calculated. With the use of structural equation models these correlations were broken down to additive genetic (A), common (C) and unique (E) environmental correlation components.

Results: The EFV was 98.1±45.2 cm^3, the WC was 98.0±14.1 cm, and the BMI was 27.8±5.2 kg/m^2 (mean±SD). The intra-pair correlation between EFV, WC and BMI values were stronger in MZ twins as compared to DZ twins (rMZ_{EFV}=0.75, rDZ_{EFV}=0.27; rMZ_{WC}=0.70, rDZ_{WC}=0.40; rMZ_{BMI}=0.67, rDZ_{BMI}=0.16; all p<0.05), which implies a strong genetic dependence of these parameters. The structural equation models confirmed these findings: A_{EFV}=75%, A_{WC}=71%, A_{BMI}=66%; E_{EFV}=25%, E_{WC}=29%, E_{BMI}=34%. No role of common environmental factors was found.

Conclusion: In this classical twin study we were able to show that genetic but not environmental factors have substantial influences on EFV, similarly to BMI and WC. As both abdominal obesity and increased volume of epicardial fat are linked to the development of

cardiovascular diseases, early and sustained preventive measures are needed to reduce the amount of these pathogenic fat depots.

Strain and strain rate by speckle-tracking echocardiography reflect both the effects of exercise training and detraining in a rat model of athlete's heart

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Recently our working group provided detailed morphologic and hemodynamic characterization on exercise-induced left ventricular (LV) hypertrophy in a rat model, confirming increased contractility. In the current study we aimed to assess whether strain parameters by speckle-tracking echocardiography (STE) are able to describe the effects of training and detraining on LV function.

Rats were divided into trained (n=12) and control (n=12) groups. Trained rats swam 200 min/day for 12 weeks, then remained sedentary for 8 weeks. Echocardiography was performed at baseline, 12 and 20 weeks using a 13MHz linear transducer to obtain LV long- and short-axis recordings for STE analysis. Global longitudinal and circumferential strain (GLS, GCS) and systolic strain rate (LSr, CSr) were measured. After the detraining period, LV pressure-volume (P-V) analysis was performed to calculate contractility indices (i.e. slope of the end-systolic P-V relationship [ESPVR]).

Echocardiography showed the development of LV hypertrophy in the trained group (trained vs. control; LV mass index: 2.4±0.1 vs 2.0±0.1g/kg, p<0.05). This difference disappeared after detraining (2.3±0.1 vs 2.4±0.1g/kg, NS), which was confirmed by post-mortem measured heart weight and histological morphometry. GCS, CSr and LSr were all increased after the training period (GCS: Figure; CSr:

−5.6±0.3 vs −4.0±0.3; LSr: −4.6±0.2 vs −3.9±0.2Hz, all p<0.05). After detraining, supernormal values reversed to the control level and ESPVR did not differ either (1.8±0.1 vs 1.8±0.2mmHg/μL, NS).

Morphologic and functional properties of exercise-induced LV hypertrophy completely regressed after the detraining period. Both changes induced by exercise training and effects of detraining reflected by STE, allowing a consecutive evaluation of LV function in rat models.
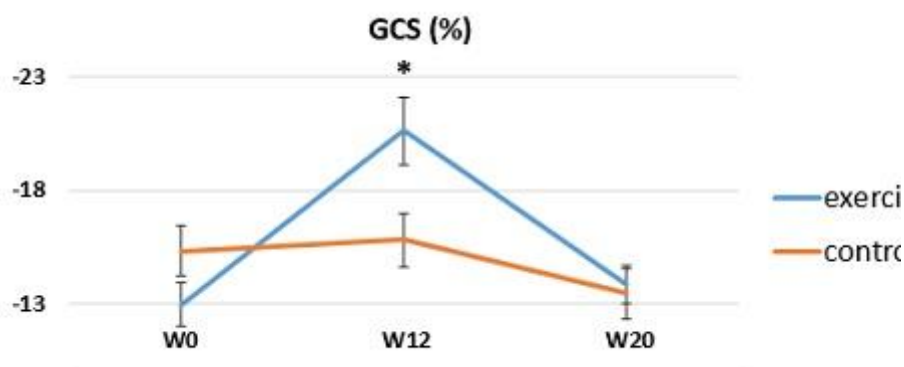
The ratio of the neutrophil leukocytes to the lymphocytes predicts the outcome after cardiac resynchronization therapy

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Topic(s):
Resynchronisation therapy

Background: The low lymphocyte counts and high neutrophil leukocyte fractions have been associated with poor prognosis in

chronic heart failure. We hypothesized that the baseline ratio of the neutrophils to the lymphocytes (NL ratio) would predict the outcome of chronic heart failure patients undergoing cardiac resynchronization therapy (CRT).

Methods: The qualitative blood count and the serum levels of NT-proBNP (N-terminal of the prohormone brain natriuretic peptide) of 122 chronic heart failure patients and 122 healthy controls were analysed. We considered the 2-year mortality as primary endpoint and the 6-month reverse remodelling ($\geq$15% decrease in the end-systolic volume) as secondary endpoint. Multivariable adjusted logistic and Cox regression analyses were applied and net reclassification improvement (NRI) and integrated discrimination improvement (IDI) were calculated.

Results: The NL ratio was elevated in chronic heart failure patients as compared to the healthy controls (2.93 [2.12–4.05] vs. 2.21 [1.64–2.81], p<0.0001). The baseline NL ratio exceeding 2.95 predicted the lack of the 6-month reverse remodelling (n=63, odds ratio=0.38 [0.17–0.85], p=0.01; NRI=0.49 [0.14–0.83], p=0.005; IDI=0.04 [0.00–0.07], p=0.02) and the 2-year mortality (n=29, hazard ratio=2.44 [1.04–5.71], p=0.03; NRI=0.63 [0.24–1.01], p=0.001; IDI=0.04 [0.00–0.08], p=0.02) of the patients independently of NT-proBNP levels or other factors.

Conclusions: The NL ratio is elevated in chronic heart failure and predicts outcome after CRT. According to the reclassification analysis, 4% of the patients were better categorized in the prediction models by combining the NT-proBNP with the NL ratio. Thus, a single blood count measurement could facilitate the optimal patient selection for the CRT.

Gender differences in morphological and functional aspects of athletes heart in a rat model

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Topic(s):

Exercise testing and training

Citation:
European Heart Journal (2015) 36 (Abstract Supplement), 460

Background: Long-term exercise training is associated with characteristic morphological and functional changes of the myocardium, resulting in a condition called athlete's heart. Referring to the latest studies, sex hormones may be involved in the regulation of exercise-induced left ventricular (LV) hypertrophy.

Purpose: We aimed at understanding the gender-specific functional and morphological alterations in the LV and the underlying molecular changes in a rat model of athlete's heart.

Methods: We divided our young, adult male and female rats into control and exercised groups. Athlete's heart was induced by swim training. The exercised rats were exposed to 200 min/day swimming for 12 weeks. Control rats were taken into the water for 5 min/day. Following the training period we assessed LV hypertrophy with echocardiography. LV pressure-volume (P-V) analysis was performed to investigate in vivo LV function. Additionally, molecular biological studies (qRT-PCR, Western blot) were performed. Interaction between gender and training was tested by two-way ANOVA.

Results: Echocardiography showed LV hypertrophy which was confirmed by LV wall thickness and mass values, nevertheless it was more pronounced in females. Post-mortem measured heart weight/tibial length ratio (+31.2% female vs. +14.5% male, $p < 0.05$) also verified gender differences in LV hypertrophy. The induction of Akt signaling was more significant in females compared to the males (p-Akt/Akt ratio: +57.7% female vs. +21.4% male, $p < 0.05$). There is also a characteristic difference in the mitogen-activated protein kinase (MAPK) pathway as suppressed phosphorilation of p44/42 MAPK (Erk) was observed in female exercised rats, but not in male ones. α-myosin heavy chain (MHC)/β-MHC ratio did not differ in males, but increased markedly in females (+140.6% female vs. +16.9% male, $p < 0.05$). Despite the more significant hypertrophy in females, characteristic functional parameters of athletes's heart did not show notable differences between the genders during invasive hemodynamic measurements. LV P-V analysis showed increased stroke volume and stroke work, improved contractility and mechanoenergetics and unaltered LV

stiffness in both males and females.

Conclusions: Our results confirm that there is a more pronounced exercise-induced LV hypertrophy in females that has no functional consequence compared to the males. The gender-specific response of the LV to exercise is modulated by characteristic molecular pathways.

Left ventricular contractility of athlete's heart: assessment by speckle tracking echocardiography and invasive pressure-volume analysis in rats

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Topic(s):
Exercise testing and training

Background: Long-term exercise training is associated with characteristic structural and functional cardiac adaptation (athlete's heart), which involves improved cardiac contractility. Contractile function is considered to be precisely measurable only by invasive hemodynamics.

Purpose: We aimed to correlate strain values measured by speckle tracking echocardiography (STE) with sensitive contractility parameters of pressure-volume (P-V) analysis in a rat model of exercise-induced left ventricular (LV) hypertrophy.

Methods: LV hypertrophy was induced in exercised group (n=10) by swim training (12 weeks, 200 min/day). Untrained rats (n=12) were taken into the water for 5 min/day. Echocardiography was performed using a 13 MHz linear transducer to observe LV morphological alterations and to obtain LV long- and short-axis recordings for speckle-tracking analysis. LV P-V analysis was performed using a pressure-conductance microcatheter and load-independent contractility indices were obtained. We used Pearson correlation to observe the relation between these parameters.

Results: According to LV wall thickness values measured by echocardiography, trained rats had increased LV mass index (trained vs control; 2.76±0.07 vs 2.14±0.05 g/kg, p<0.01), which was confirmed by post-mortem heart weight/tibial length ratio. Invasive hemodynamics revealed increased ejection fraction, stroke volume and stroke work in athlete's heart. P-V loop derived load-independent contractility parameters were significantly improved in the trained group [slope of the end-systolic P-V relationship (ESPVR): 3.58±0.22 vs 2.51±0.11 mmHg/μl; p<0.01]. STE analysis showed supernormal global circumferential strain (GCS: −19.4±2.3 vs. −14.9±2.0%, p<0.01) and circumferential strain rate (CSr: −5.0±0.4 vs. −3.8±0.4 s^{-1}, p<0.01) in exercised rats. These alterations were also observed regarding global longitudinal strain and strain rate. Contractility indices measured by P-V analysis strongly correlated with strain and strain rate parameters [ESPVR vs. GCS (r=−0.83, p<0.01), CSr (r=−0.75, p<0.01)].

Conclusions: In our rat model, strain and strain rate parameters closely reflected the improvement in intrinsic contractile function induced by exercise training. STE can be a feasible and useful method to follow up development of athlete's heart in animal models.

Invasive treatment strategies of iatrogenic pulmonary vein stenosis in patients after atrial fibrillation ablation

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Topic(s):
Atrial fibrillation (AF)

Background: Atrial fibrillation ablation has become the gold standard treatment of paroxysmal atrial fibrillation. Pulmonary vein stenosis (PVS) is a rare complication of the procedure. Although it can be treated with percutaneous angioplasty (PTA)

and stent implantation, the management of the disease can be challenging.

Aims: Safety and efficacy of pulmonary vein PTA and stenting was investigated.

Methods: The presence of significant PVS was verified with CT angiography. In all PVS patients PV PTA was performed. Long sheat was introduced from the right femoral vein to the right atrium. After transseptal punction selective pulmonary vein angiography, pressure measurements and then balloon dilatation and/or stent implantation was performed.

Results: 3050 atrial fibrillation ablations has been performed in our clinic since 2005. Altogether 10 symptomatic PVSs (0.32%) were diagnosed, which were verified with CT angiography and were treated with PTA. Balloon angioplasty alone were performed in 15 veins of 5 patients, in one case drug eluting balloon was used. Furthermore, in 5 other patients BMS stents and in 3 patients self expanding DES stents were used (4 veins). Total PV occlusion was found in 3 cases, which could also be successfully treated with PTA. In one patient rupture of the PV was noticed after the balloon dilatation of the PV, where surgical patch plasty of the PV was necessary. In one patient distal, in an other patient proximal dislocation of the implanted inflatable stent was noticed, none of them required surgical intervention. During PTA of a totally occluded PV distal rupture occured after balloon dilatation causing massive haemoptoe, but it could be effectively treated with balloon reinflation. Restenosis could be observed after the first intervention in 8 patients, all of them were treated with reintervention, 3 out of 8 required a third intervention. In these cases 8 mm size self-expanding DES stents were implanted. After re-intervention no significant restenosis evolved.

Conclusion: Pulmonary vein PTA seems to be a feasible method to treat iatrogenic PVS, however even in high volume centers with experienced operators the risk of specific comlications is notable. The occurence of restenosis after balloon dilatation alone or BMS stent implantation remains high. In the presence of verified PVS self expanding DES implantation seems to be the most effective method of treatment.

The effect of treatment optimization on the suitability of ARNI among patients followed at a heart failure outpatient clinic

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Background: It is well-known that the PARADIGM-HF trial, that examined LCZ696 or enalapril therapy on top of other evidence-based treatments in HFrEF, showed a huge drop in the primary outcome in favour to the new drug. However there are some questions about the use of LCZ696 in every day clinical practice.

Aim: To assess the proportion of pts suitable for ARNI according to the screening and randomization criteria of the PARADIGM-HF trial {NYHA II-IV; LVEF≤35%; systolic blood pressure (SBP)≥100 and 95mmHg; eGFR≥30ml/min/1.73m^2; serum potassium (seK)≤5.2 and 5.4mmol/l; tolerated dose of an ACEi/ARB equivalent to at least 10 mg of enalapril twice daily; elevated level of BNP} after treatment optimization (TO) and one month later.

Patients and methods: The primary cohort (PC) included 596 consecutive HFrEF pts (LVEF: 29.8±7.9%; NYHA: 3.1±0.7; blood pressure: 126.6±23.3/80.2±13.3mmHg; ischemic etiology: 46.8%; diabetes: 34.4%; male: 75.5%; age: 62.7±25.4 years; eGFR: 54.1±25.1ml/min/1.73m^2) who were followed prospectively at our heart failure outpatient clinic. At baseline the use of guideline-recommended, evidence-based treatments was quite low: ACEi/ARB in 36.1%, BB in 35.2%, MRA in 30.7%, CRT-P/CRT-D in 7.5%, ICD in 1.6%. The proportion of pts suitable for ARNI was examined first after TO, according to the screening criteria of the PARADIGM-HF trial, and secondly 1 month later according to the randomization criteria of the study. BNP's measurement was not available at the time of the analysis.

Results: After TO {ACEi/ARB (91.6%, at a dose equivalent to at least 10 mg of enalapril twice daily: 60.4% of PC), BB (92.3%, at

target doses: 60.9% of PC), MRA (53.9%), CRT-P/CRT-D and ICD (16.6% and 2.8%, respectively)} the proportion of pts suitable for ARNI was 11.4% (68pts). The causes of unsuitability were NYHA I (30.7% of PC), LVEF>35% (45.3% of PC), SBP<100mmHg (22.8% of PC), eGFR<30ml/min/1.73m^2 (30.7% of PC), seK>5.2mmol/l (12.4% of PC), and the low tolerated dose of an ACEi/ARB (31.2% of PC). Of the 68 pts suitable for ARNI after TO, 7 pts dropped out one month later according to the randomization criteria of the trial mostly because of SBP<95mmHg (2 pts); seK>5.4mmol/l (3 pts), or worsening renal function (5 pts).

Conclusions: Treatment with ARNI may be an important, new possibility for the management of pts with HFrEF. Among real-life HFrEF pts treated optimally, the proportion of pts suitable for ARNI according to the PARADIGM-HF trial criteria seems to be moderate.

Does the timing of the initiation of intraaortic balloon pump therapy affect mortality in patients with acute coronary syndrome complicated by cardiogenic shock?

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Topic(s):
Acute intensive cardiovascular care

Introduction: Based on literature data, the routine use of intraaortic balloon pump (IABP) in the treatment of acute coronary syndrome (ACS) complicated by cardiogenic shock is questionable. However, the available studies did not subselect patients in whom the cardiogenic shock has been developed later than the time of percutaneous coronary intervention (PCI), therefore the IABP therapy was initiated as a rescue therapy, with a certain time period following PCI.

Purpose: The present study aimed to investigate wheter the timing of initiation of IABP therapy has any effect on in-hospital-, 30 days-,

and 1 year mortality.

Methods: Patients with ACS with the need of IABP therapy due to cardiogenic shock between 2009 and 2012 were included in the study. Anamnestic and procedural data were collected. We focused on the determination of the area of myocardium at risk (AMR) affected by the culprit lesion. AMR was calculated in all patients with the use of Holistic Coronary Care sofware, a program developed by our study group.

Results: Among a total of 290 patients 45 recieved IABP as a rescue therapy. Among baseline clinical parameters the left ventricular ejection fraction (LVEF) and the glomerular filtration rate (GFR) was significantly higher in the rescue IABP group (LVEF 39% SD:8 vs. 34% SD:9, p=0.005; GFR [ml/min/1.73 m^2]: 69 SD:22 vs. 60 SD:23 p=0.01). There was no significant difference in the calcualted AMR between patients with rescue IABP therapy and those in whom IABP was inserted earlier, during the PCI (62.3% SD 25.8 vs. 58.8% SD 25.5; p=0,098). The in-hospital mortality rate did not differ significantly in the two groups, while duration of hospitalization was significantly longer (22 vs. 17 days p=0,05) and the mortality rate was significantly higher at both 30 and 365 days in the rescue IABP therapy group as compared to those with earlier initiation of IABP therapy (16% vs. 3.8% p=0.018; 29% vs. 6% p=0.001 for 30 days and 1 year, respectively).

Conclusion: Patients with ACS who recieve IABP therapy during the PCI due to an early development of cardiogenic shock have better survival at 30 and 365 days as compared to patients with the need of rescue IABP therapy.

Clinical predictors of mortality following rotational atherectomy and stent implantation in high risk patients

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Topic(s):
PCI: long-term outcome

Background: Contemporary rotational atherctomy (RA) is mainly used to facilitate stenting in complex lesions. Outcomes involving RA and stenting have been investigated, yet high risk patients have not been adequately described.

Purpose: Our aim was to assess procedural success and determine clinical predictors of post-procedure mortality, following RA and stenting in high risk patients.

Methods: Data of 218 consecutive patients who underwent RA were evaluated in a prospective register. The primary end-point was the composite of: angiographic success of the procedure and long term mortality. Secondary end-points were procedural success, consumption of the angioplasty equipment and peri-procedural major adverse events (MACE). The impact of the relevant angiographic and clinical characteristics on long term mortality were analyzed using uni- and multivariate Cox regression analysis.

Results: Mean age was 70±8.2 years, diabetes was present in 44%, chronic renal failure in 29%. Prior myocardial infarction and three vessel disease amounted to 42.2% and 32.6%, respectively. Altogether, 52.8% of patients underwent RA after a failed, non-RA intervention attempt and 30.7% of cases presented as acute coronary syndromes. Angiographic success was 100% and all patients received stents after RA. Peri-procedural MACE occurred in five patients (2.3%). Post-procedural death was investigated, with a mean follow-up of 36 months. Mortality amounted to 37.2%. Multivariate analysis revealed that left ventricular ejection fraction <50%, glomerular filtration rate <60 ml/min, cardiogenic shock and diabetes were the only independent mortality predictors.

Conclusions: We have found that RA and stenting is a feasible and viable option in an elderly high-risk population, with exceptional procedural success and acceptable long term results.

Impact of matrix metalloproteases and their inhibitors in the athlete's heart

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Topic(s):
Sports cardiology

The physiological mechanisms behind exercise-induced myocardial hypertrophy are not clearly characterized and subject to intense research. Matrix metalloproteases (MMP) and their tissue inhibitors (TIMP) are promising biomarkers of numerous cardiac diseases including pathological left ventricular hypertrophies. Our aim was to assess the correlations between the physiological hypertrophy of athlete's heart and the serum levels of MMPs and TIMPs.

Our study included elite athletes competing in waterpolo, kayaking, canoeing or rowing (EA; n=75, age: 26±8 years, 77% male) compared to age- and gender-matched healthy sedentary volunteers (CTL; n=33). The left (LV) and right ventricular (RV) end-diastolic volume (EDVi) and mass (Mi) indexed to body surface area were measured by cardiac magnetic resonance imaging (Philips Achieva 1.5T, QMASS 7.1 software). Serum concentrations of the enzymes (MMP-2, MMP-9, TIMP-1, TIMP-2) were determined by enzyme-linked immunosorbent assay (R&D Systems, QuantiKine).

Not surprisingly, the LV and RV volumes and masses were markedly increased in the athletes compared to the control group (EA vs. CTL; LVEDVi: 119±14 vs. 93±13 ml/m^2; RVEDVi: 124±17 vs. 95±15 ml/m^2; LVMi: 84±18 vs. 59±12 g/m^2; RVMi: 31±6 vs. 24±4 g/m^2, all p<0.001). Despite the notable cardiac remodelling, we did not find significant differences in the serum levels of the measured enzymes between the two groups. In athletes, significant negative correlations were found between MMP-2 and LV and also RV mass indices (LVMi: r=−0.35, p=0.002; RVMi: r=−0.35, p=0.009) and end-diastolic volume indices (LVEDVi: r=−0.23, p=0.048; RVEDVi: r=−0.25, p=0.029). A similar inverse relationship was observed between TIMP-2 and LVMi and also RVEDVi (LVMi: r=−0.38, p=0.001; RVEDVi: r=−0.24, p=0.039). MMP-9 showed a significant positive correlation with the LV end-diastolic volume (LVEDV: r=0.27, p=0.019). In the control group, we did not notice these relationships.

In contrast to pathological LV hypertrophies, serum levels of MMP-2 showed an inverse relationship to the ventricular volumes and masses in the elite athlete group. The dissimilar correlations of MMP-2 and MMP-9 also imply a different regulation of these enzymes in the athlete's heart. MMP-2 may be a useful biomarker in clinical practice to distinguish between physiological and pathological hypertrophies and to recognize overlapping cardiac diseases.

Differentiation of arrhythmogenic right ventricular cardiomyopathy and athlete's heart using cardiac magnetic resonance imaging

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The diagnosis of arrhythmogenic right ventricular cardiomyopathy (ARVC) is based on the revised Task Force Criteria defined in 2010, which includes right ventricular end-diastolic volume index (RVEDVi), right ventricular ejection fraction and wall motion abnormalities evaluated using cardiac magnetic resonance (CMR) imaging. However, the elevated RVEDVi can be a result of sport adaptation as well, the revised Task Force guideline contains no criteria for professional athletes.

Our goal was to determine the CMR parameters which can help to distinguish ARVC and athlete's heart.

Between 2010 and 2014 CMR examination was performed on 436 patients because of the suspicion of ARVC. In 34 patients (41±11y,22 male) the CMR showed major criteria, and fulfilled revised Task Force Criteria. Additionally 54 professional athletes free of complaint (25±5y,35 male) and 56 healthy volunteers (28±5y,36 male) were examined by CMR. Left (LV) and right ventricular (RV) end-diastolic (ED), end-systolic, stroke volume indices, ejection fractions (EF) were compared and derived parameters were calculated: LVEDV/RVEDV and LVEF/RVEF. Furthermore, in male patients two subgroups were established with single right ventricular involvement (SI) (n=10) and biventricular involvement (BI) (n=12).

RVEDVi of ARVC patients and ahlete's were higher than the control group's (male:130.5; 133.6 vs 98 ml/m^2, p<0.001; female:128.1; 111.1 vs 82 ml/m^2, p<0.05), there was no significant difference between the RVEDVi of ARVC patients and athletes. RVEF was significantly lower in both male and female ARVC patients compared to the athletes and healthy volunteers (male:45 vs 54.6 vs 57.2%; female:42.4 vs 58 vs 60.7%).

LVEDV/RVEDV of female ARVC patients and LVEDV/RVEDV and

LVEF/RVEF of male patients with SI showed significant difference compared to the athlete's group (ARVC vs athletes: female:0.81 vs 0.97; male:0.84 vs 0.95; 1.2 vs. 1.05), but none of the derived CMR parameters showed significant difference between male BV patients and athletes.

In 5 athletes (28±4.1y,4 male) ARVC was diagnosed according to RV wall motion abnormality, late enhancement, RVEF and derived parameters. RVEF and LVEDV/RVEDV of athletes with ARVC were below the 5th percentile, whereas LVEF/RVEF was above the 95th percentile of healthy athletes.

Consequently, RVEDVi shows no difference between ARVC patients and athletes, in healthy athletes RVEDVi is in the range of the proposed Task Force Criteria. RVEF was the most useful parameter in the differentiation of ARVC and athlete's heart. In SI patients LVEDV/RVEDV and LVEF/RVEF can support the diagnosis.

Improved visualization of the coronary arteries using model-based iterative reconstruction for cardiac CT

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On behalf: Cardiovascular Imaging Research Group

Topic(s):
X-ray Computed Tomography (CT)

Purpose: To evaluate the image quality characteristics of coronary CT angiography (CTA) images reconstructed with standard filtered back projection reconstruction (FBR), hybrid iterative reconstruction (HIR) and model-based iterative reconstruction (IMR) techniques.

Methods: Raw data of 52 patients (39 male, age 64.7±9.3 years, BMI 28.2±5.6kg/m^2) who underwent 256-slice coronary CTA were reconstructed with FBR, HIR and IMR. Two readers evaluated the datasets qualitatively and quantitatively. A four-point scale was used to rate overall image quality from 1=excellent to 4=poor, non-diagnostic. Image noise was graded from 1=no image noise to 4=severe noise, while image sharpness was evaluated on a five-point scale. Mean image noise (SD) and contrast-to-noise ratio (CNR)

were measured in proximal and distal coronary segments.

Results: Qualitative analysis showed that IMR improves image quality and image sharpness as compared to FBR and HIR (p<0.0001 all). Image noise was significantly lower with HIR as compared to FBR and was further reduced with IMR as compared to HIR (p<0.0001 all). The mean image noise as measured in the ascending aorta was lowest with IMR (42.1±10.7 vs. 28.7±7.2 vs. 12.9±2.7; FBR vs. HIR vs. IMR, respectively; p<0.001 all), while mean attenuation did not differ among the three reconstruction methods (517.1±93.6 vs. 517.9±93.1 vs. 517.7±93.1 HU, p=1.0 all). Proximal CNR in FBR, HIR and IMR was 17.4±5.8 vs. 25.3±8.4 vs. 54.2±12.0 (p<0.001 all), while distal CNR was 16.2±5.0 vs. 23.5±7.4 vs. 55.2±12.4, respectively (p<0.001 all).

Conclusion: IMR significantly improves image quality accompanied by a substantial increase in CNR and decrease in image noise in coronary CTA.

The phosphodiesterase-5 inhibitor vardenafil protects against diabetic cardiomyopathy in type-2 diabetes mellitus

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Topic(s):
Metabolism and metabolic syndromes

Purpose: Diabetes mellitus (DM) is associated with a special heart disease, termed diabetic cardiomyopathy. The pathophysiological role of cyclic guanosine monophosphate (cGMP) signalling has been intensively investigated in DM. The second messenger cGMP, broken down by the phosphodiesterase-5 enzyme (PDE5), has been shown to exert cytoprotective effects. We investigated the effect of chronic inhibition of PDE5 by vardenafil in type-2 DM related cardiomyopathy.

Methods: For type-2 DM Zucker Diabetic Fatty (ZDF; homozygous recessive (fa/fa)) rats were used. Heterozygous (fa/+) or homozygous dominant (+/+) ZDF Lean (ZDFL) rats served as controls. Animals received either vehicle (ZDFL, ZDF) or 10mg/kg BW vardenafil per os (ZDFLVard, ZDFVard) from 7 to 32 weeks of age. Cardiac morphology was followed by

echocardiography. Left ventricular (LV) function was assessed using a pressure-volume (PV) conductance microcatheter system. Gene expression analysis of atrial natriuretic factor (ANF; qRT-PCR), cardiomyocyte diameter/tibia length (CD/TL) and Masson's staining (fibrosis score (FS)) were used to prove pathological myocardium hypertrophy.

Results: Cardiac hypertrophy (echocardiography: LV anterior wall thickness in systole (LVAWs): 2.81±0.1 mm; relative wall thickness (RWT): 0.49±0.02; LVmass/TL: 0.30±0.01 g/cm; CD/TL: 3.53±0.02 μm/cm; ANF: 3.04±0.26 vs ZDFL (LVAWs: 2.53±0.04 mm; RWT: 0.43±0.02; LVmass/TL: 0.23±0.004 g/cm; CD/TL: 3.09±0.02 μm/cm; ANF: 0.92±0.17); p<0.05) and fibrotic remodelling (FS: 1.05±0.09 vs ZDFL (0.57±0.13); p<0.05) have been observed in ZDF. Drug treatment significantly decreased myocardial hypertrophy and fibrosis (LVAWs: 2.47±0.05 mm; CD/TL: 3.15±0.02; ANF: 1.39±0.21; FS: 0.59±0.08 vs ZDF;p<0.05) in DM. PV analysis showed impaired diastolic function and increased cardiac stiffness (time constant of LV pressure decay (τ): 9.17±0.25 ms; slope of end-diastolic pressure volume relationship (EDPVR): 0.078±0.002 mmHg/μl vs ZDFL (τ: 8.18±0.13 ms; EDPVR: 0.045±0.003 mmHg/μl); p<0.05) while contractility parameters and blood pressure remained unchanged in ZDF. Vardenafil improved diastolic parameters (τ: 8.62±0.34 ms, EDPVR: 0.062±0.006 mmHg/μl vs ZDF; p<0.05). Vardenafil did not have effect in ZDFL.

Conclusions: We reported that chronic administration of vardenafil prevents DM associated myocardial complications. PDE5 inhibition might be an important target to improve the cardiovascular outcome in diabetic patients in the future.

Heritability of coronary calcium quantity and total plaque burden: a classical twin study

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Topic(s):
Risk scores

Citation:

Through the comparison of monozygotic (MZ) and dizygotic (DZ) twins phenotypic similarities can be quantified and the weight of genetic and environmental factors can be determined in an unique way. It has been reported that coronary atherosclerosis has a strong genetic determination. However, it is unclear if coronary calcium quantity and total plaque burden are inherited similarly. Our goal was to assess the magnitude of genetic and environmental impact on coronary calcium quantity and total plaque burden.

Coronary CT-angiography was performed in 208 twin subjects, of whom 62 were MZ pairs and 42 were DZ pairs (mean age: 58.1±8.7 vs. 55.8±9.8, p=0.218, respectively). Total Ca-score was assessed by Agatston-score measurement. Total plaque burden, which incorporates non-calcified, calcified and partially calcified plaques was assessed by the segment involvement score (SIS: total number of segments with plaque) and segment stenosis score (SSS: sum of all stenoses, minimal = 1, mild = 2, moderate = 3, severe = 4). SSS index (SSSi) was calculated by SSS/total segment number. SIS index (SISi) was calculated by SIS/total segment number. Concordance between MZ and DZ pairs were assessed by non-parametric correlations. Rough heritability was calculated according to the Falconer-method.

The Agatston-score was >0 in 38.7% of the MZ twins (median:132.3 [IQR: 27.5–387.4]), and in 40.5% of the DZ twins (median: 107.8 [IQR: 35.9–230.3]), p=0.880. The SISi and SSSi were positive in 55.6% of MZ and in 55.9% of DZ twins. The median SISi of MZ versus DZ twins was 0.2 (IQR: 0.1–0.4) versus 0.2 (IQR: 0.1–0.4), respectively, p=0.972. The median SSSi of MZ versus DZ twins was 0.3 (IQR: 0.1–0.5) versus 0.3 (IQR: 0.1–0.7), respectively, p=0.940. Relatively strong heritability was found regarding Ca-score (h^2=1.015), while the plaque burden showed a weaker genetic dependency (SSSi: h^2=0.632 and SISi: h^2=0.466).

This classical twin study shows that coronary calcium quantity has a relatively strong heritability, whereas plaque burden, which incorporates non-calcified, calcified and partially calcified plaques, is more determined by environmental factors. The latter implies that non-calcified plaque development is predominantly affected by environmental factors, which underscores the importance of preventive measures in cardiovascular risk reduction.

Seasonal variation of the critical limb ischemic events in the whole Hungarian population

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Topic(s):
Pathophysiology, epidemiology

Background: Seasonal manifestations of cardiovascular diseases (CVD) are described in case of acute myocardial infarction, sudden cardiac death, atrial fibrillation, aortic rupture/dissection, Stroke, deep venous thrombosis and pulmonary embolism. Paucity of data is available concerning critical limb ischemia (CLI) on this regard.

Purpose: To assess the seasonal trend of critical limb ischemia events in the whole Hungarian population

Methods: Based on the health care administrative data (disease classification and procedure codes) of the whole Hungarian population, in a nine years period (2004–2012), all the events were detected which meet the criteria of CLI. Case detection was based on finding the PAD related major limb amputations and lower limb revascularization (surgical/endovascular) accompanied with pain/tissue necrosis. Seasonality was assessed in an Age-period model.

Results: In the whole Hungarian population, over a nine year period (2004–2012), in 44.200 subjects, 55.900 events were identified which met the definition of CLI. PAD related major amputations represented 70%, lower limb revascularization with pain/tissue necrosis was detected in 30% of the cases. The incidence rate of CLI events (taken together and separately also) showed significant decline in late summer and autumn. This was consistent over the whole observational time.

Conclusion: This analysis, as the most complete report so far showed consistent results with other smaller studies addressing seasonality of CLI. Biological plausibility is supported by other data showing that cardiovascular risk factors are also seasonal, characterized by a decline in summer. A meaningful temporal relationship, in this manner is also presumable.

Early release kinetics of N-terminal pro-B-type natriuretic peptide in

patients after percutaneous transluminal septal myocardial ablation

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Topic(s):
Percutaneous / endovascular treatment

**Background and introduction:** In symptomatic patients with obstructive form of hypertrophic cardiomyopathy (HCM), septal alcoholic ablation (SAA) has been shown to be an alternative to surgical myectomy. N-terminal pro-B-type natriuretic peptide (NT-proBNP) is a powerful biomarker in various cardiovascular diseases as well as in HCM. The aim of present study was to examine the effect of the SAA caused left ventricular outflow gradient and wall stress reduction on serum NT-proBNP levels.

Methods: We analysed the early release kinetics of NT-proBNP in 9 patients with hypertrophic obstructive cardiomyopathy undergoing SAA from June 2011 to January 2014. Serum samples were collected in gel tubes tubes prior to and at 1, 2, 3, 4 and 6 hour after SAA. An electrochemiluminescence immunoassay using monoclonal antibodies was used to measure serum NT-proBNP levels (NT-proBNP assay, Elecsys Analyzer Cobas 4010, Roche Diagnostics, Mannheim, Germany).

Results: The SAA in nine patients resulted in complete success in eight and partial success in one. In all but one of the cases the serum NT-proBNP values decreased during the first 4 hours. Decreasing mean serum NT-proBNP concentrations were observed at all time points post procedure. The change compared to baseline value was significant at 1, 2 and 4 hour after SAA (P value 0.040, 0.042, 0.038, respectively).

Conclusions: Our results show decreasing serum NT-proBNP levels after induction of myocardial infarction during septal alcoholic ablation. These findings suggest that the observed changes in serum NT-proBNP levels may be related to the decrease of the left ventricular wall stress due to the procedure related reduction of the left ventricular outflow gradient.
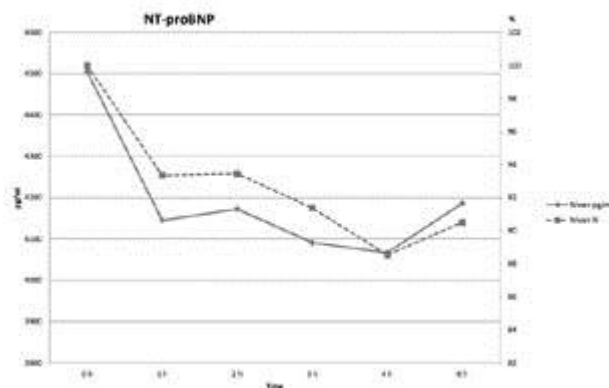
NT-proBNP levels and percent change

Transseptal endocardial left ventricular lead implantation after failed CRT implantation- long term results

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Topic(s):
Resynchronisation therapy

Introduction: CRT implantation is a well estabilished therapy in chronic heart failure patients. Transvenous left ventricular (LV) lead positioning might be challenging or in some cases impossible.

Objectives: The aim of this study was to investigate the effectiveness and safety of transseptal endocardial left ventricular lead implantation (TELVLI) in severe heart failure patients, and evaluate the long term follow-ups of the patients.

Methods: TELVLI was performed in 35 patients (30 men, 64±6 years, NYHA III-IV stage). Transseptal (TS) puncture was performed via the femoral vein. Intracardiac ulrasound was used to guide the puncture in 25 pts. The site of the puncture was dilated with a 6mm (3 pts), later with an 8 mm balloon (32 pts). After the puncture of the left subclavian vein, an electrophysiological deflectable CS catheter was introduced into the CS sheath. The CS catheter was used to reach the left atrium and the left ventricle

through the dilated transseptal puncture hole. At the latest LV activation site 65 cm active fixation bipolar lead was screwed into the LV wall, at the site of the latest activation.

Results: The lead was fixed in the left ventricle in all cases with good pacing threshold (0,84±0,4 V;0,4 ms). Puncture complication, pericardial effusion was not observed. Because of intraoperatively started anticoagulation, pocket haematoma was observed in three (9%) and needed evacuation in one case (3%). Follow-up was longer than one month in 34 patients [38 (22–49) months]. Significant improvement of NYHA was observed in all but one case (97%), at the first month control LV EF was 30±9% vs 38±6%. Early lead dislocation was noticed in two cases (6%), reposition was performed using the original puncture site in one, and transvenous implantation was succesfully carried out in the other case. Explantation of the system was necessary because of pocket infection in four cases (11%), in two of these cases TELVLI was carried out succesfully 3 months later, in one patient 22 months later. All patients were maintained on anticoagulation therapy with INR between 2–3. No thromboembolic complication was noticed during the follow up. 13 patients were lost, one of them died five years after the implantation in renal failure, the other patient died in malignant tumor 4 years after the implantation, 11 patients died due to the progression of the heart failure in average 16 months after the implantation.

Conclusion: TELVLI approach might be a very promising alternative technique of the surgical epicardial procedure when transvenous implantation could not be applied.

Demonstration of the functional consequences of the coronary stenosis on the basis of the flow-pressure relations using 3D-QCA morphological data

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Topic(s):
Invasive and functional coronary imaging

Background: The virtual functional assessment index (vFAI) has been suggested recently for demonstration the functional consequences of the coronary lesions. The vFAI was derived from the data of the flow-pressure curves generated by solving the Navier-Stokes equations using three-dimensional quantitative coronary angiography (3D-QCA) reconstructions. This new index showed good correlation with the fractional flow reserve.

Aims: To develop a smart model to calculate the vFAI using 3D-QCA data and the simple Hagen-Poiseuille and the Bordan-Carnot fluid dynamic equations as well as to compare these results to the measured FFR values.

Methods: A total of 45 coronary lesions of 33 patients were investigated. Intracoronary pressures measurements were performed. X-ray angiographic images were recorded by flat panel systems. The lumen of the interrogated vessel segments from the origin of the target vessel to the pressure sensor was reconstructed in 3D using a dedicated 3D QCA software package.

Results: Significant tight correlation was found between the calculated vFAI and the measured FFR values (r=0.81; p<0.0001). The cut off value of the vFAI of 0.92 provided a good sensitivity (95%) with 71% specificity to predict the diagnostic FFR ≤0.8 values. The area under the curve was calculated to be 0.86 according to the ROC analysis.

Conclusions: The vFAI demonstrates comprehensively the pathophysiological consequences of the coronary lesions. The level of correlation between the vFAI values and the measured FFR values calculated using the simple approach developed by our team matches the performance of the previously described method that uses dedicated software and time-consuming fluid dynamic computations.

Endothelial derivatives of human pluripotent stem cells show antiplatelet effects in 3D culture -steps towards vascular tissue engineering

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Background and purpose: Endothelial derivatives of human pluripotent stem cells may offer regenerative treatments in ischemic cardiovascular diseases. Here we studied differentiation conditions toward mature endothelial population as well as fate and function of these cells during 3D culturing.

Methods and results: To optimize endothelial development, human embryonic stem cells (hESC) were differentiated via embryoid body (EB) or monolayer method under normoxic and hypoxic conditions. CD31-positive endothelial cells (EC) were sorted by FACS and compared with human induced pluripotent stem cell-derived endothelial cells (hIPSC-EC) and human adult coronary arterial endothelial cells (HCAEC). Both hESC-EC and hIPSC-EC showed mature endothelial characteristics such as cobblestone pattern, ac-LDL uptake, and tube formation in vitro. Proteome profiling revealed high abundance of angiogenesis-related proteins in cell lysates and supernatant. As assessed by qPCR, angiopoietin2 mRNA levels increased in hESC-EC when differentiated via EB method (EB in normoxia 353.17 ± 86.29; EB in hypoxia 323.89 ± 86.63, monolayer 27.20 ± 9.92 vs. hESC, $p<0.001$). Expressions of arterial (EphrinB2, Notch1–2) and venous (EphB4) endothelial markers were increased, suggesting the presence of mixed endothelial population in culture. However, no significant differences were found in ratio of arterial and venous subpopulations in the different developmental protocols. For engineering 3D vascular constructs decellularised human aortic slices ($300\mu m$) were repopulated with hESC-EC and hIPSC-EC and cells remained viable on engineered matrices in vitro. Engineered bioscaffold were incubated with platelet rich plasma from healthy adults. 3D culture conditions activated antiplatelet effects of the cells (as shown by secreted levels of chemokine Rantes (pg/ml): hESC-EC 229.6 ± 37.9, hESC-EC on bioscaffold 83.6 ± 52.1; hIPSC-EC 234.9 ± 22.8, hIPSC-EC on bioscaffold 127.9 ± 63.6, $p<0.01$, n=6).

Conclusions: Differentiation conditions modulate endothelial development and angiogenic gene expression. 3D culturing increased antiplatelet effects. Functionally active endothelial derivatives of human pluripotent stem cells promises vascular tissue engineering for therapeutic purposes.

Asymmetric dimethylarginine (ADMA) in the pericardial fluid may contribute to the development of cardiac hypertrophy

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Background: Pericardial fluid (PF) contains several biologically active substances, which may play a role in modulation of cardiac function and morphology. Nitric oxide (NO) has been implicated in cardiac function and remodeling, whereas asymmetric dimethylarginine (ADMA) has been shown to inhibit NO-synthase (NOS).

Purpose: To test the hypothesis that L-arginine (L-Arg) precursor of, and ADMA a false substrate of NOS are present in PF of cardiac patients and their altered levels may contribute to altered cardiac morphology.

Methods: Levels L-Arg and ADMA in plasma and PF, and echocardiographic parameters of patients undergoing coronary artery bypass graft (CABG, n=28) or valve replacement (VR, n=25) were determined.

Results: In VR patients 35.7% and in CABG 80% demonstrated LV hypertrophy. In all groups, plasma and PF L-Arg levels were higher than that of ADMA. Plasma L-Arg level was significantly ($p < 0.05$) higher in CABG than VR (75.7±4.6 µmol/L vs. 58.1±4.9 µmol/L), whereas PF ADMA level was significantly higher in VR than CABG (0.9±0.0 µmol/L vs. 0.7±0.0 µmol/L). L-Arg/ADMA ratio was significantly lower in the VR than CABG (VRplasma: 76.1±6.6 vs. CABGplasma: 125.4±10.7; VRPF: 81.7±4.8 vs. CABGPF: 110.4±7.2). There was a positive correlation between plasma L-Arg and ADMA in CABG (r=0.539); and plasma and PF L-Arg in CABG (r=0.357); and plasma and PF ADMA in VR (r=0.529); and PF L-Arg and ADMA in both CABG and VR (CABG: r=0.468; VR: r=0.371). The following echocardiographic parameters were higher in VR

compared to CABG: interventricular septum (14.7±0.5 mm vs. 11.9±0.4 mm); posterior wall thickness (12.6±0.3 mm vs. 11.5±0.2 mm); left ventricular (LV) mass (318.6±23.5 g vs. 234.6±12.3 g); right ventricular (RV) (33.9±0.9 cm^2 vs. 29.7±0.7 cm^2); right atrial (18.6±1.0 cm^2 vs. 15.4±0.6 cm^2); left atrial (19.8±1.0 cm^2 vs. 16.9±0.6 cm^2) areas. There was a positive correlation between plasma ADMA and RV area (r=0.453); PF ADMA and end-diastolic (r=0.434) and systolic diameter of LV (r=0.487); and negative correlation between PF ADMA and LV ejection fraction (r=−0.445) in VR.

Conclusions: We suggest that elevated levels of ADMA in the pericardial fluid of cardiac patients indicate a reduced bioavailability of NO, which can contribute to the development of cardiac dysfunction, hypertrophy, and remodeling.

Exercise detection with 3-Axis accelerometer of a total intracardiac leadless pacemaker

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Topic(s):
Antibradycardia pacing

Background: Conventional pacemaker systems use accelerometers or other extracardiac sensors to adapt stimulated heart rate to actual patient activity. The Micra Trans-Catheter Pacemaker (TCP) is implanted in the right ventricle and incorporates a 3-axis accelerometer to detect patient (pt) activity. The TCP incorporates filtering to accentuate physical motion over cardiac motion.

Purpose: To describe the performance and stability of the activity detection during exercise and different body positions.

Methods: Pts underwent postural and hallwalk testing at pre-discharge, 1 month, 3 month and 6 month. The activity units were measured in each accelerometer vector during different postures and activity (Figure). An excellent vector was

defined as having activity units at least >10 above the highest resting posture, >5 units was considered adequate.

Results: Overall 40 pts (76±7.8 yrs, 10 female, 30 atrial fibrillation) were implanted with the TCP. At least one vector testing was available in 39 pts; repeated testing was available in 27 pts. Although activity detection occurred at rest (due to cardiac motion) and position differences were observed in 23 pts, 38 of 39 had either one excellent (20 pts) or adequate (18 pts) vector. In repeat testing, if an excellent vector was programmed initially, this vector remained excellent (15/15). In pts programmed to an adequate vector at baseline, 10/12 patients were still adequate and 2 were programmed to a different vector.

Conclusions: Although posture dependent activity differences were observed, detection of physical exercise and appropriate rate response with intracardiac accelerometer in a TCP was demonstrated. A simple exercise test allows selection of the accelerometer vector with the greatest activity to rest ratio.
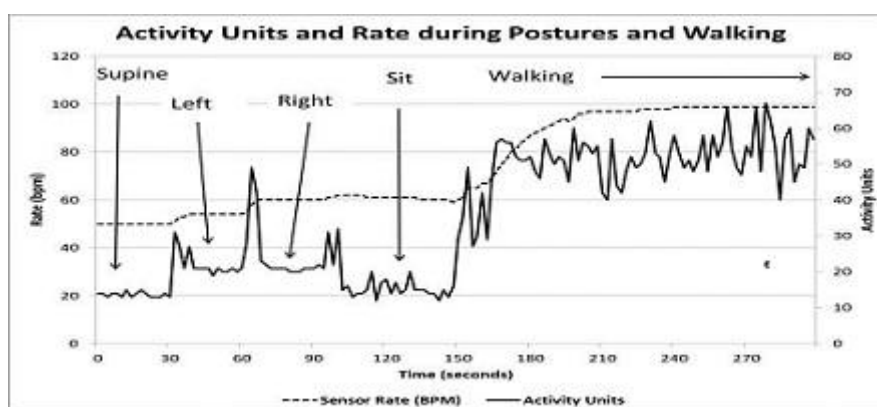
Prognostic significance of the culprit vessel in patients with ST-segment elevation myocardial infarction treated with primary coronary intervention

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Topic(s):
Infarction acute phase STEMI

Citation:

Background: Patients (pts) with ST elevation myocardial infarction (STEMI) could benefit from primary percutaneous coronary intervention (pPCI). We have very few data on prognostic significance of culprit vessel (CV) treated with pPCI.

Aim: Our aim was to study the prognostic significance of CV in pts with STEMI treated only one CV with pPCI

Methods: A total of 10763 STEMI pts undergoing pPCI were found in the National Myocardial Infarction Registry in whom only one CV was treated with successful intervention. The pts were allocated to four groups, according to localization of the CV. All pts were followed for one year and the vital status were collected from the national data.

Results: Pts characteristics according to CV were summarized in Table 1. The LM group was significantly older, the prevalence of PAD and previous myocardial infarction were significantly higher than in the LAD and RCA group. During hospitalization, cardiogenic shock was more often (26.7%) in the LM group compared to LAD, LCx RCA groups (6.7%, 5.7%, 5.5% respectively). Thirty days mortality was highest in LM group (25%) compared to LAD, LCx, RCA groups (9.2%, 6.3%, 6.4% respectively). One-year mortality was also highest in LM group (32%) compared to LAD, LCx and RCA groups (15.5%,12.3%, 11.1% respectively). Both date the mortality was significantly higher in LM and LAD groups compared to all others (p=0.013).

Conclusion: CV has prognostic significance in patients with STEMI in spite of successful pPCI. Pts have the worst prognosis if the CV the LM or LAD artery in spite of pPCI.

Pts groups according to culprit vessel

	LM	LAD	LCx	RCA	Difference (p)
Number of pts	107	4765	1481	4404	
Age year±SD	66.3±12.8*	63.1±13.4	62.7±12	63.3±12.1	*LM vs. all others (p<0.05)
Male (%)	72	62.1	66.4**	61.6	**LCx vs. (LAD, RCA p=0.002)
Hypertension %	73.7	71	73.1	72.7	NS
Diabetes %	30.5	25.5	25.6	26.2	NS
PAD %	19.8***	8.6	10.1	10.7	***LM vs. all

					others (p=0.006)
Previous MI%	24.7****	14.2	18.5	14.8	****LM vs. LAD, RCA p=0001
Previous stroke %	10.4	7.7	8.1	8.8	NS

LM, left main; LAD, left anterior descendens artery; LCx,left circumflexus artery; RCA, right coronary artery; PAD, periferal artery disease, MI, myocardial infarction, SD,standard deviation.

Elevated carbohydrate antigen 125 (CA-125) predicts poor prognosis in cardiac resynchronization therapy of chronic heart failure patients

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Topic(s):
Resynchronisation therapy

Background: Traditionally, CA-125 (carbohydrate antigen 125) has been used to detect ovarian cancer, however recent studies demonstrated that chronic heart failure patients have increased CA-125 levels associated with poor prognosis. CA-125 is produced in the cardiovascular system mainly by mesothelial cells. The increase in its levels is in connection with fluid overload and wall stress of both the left and right heart on the one hand and with inflammatory stimuli on the other. We evaluated the predictive value of CA-125 in the clinical outcome of chronic heart failure patients with cardiac resynchronization therapy (CRT).

Methods: We determined CA-125 levels of 132 chronic heart failure patients in a single center prospective observational study before and 6 months after CRT implantation using chemiluminescent immunoassay (LIAISON® CA 125 II™). Reverse remodeling, as echocardiographic response to CRT, was defined as at least a 15% decrease in the left ventricular end-systolic volume. We considered 2-years mortality as the endpoint of the study.

Results: CRT decreased the CA-125 levels 6 months after the implantation

(21.9 [10.9–52.9] vs. 18.5 [9.0–34.7] U/ml, p=0.0008). Responders to CRT (n=62) showed lower CA-125 levels at baseline (17.7 [9.2–31.9] vs. 24.2 [12.7–93.0] U/ml, p=0.09) and 6 months later (13.4 [7.7–21.2] vs. 23.0 [11.7–50.8] U/ml, p=0.004) as compared to the non-responders, however the CRT decreased the CA-125 levels in both groups (p=0.01).

Those 104 patients who survived the 2-year post-implant period had significantly lower CA-125 levels at baseline (19.3 [9.8–41.0] vs. 44.5 [20.0–126.0] U/ml, p=0.001) and adjusted multivariable Cox regression analysis demonstrated that CA-125 levels exceeding 22.5 U/ml predicts the 2-years mortality of the patients (hazard ratio=2.84 [1.17–6.86], p=0.02; area under the curve=0.68 [0.57–0.78], Sensitivity= 75%, Specificity= 58%, p=0.003).

Conclusions: CRT decreased the levels of CA-125 and patients with reverse remodeling had even lower CA-125 levels. Elevated CA-125 levels before the CRT implantation predicted the 2-year mortality of the patients. According to these results CA-125 could be a promising biomarker in the optimal patient selection for the CRT.

Pre-operatively elevated hepatocyte growth factor levels predicts 2-year mortality risk following cardiac resynchronization therapy

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Topic(s):
Resynchronisation therapy

Introduction: Cardiac resynchronization therapy (CRT) improves mortality in chronic heart failure (HF) patients with ventricular dyssynchrony, although some patients do not improve clinically and pass away unexpectedly despite optimal medical therapy and correct CRT indications. Hepatocyte growth factor (HGF) exerts antiapoptic and antifibrotic effects on various cells and cardioprotection was observed in animal models. The HGF predicted the long-term mortality of chronic heart failure patients on conventional medical therapy. The aim of the present study was to assess whether HGF predicts the short- and

long-term survival of patients undergoing CRT.

Methods: We enrolled 132 HF patients undergoing CRT. Plasma HGF levels were analysed by ELISA (R&D Systems, Minneapolis, Minnesota, USA) from venous blood samples obtained at baseline and 6 months later. Primary end-point was the 2-year all-cause mortality, secondary end-point was the 6-month mortality/hospitalization due to HF progression. Multivariable adjusted logistic and Cox regression analyses were applied. The basic models included New York Heart Association (NYHA) functional state, left bundle branch block (LBBB), QRS>135 msec, beta blocker, angiotensin convertase inhibitor or angiotensin receptor antagonist and mineralocorticoid receptor inhibitor therapy.

Results: The baseline HGF level decreased significantly 6 months after implantation (1275 [969–1768] vs. 1091 [865–1333] pg/ml, p=0.0009). The increasing levels of the HGF at baseline predicted both the 6-month mortality/hospitalisation (Odds ratio= 1.75 [1.14–2.68], p=0.009, per 1 standard deviation (SD) increase) and the 2-year mortality (Hazard ratio= 1.39 [1.06–1.82], p=0.01, per 1 SD increase) of the patients independently of the medical therapy, NYHA class, QRS width and LBBB.

Conclusions: The cardiac resynchronization therapy decreased the levels of the preimplant HGF. Increasing levels of the HGF predicted both short-term and long-term survival of chronic heart failure patients, thus HGF might be beneficial in the optimal patient section for CRT.

Clinical presentation at first heart failure hospitalization does not predict recurrent heart failure events in mild HF patients

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Topic(s):
Resynchronisation therapy

Background: Whether clinical presentation at first heart failure (HF) hospitalization predicts subsequent HF events in mild HF patients with an

implanted ICD or CRT-D, is not well understood.

Methods: Data on HF hospitalizations were prospectively collected for patients enrolled in MADIT-CRT. Predictors of subsequent HF hospitalization (HF2) after the first HF (HF1) event were assessed using Cox proportional hazards regression model.

Results: There were 193 patients with one HF hospitalization and 156 patients with subsequent HF2 events after the first admission. Patients with prior HF hospitalization (p=0.008), larger left ventricular volumes (p=0.01 for both), left atrial volume (p=0.002) and prescribed diuretics (p=0.019) had a higher probability of subsequent HF2 hospitalization. At the first HF hospitalization, dyspnoe at rest was predictive of subsequent HF2 hospitalizations (p=0.04) in a univariate model, but not after adjustment for baseline covariates. Other symptoms at admission were not predictive for subsequent HF2 hospitalization. Multivariate predictive model showed RBBB (HR=1.76, 95% CI: 1.10–2.83, p=0.02), QRS <150 ms (HR=1.44, 95% CI: 1.04–2.00, p=0.03), prior CHF hospitalization (HR=1.51, 95% CI: 1.10–2.07, p=0.01), and LVEDV index (HR=1.10, 95% CI: 1.05–1.16, p<0.001) to be associated with a higher risk for subsequent HF2 hospitalization. Cardiac support during first HF hospitalization was associated with a 3.2-times higher risk of subsequent HF2 hospitalization (95% CI: 1.30–7.98, p=0.01).

Conclusions: Left ventricular volumes, RBBB and narrow QRS on the ECG, and prior HF hospitalization predict subsequent HF2 hospitalization in mild HF patients. Clinical presentation at first HF admission is not useful to predict subsequent events. Cardiac support during first HF hospitalization is associated with more frequent subsequent HF hospitalizations and might be a useful surrogate marker for identifying a high risk patient population.

Clinical determinants of arterial thrombus structure: ultrasctructural and immunohistochemical studies

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Topic(s):
Thrombosis and coagulation

Citation:
European Heart Journal (2015) 36 (Abstract Supplement), 226

Introduction: Clot structure profoundly affects the clinical outcome of thrombotic diseases.

Purpose: We studied the associations between clinical data and the structure of coronary and peripheral arterial thrombi.

Methods: Patients of various age (36–98 years) and sex (40% female) were recruited over 22 months. Coronary thrombi were obtained by PCI-thromboaspiration following AMI (n=100), peripheral clots were removed by endarterectomy (n=50). Samples were processed by scanning electron microscopy for fibrin fiber diameter, relative occupancy by red and white blood cells, platelets, fibrin and by confocal microscopy with indirect immunostaining for fibrin and platelet receptor GpIIb/IIIa. Morphometric analysis was performed on 15 images/thrombus. Hypothesis tests and regression analysis were used to assess the correlation between structural features and selected clinical data, e.g. age, sex, antiplatelet therapy, ECG findings, ischaemic time, smoking, co-morbidities.

Results: Coronary clots contained less (mean 70.5% vs. 83.9%) and finer (mean fiber diameter 122 vs. 135 nm) fibrin than peripheral clots, while thrombi from smokers contained more fibrin than non-smokers (mean 78.1% vs. 62.2%) ($P<0.05$). In the first 24 h, fibrin content of coronary clots decreased with time, whereas in peripheral clots platelet content increased in the first 7 days. Higher clot platelet content was found in smaller vessels and at higher hematocrit values. A J-shaped dependence was found between systemic and intrathrombotic platelet count, which correlation was enhanced by aspirin and clopidogrel in peripheral thrombi and by smoking and dyslipidaemia in AMI patients.

Conclusion: Systemic and local factors are associated with characteristic thrombus morphology at different vascular locations.
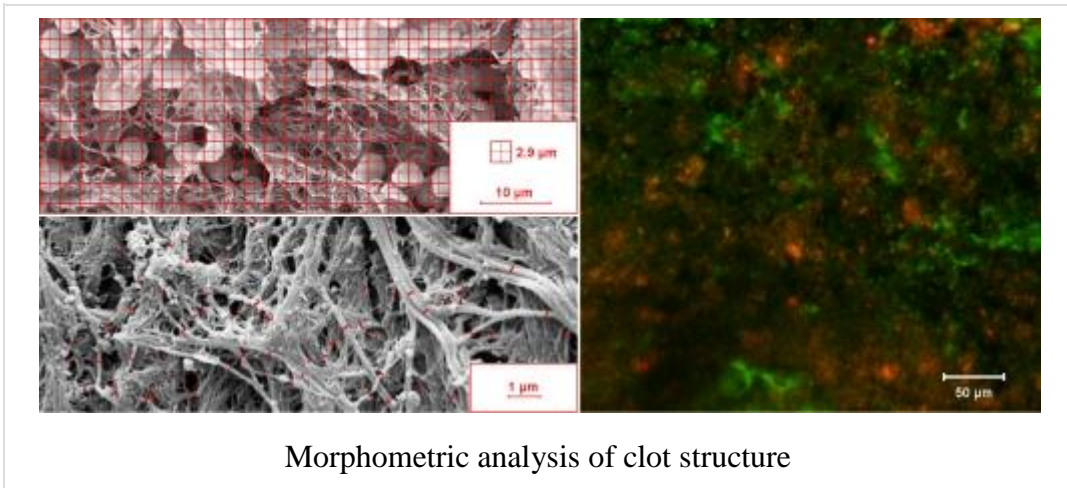
Morphometric analysis of clot structure