1038
Repolarization abnormalities during eeg-exercise test: are they really an expression of coronary flow reserve impairment?
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Background: The appearance of a down-slope of ST wave on eeg during an exercise-eeg test (ExT) is commonly considered as a marker of myocardial ischemia and therefore of coronary dysfunction. Coronary flow reserve (CFR) represents a functional parameter of the coronary circulation and, at present, can be measured by transthoracic echocardiography (TTE) during angiostressor stress on the mid-distal left anterior descending (LAD) and right coronary (RCA) arteries.

Methods: Starting from January 2003, we studied 438 patients suspected of having coronary artery disease: each of them underwent a treadmill exercise test, adopting the Bruce protocol, and coronary flow evaluation by transthoracic echocardiography. Seventy patients with poor acoustic windows were excluded as they did not allow correct evaluation of coronary flow in both coronary arteries. Within 3 months all pts underwent coronary angiography. We subdivided the patients by applying the conventional positive criteria of ExT. We considered the pts with positive ExT (218 pts) as group 1 and the pts with negative ExT as group 2 (220 pts). The coronary flow and reserve were evaluated by stress echocardiography TTE (S3-S8 probe, second harmonic 3,6-7 MHz, HP 5500-7500, Philips technology). The mid-distal LAD coronary artery was imaged from a modified apical two-chamber view and mid-distal right coronary was mapped by highlighting the diaphragmatic wall of LV. The peak diastolic coronary flow velocity of each coronary artery was recorded by pulsed Doppler under the guidance of Color Doppler flow mapping. CFR was calculated as the ratio of dipyridamole/rest peak diastolic flow velocity (0,84 mg over 10 m’).

Results: The CFR value of LAD was detected in 405/418 (92,4%) and in 318/438 (72%) for RCA. We matched the mean CFR value between LAD and RCA in the two different groups: Group 1 showed a mean down-slope of 1,9±0,6 and Group 2 2,5±0,9, p=0.013/0.001. The mean value of CFR resulted lower in Group A (2,32±0,41) vs Group B (2,51±0,40) (p=0.037).

Conclusion: By analysing the two major coronary arteries, LAD and RCA, we conclude that an impairment of coronary reserve may play an important role in inducing a down-slope of ST wave during ExT. CFR reduction induces a subendocardial flow redistribution that may give reporalization abnormalities on Ecg.

1039
Contribution of distal left anterior descending flow reserve by echo for risk stratification in chronic coronary artery disease
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Introduction: The non-invasive evaluation of left anterior descending artery (LAD) flow reserve (CFR) is feasible using transthoracic Doppler echo. LAD CFR, despite its proven accuracy for LAD patency diagnosis, has not been validated as a prognostic indicator. We investigated the LAD CFR prognostic yield in pts with chronic coronary artery disease (CAD).

Methods: 216 consecutive pts with chronic CAD were studied for LAD CFR, (age 63±11, ajection fraction 47±9, 20% females, 21% with previous anterior MI, 22% with other MI, 22% with previous CABG, 11% with diabetes). 119 pts had coronary angiography within 3 months from the index echo study. 20% had >70% and 44% >50% LAD diameter stenosis).

Results: Pts with CE or REVASC had lower CFR LAD (2.1±0.7 or 1.6±0.7 vs 2.5±0.9, p=0.013/0.001).

Using ROC analysis for CE, a CFR value >1.6 had sensitivity 0.67, specificity 0.78 (area under the curve=0.76, p=0.01) for REVASC. Using Kaplan Meier analysis, CFR >1.8 was related both to CE (log rank=5.3, p=0.02) and REVASC (log rank=16.7, p<0.00).

The prognostic contribution of LAD CFR was unaffacted when the subgroup of pts with a greater than 50% LAD stenosis was considered (log rank=2.82, p=0.07).

The use of b-blockers or statins did not affect the prognostic yield of CFR LAD (log rank=4.9/0.02 and 15.3/0.00 respectively).

Conclusion: LAD CFR evaluation noninvasively by Doppler echo provides important mid term diagnostic yield for cardiac events in pts with chronic CAD. The prognostic contribution is incremental to the TI201 scintigraphy results, is independent from the presence of >50% LAD stenosis and it is not affected by the use of b-blockers or statins.

1040
Short-term and long-term cardiac events in patients with no-reflow phenomenon: analysis using transthoracic color Doppler echocardiography
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Background: Our recent studies have shown that coronary flow velocity pattern (CFVP) with a rapid diastolic deceleration (DST) is a marker of severe microvascular injury (no-reflow phenomenon) and predicts in-hospital complications and survival in patients with anterior acute myocardial infarction (AMI). However, the relationship between CFVP and the long-term prognosis has not been elucidated.

The purpose of this study was to investigate the relationship between CFVP noninvasively measured by transthoracic color Doppler echocardiography (TTDE) and short-term and long-term cardiac events in patients with anterior AMI.

Methods: The study population consisted of 73 consecutive patients with a first-time anterior AMI successfully treated with percutaneous coronary intervention. Using TTDE, we measured coronary flow velocity in the left anterior descending artery 12 to 48 hours after the intervention. We defined severe microvascular injury as a DST ≤ 600ms. The patients were prospectively followed for the occurrence of adverse cardiac events that include cardiac death, cardiac tamponade or rupture, malignant arrhythmias and worsening congestive heart failure needs hospitalization. Event free survival was plotted according to the Kaplan-Meier method and compared with the log-rank test.

Results: Using TTDE, coronary flow velocity measurement was possible in 66 of 73 patients (90%). 43 patients with DDT>600ms and 23 patients with DDT ≤ 600ms. Although in-hospital event-free rate was significantly lower in patients with
DDT < 600ms than with DDT ≥ 600ms (56.5% versus 95.4%, p < 0.0002). There was no significant difference between the two groups for the occurrence of cardiac events after their hospital discharge (mean follow-up period, 3.7±1.7 years).

Conclusion: Patients with no-reflow phenomenon after successful coronary reperfusion showed poor clinical outcomes during the acute phase. However, patients who survived the acute phase, their long-term prognosis is equivalent to those without no-reflow phenomenon.

1041
High rejection score is associated with lower coronary flow reserve in heart transplant recipients with normal coronary angiography

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Background: Coronary flow reserve (CFR) is increasingly being used to assess the functional significance of cardiac allograft vasculopathy (CAV). The factors determining CFR in heart transplant recipients with normal coronary angiography are ill defined.

Methods: 38 consecutive patients (24 male, aged 50±13 years at heart transplantation) were studied at 6±4.5 years after heart transplantation. Rejection scores (RS) on endomyocardial biopsy were calculated (ISHLT grades: 0 = 0; 1A-1B = 2; 2-3; 3A-4; 3B-5; 4-6) in the first year and during the whole follow-up. RS including electron microscopy scores (≥3A) were also calculated. Coronary blood flow reserve in the left anterior coronary descending artery was assessed by contrast enhanced transthoracic echocardiography (CE-TEE) at rest and during intravenous infusion of adenosine (0.14 mg/kg). CFR was obtained as the ratio of hyperemic diastolic peak velocity (DPV) to resting DPV. All patients had normal findings on left ventricular angiography and coronary arteriography and a normal left ventricular mass. Comparison of means was made by Student’s t test. A p value <0.05 was considered to be significant.

Results: 7 patients (19%) had a CFR < 2.9 (group A) and 21 (55%) had a CFR ≥ 2.9 (group B). Systolic and diastolic blood pressure, heart rate and blood pressure grim differences were similar in both groups. A group A had a higher number of treated rejections in the first year (4.5±2.6 vs 2.3±2.2, p=0.01) and in the whole follow-up (5.1±3 vs 2.6±2, p=0.01). RS in the first year and in the whole follow-up were higher in group A (1.7±1.0 vs 1.2±0.4, p=0.04, 1.6±0.5 vs 1.1±0.4, p=0.02, respectively) as well as RS including only severe grades (≥3A) in the first year (0.26±0.14 vs 0.14±0.13, p=0.04) and in the whole follow-up (0.23±0.17 vs 0.13±0.09, p=0.04).

Conclusions: In heart transplant patients with angiographically normal coronary arteries, CFR by CE-TEE was inversely related to the number of previous rejection episodes. Since a high rejection burden is associated with increased risk of CAV, a CFR reduction may be an early marker of CAV. Prospective studies are warranted.

1042
Determinants of coronary flow velocity reserve in healthy young men

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Introduction: The objective of this study was to identify risk markers for attenuated coronary artery function that exist already in healthy young men without incident atherosclerosis. The identification of early markers for development of atherosclerosis may help in early detection of subjects at higher risk, and may help in reducing the morbidity and mortality related to this disease.

Methods: Coronary blood flow velocity was measured with transthoracic Doppler echocardiography at baseline and during adenosine infusion in 37 healthy non-smoking men (mean age 27±4.0 years). Body composition and distribution of fat tissue was assessed with anthropometric measures and regulation of fat metabolism by determination of adiponectin and leptin levels. Physical capacity was assessed with ergospirometry.

Results: The mean body mass index of the subjects was 23.1±1.9 kg/m², waist to hip ratio 0.84±0.04, and coronary blood flow velocity reserve (CFVR) 3.5±0.61. In univariate analysis, obesity indices at study outset, leptin, adiponectin, Max load/W/kg and VO2 peak (ml/kg/min) in ergospirometry were not pressure product and heart rate at rest were significantly correlated with CFVR. In multivariate analysis, Max load/W/kg and waist to hip ratio were the only independent predictors of CFVR. We found no relationship between CFVR and serum lipids or body mass index.

Conclusions: We conclude that increased abdominal fat and decreased aerobic fitness are independent predictors of attenuated coronary reactivity in healthy men already at a young age.

1043
Short-term simvastatin therapy improves coronary flow reserve in uncomplicated hypertensive patients with hypercholesterolemia

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Purpose: The reduction of coronary flow reserve (CFR) in arterial hypertension can be due to high blood pressure (BP), abnormal left ventricular (LV) structure but even to concomitant hypercholesterolemia. The present study aimed to assess short-term effect of simvastatin (SIM) on CFR in uncomplicated hypertensive patients with hypercholesterolemia.

Methods: Eighteen patients (M/F=12/6, mean age ± 48.2 years with 11 WHO stage arterial hypertension and hypercholesterolemia (total cholesterol [TC] >200 mg/dl), whose diastolic BP had been already normalized (<90 mmHg) by drugs, were given 4-week SIM 20 mg o.i.d. in addition to on-going antihypertensive therapy. Exclusion criteria were coronary heart disease (angina pectoris and/or ECG signs at rest and/or at maximal treadmill exercise), diabetes mellitus, heart failure, cardiomyopathies, valvular heart disease. At the beginning and at the end of treatment patients underwent blood drawing for TC and HDL-cholesterol (HDL-C), and transthoracic Doppler echocardiography for both standard assessment and evaluation of CFR in distal left anterior descending artery by using low-dose dipyridamole (Dp) (0.56 mg/ml in v). CFR was estimated as the ratio between coronary diastolic peak velocity after Dp and at rest.

Results: After 4-week therapy, TC and TC/HDL-C ratio (both p<0.01) were reduced, without changes of BP, heart rate, LV mass index, relative wall thickness, fractional shortening and Doppler diastolic indexes. Due to increase of coronary Dip velocities (p<0.01), CFR was improved by SIM (from 1.06±0.02 to 2.2±0.94, p<0.005), without changes of double product before and after therapy. This improvement remained significant even after adjusting coronary flow velocities for respective diastolic BP. In addition, it was not significantly associated to changes of TC, HDL-C and TC/HDL-C ratio. In relation to the interval of agreement for repeated measurements (second versus first exam from 10% to 4%) determined in 6 volunteer hypertensives who had repeated CFR in 3-5 days, CFR increment was considered clinically relevant, i.e. > or = 8%, in 66.6% of cases (12/18).

Conclusions: In uncomplicated hypertensive patients with normalized BP, short-term SIM therapy improves an improvement of CFR which is not associated to cholesterol changes, thus appearing due to a direct effect on coronary microcirculation. This finding supports guidelines’ indication of aggressive management of the full spectrum of concomitant cardiovascular risk factors in hypertensive patients with pre-clinical cardiovascular disease.