111 Prognostic value of cardiac metaiodobenzylguanidine in patients with advanced heart failure: relationship with peak oxygen consumption and brain natriuretic peptide

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Objectives: We sought to prospectively compare the prognostic value of cardiac iodine-123 (I-123) metaiodobenzylguanidine (MIBG) imaging with peak oxygen consumption (VO2) and plasma BNP level in patients with advanced heart failure (AHF) waiting for heart transplant.

Background: In mild to moderate heart failure, cardiac fixation of MIBG reflecting presynaptic uptake is reduced, exercise capacity is altered and plasma BNP level is increased. In AHF, prognostic value of these parameters is still unknown.

Methods: Fifty one patients with advanced heart failure were studied with planar MIBG imaging, cardiopulmonary exercise tests, hemodynamic and neurohormonal parameters. Early (30 min) and late (4 h) MIBG acquisition, as well as their ratio (washout rate, WOR) were determined. Prognostic value was assessed by survival curves (Kaplan-Meier method) and uni- and multivariate Cox analyses.

Results: Early and late cardiac MIBG uptake were correlated with ejaculation fraction (r=1.33 and r=0.42). With a median follow up of 494 days, NYHA (p=0.03), plasma BNP (p=0.002), peak VO2 (p=0.03) were predictive of death or heart transplantation, but only plasma BNP emerged by multivariate analysis. WOR<36.63% (1st quartile) was predictive on kaplan-Meier analysis.

Conclusions: In AHF patients, VO2 and BNP plasma level are stronger prognosticator than MIBG imaging related parameters. MIBG should be reserved to patients with mild to moderate heart failure while BNP remains the most powerful prognostic index whatever the severity of heart failure.

112 Levosimendan improves hemodynamics functions without sympathetic activation in severe heart failure patients: direct evidence from sympathetic neural recording

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Background: Levosimendan is a new inodilatory agent with calcium sensitizing activity. A major concern regarding the use of inotropic agent in heart failure is their effect on the sympathetic tone. This effect could explain increase in short term mortality with other inotropes. In this setting, the aim of our study was to assess the effect of levosimendan on sympathetic tone measured directly by microneurography.

Methods: In a group of acute decompensated heart failure patients, we assessed cardiac performance by digital plethysmography (Finometer©) measurement. Sympathetic tone was assessed through recording of muscle sympathetic nerve activity by microneurography. Recording were done blindly, for each patient after dobutamine perfusion was stopped (baseline) and 48 hours after levosimendan infusion. Clinical, biological and morphological data were collected. We compared cardiac parameters and sympathetic nerve activity before and after administration of levosimendan.

Results: 13 patients with refractory chronic heart failure were recruited (aged 48±3.6 years). Systolic blood pressure and rate pressure product (mmHg x Beat/min) decreased significantly after levosimendan infusion (p<0.05). Cardiac output and stroke volume assessed by Finometer were significantly increased after levosimendan infusion (p<0.05). A significant decrease of muscle sympathetic nerve activity is observed after levosimendan infusion (p<0.01). Levosimendan cause a significant reduction of plasma brain natriuretic peptide (BNP) after the initiation of the drug (p<0.01).

Conclusion: Levosimendan induced improvement of cardiac performance is associated with a decreased in MSNA. This study show for the first time that levosimendan has no direct detrimental effect on the sympathetic nervous system.

113 Significance of increased plasma BNP level in Patients with Hypertrophic Cardiomyopathy

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Background: Plasma BNP is widely used in the management of patients with systolic heart failure; however it has been less studied in patients with hypertrophic cardiomyopathy. We hypothesized that increased plasma BNP level could be associated with heart failure symptoms and increased left ventricle filling pressure in patients with HCM.

Methods: We studied 62 consecutive patients with HCM admitted for evaluation in our outpatient clinic. In all patients, clinical examination, complete echocardiography and plasma BNP and creatinine measurements were performed.

Results: The mean BNP value was 297±282 pg/mL. In univariate analysis, BNP showed a significant relationship to age (R_ = 0.1862; p = 5.10-4), magnitude of dyspnea, expressed by New York Heart Association (NYHA) functional class: I, 114±114 pg/mL; II, 224±168 pg/mL; III, 523±280 pg/mL; IV, 816±368 pg/mL (p < 10-4), atrial fibrillation (p < 0.009) and creatinine clearance (R_ = 0.2328; p < 10-4). BNP levels were also correlated with lateral annular Ea velocity (R_ = 0.2148; p = 10-4), increased LV filling pressure defined as E/A > 2 or E/Ea > 10 (R_ = 0.376; p < 10-4), left atrial size (R_ = 0.1686; p = 9.10-4), systolic pulmonary arterial pressure (R_ = 0.2399; p < 10-4). There was no relation between BNP and LV outflow tract gradient at rest or maximal LV wall thickness. Variables with significant multivariable relationship with BNP were NYHA functional class, mitral lateral Ea velocity, increased LV filling pressure, and creatinine clearance.

Conclusion: BNP levels in patients with HCM are related to the presence and magnitude of heart failure symptoms and LV filling pressure. Its prognostic value should be evaluated in these patients.

114 Metaboreflex is deactivated by hyperoxia in chronic heart failure

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Introduction: In healthy subject hyperoxia enhances metaboreflex sensitivity during static exercise. However the influence of chronic heart failure on metaboreflex sensitivity remains a matter of controversies. Moreover the effect of hyperoxia on this reflex in CHF patients is unknown. This is of importance since these patients regularly receive chronic administration of nasal oxygen during hospital admission.

Methods: The effects of breathing 21% (normoxia) and 100% oxygen (hyperoxia) at rest and during isometric handgrip at 30% of maximal voluntary contraction on MSNA, heart rate (HR), blood pressure (systolic, diastolic, mean and pulse pressure) and O2 saturation (D-O2) were determined in 14 patients with heart failure. The isometric handgrips were followed by 3 min of post-exercise circulation arrest (PE-CA) to allow metaboreflex activation in the absence of other reflex mechanisms.

Results: In normoxia, handgrip and PE-CA induced an expected increase in MSNA and hemodynamic parameters (BP, HR ; all p<0.05). Hyperoxia enhanced resting diastolic, mean blood pressure and Sao2 (all p<0.05), but without effects on MSNA responses. Hyperoxia did not modify expected
response of sympathetic and hemodynamic parameters during exercise (all p<0.05) but response after PE-CA was blunted.

Conclusion: In patients with chronic heart failure, hyperoxia did not alter mecanoreflex MSNA activation. In contrast, hyperoxia attenuates metaboreflex activation. This effect could lead to a diminished activation of the sympathetic nervous tone in heart failure and have beneficial effects.

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Diagnostic and management of patients with heart failure with preserved systolic function in hospital settings: a French observational cohort survey

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Background: Few data are available about real life and management of patients heart failure with preserved systolic function (HF-PSF).

Objective: To describe patients, disease characteristics and treatment strategies implemented in HF-PSF patients hospitalized for confirmed acute HF with LVEF ≥45%

Methods: An observational study was conducted in 68 hospital in France with 2 steps: (1) a registry part in patients hospitalized for confirmed acute HF for estimation of proportion of HF-PSF patients in the overall HF patients, (2) a detailed part with data collection of patients recently diagnosed for HF-PSF (LVEF ≥45% evaluated within 8 days following hospitalization date).

Results: 707 HF patients were enrolled in the registry with a proportion of 51% with HF-PSF. In detailed part 364 HF-PSF patients were selected, with a mean age of 79 years, 59% female, and a mean BMI 27.7 kg/m².

Main cardiovascular characteristics of HF-PSF patients were: atrial fibrillation (51%), coronary heart disease (32%), peripheral arterial disease (15%) and stroke (15%) as CV antecedents and hypertension (78%), obesity (45.5%) and diabetes (29%) as risk factors.

Mean values were: blood pressure 133/86 mmHg, HR 92 beats/min, creatinine 13.8 mg/dl, haemoglobin 12.0 g/dl. BNP was performed in 243 patients with a median value of 684 pg/ml and NT-pro-BNP in 77 patients with a median value of 3999 pg/ml. Mean ejection fraction was 58±8%.

Non CV co-morbidities were: renal failure(39%), COPD(20%), walking disorders (22%), depression(12%), cognitive disorders(8%) and cancers(5%).

Treatment at discharge included: diur. (85%), ACE-i(55%), BB (56%), Ca antag (27%), ARB (20%), aldosterone blockers (13%), digoxin (16%), anticoagulants (52%), statins (48%), aspirin (32%) and amiodarone (28.5%).

Conclusion: Much is not known about the epidemiology and management of HF-FSP in France but our study try to improve the knowledge on this disease with real life data even if until today there is no specific treatment.

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Cardiac remodeling and failure late after myocardial infarction is exacerbated by tissue hypothyroidism

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Previous studies have shown that thyroid hormone (TH) signaling is altered after acute myocardial infarction or myocardial hypertrophy with potential physiological consequences. We investigated whether such changes are related to the severity of cardiac dysfunction.

Myocardial infarction was induced in rats by coronary artery ligation (AMI), while SHAM operated animals served as controls (SHAM, n=8). Both AMI and SHAM hearts were studied after 34 weeks. AMI were divided to heart failure (AMI-HF, n=6) and non-heart failure group (AMI-NHF, n=2) as assessed by the ratio of lung weight to body weight (LWG/BW) and right ventricle weight to body weight (RV/BW). Contractile function and left ventricular (LV) remodeling was assessed by echocardiography. TR1β was increased in both border and remote regions of viable LV of AMI-NHF (2.0 fold and 1.8 fold), while it decreased in AMI-HF (2.0 fold and 1.5 fold) vs SHAM, p<0.05. TRβ1 was reduced in border and remote regions in AMI-HF (2.8 fold and 2.0 fold) and AMI-NHF (3.6 fold and 2.0 fold) vs SHAM, p<0.05. T3 and T4 were not different between groups. Accordingly, this response corresponded to changes in cardiac function (table) and in MHC isoform expression. A marked increase in β-MHC was observed in both border and remote regions of LV of AMI-HF (76% and 75%), p<0.05 vs both SHAM and AMI-NHF while a small but significant increase in β-MHC was found in both border and remote regions of LV in AMI-NHF (62% and 60%) as compared to SHAM (48% and 50%).

<table>
<thead>
<tr>
<th></th>
<th>LGW/BW</th>
<th>RV/BW</th>
<th>LVEDD (mm)</th>
<th>LVEDS (mm)</th>
<th>EF%</th>
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<tbody>
<tr>
<td>SHAM</td>
<td>3.77 (0.15)</td>
<td>0.35 (0.02)</td>
<td>6.9 (0.15)</td>
<td>4.0 (0.2)</td>
<td>75.6 (2.3)</td>
</tr>
<tr>
<td>AMI-HF</td>
<td>3.95 (0.4)</td>
<td>0.43 (0.02)</td>
<td>8.8 (0.22)*</td>
<td>7.1 (0.3)*</td>
<td>41.2 (2.6)</td>
</tr>
<tr>
<td>AMI-NHF</td>
<td>6.90 (0.8)**</td>
<td>0.82 (0.1)**</td>
<td>10.4 (0.50)**</td>
<td>9.2 (0.5)**</td>
<td>27 (2.0)</td>
</tr>
</tbody>
</table>

*p<0.05 vs SHAM, **p<0.05 vs SHAM and AMI-HF

Post-infarct remodeling results in tissue hypothyroidism. The occurrence of heart failure is accompanied by distinct changes in TR and MHC isoform expression corresponding to a marked regression to the fetal pattern.