

H015

INITIAL HEART RATE VARIABILITY COULD HELP TO IDENTIFY THE PATIENTS WITH MYOTONIC DYSTROPHY AT RISK OF DEATHJ. -D. LUPORSI ¹, P. KAMINSKY ², B. BREMBILLA-PERROT ¹¹ *Cardiologie, CHU de Brabois, Vandœuvre-lès-Nancy, France*² *Service des maladies orphelines, CHU de Brabois, Vandœuvre-lès-Nancy, France*

Heart rate variability evaluation (HRV) is used to evaluate the prognosis in heart diseases at risk of cardiac mortality. Myotonic dystrophy (MD) is complicated by cardiac involvement. The purpose of the study was to evaluate the prognostic value of HRV determination for the stratification risk in MD.

Methods – 60 asymptomatic patients, 26 men, 34 women, mean age 39±12 years at inclusion, had a MD. The studies were performed at inclusion and repeated 4±2.5 years later. Recording of 24 hour Holter monitoring and measurement of HRV in the time domain was calculated every 5 minutes (Elatec system); standard deviation of mean RR intervals (SDNN) was determined. Left ventricular ejection fraction (LVEF) was evaluated by 2D echocardiography.

Results – 1 – General changes of studies: LVEF tended to decrease (63±8, 61.5±19.5%) ($p < 0.06$). Mean values of SDNN did not change between the first inclusion (129±41ms) and the last study (134±51ms).

2 – Modifications of studies according to initial data: LVEF was normal in 56 patients at inclusion. And decreased at second study 64±6%, 61.5±7% ($p < 0.01$). LVEF was less than 50% in 4 patients at inclusion and did not change at second study (43.5±7 vs 45±8%). At inclusion, SDNN was normal in 42 patients (>100ms) (147±35ms) and was 148±52 at second study (NS); SDNN was < 100ms in 2 of them at second study. SDNN was decreased (50 to 100ms) in 17 patients at inclusion (mean 85±9ms) and tended to increase at second study (97±34ms) (NS).

3 – Follow-up: Initial SDNN could be predictive of the mortality: four patients died from heart and respiratory failure; Three had an initial SDNN < 100ms (3/17; 18%) and the last one had a normal SDNN (1/42; 2%) ($p < 0.08$).

Conclusions – The modifications of HRV during the follow-up were not useful for the prediction of the adverse events in myotonic dystrophy, although LVEF decreased with time. However, a relatively low HRV at the first evaluation could be predictive of increasing mortality from 2 to 18%.

H016

EXTRACELLULAR CARDIAC MATRIX BIOMARKERS IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION COMPLICATED BY LEFT VENTRICULAR DYSFUNCTION AND HEART FAILURE: INSIGHTS FROM THE EPHEBUS STUDYP. ROSSIGNOL ¹, W. IRAQI ¹, M. ANGIOI ¹, R. FAY ¹, J. NUÉE ¹, J. -M. KETELSLEGGERS ², J. VINCENT ³, B. PITT ⁴, F. ZANNAD ⁵¹ *Inserm et CHU de Nancy, Dommartin-lès-Toul, France*² *Cliniques Universitaires St-Luc, Department of Internal Medicine, School of Medicine, Brussels, Belgium*³ *Pfizer Inc, New York, USA*⁴ *Department of Internal Medicine, Division of Cardiology, University of Michigan, Ann Arbor, USA*⁵ *Department of Cardiology, Heart Failure and Hypertension Unit, CHU Nancy, Nancy, France*

Background – Aldosterone stimulates cardiac collagen synthesis. Circulating biomarkers of collagen turnover provide a useful tool for the assessment of cardiac remodelling in patients with congestive heart failure (CHF) and left ventricular systolic dysfunction (LVSD) post acute myocardial infarction (AMI).

Methods and Results – In a substudy of EPHEBUS, which evaluated the effects of the selective aldosterone-receptor antagonist eplerenone versus placebo, serum levels of collagen biomarkers were measured in 476 patients with CHF following AMI complicated with LVSD. Combination of both ICTP and BNP levels above median at baseline was associated with all cause mortality and composite endpoint CV death or HF hospitalisation with hazard ratios of 2.49 ($p = 0.039$) and 3.03 ($p = 0.002$) respectively. During follow up, PINP and PIIINP levels were found consistently lower in the eplerenone group and significantly so from month 6 onwards.

Conclusions – Changes in biomarkers of collagen synthesis and degradation suggest that extra cellular matrix remodelling is an active process in patients with CHF and LVSD post-AMI. High ICTP when combined with high BNP serum levels are associated with the highest event rate. Eplerenone suppresses post-AMI collagen turn over changes.

Keywords: acute myocardial infarction, extracellular matrix, collagen biomarkers, heart failure

H017

TIME DEPENDENT ACTIVATION OF AKT-GSK3BETA AND CALCINEURIN SIGNALING PATHWAYS DURING THE DEVELOPMENT OF TAC-INDUCED LEFT VENTRICULAR HYPERTROPHY IN B6D2/F1 MICEM. PREVILON ¹, C. DACHEZ ¹, J. -J. MERCADIER ^{1,2}, P. ROUET-BENZINEB ¹¹ *Inserm UMR 698, Paris, France*² *AP-HP, Groupe Hospitalier Bichat-Claude Bernard, Paris, France*

Left ventricular hypertrophy (LVH) is an adaptive response to chronic biomechanical stress that later progresses to maladaptive hypertrophy and heart failure. To better understand the mechanisms responsible for LVH development, we studied the activation of two major kinases, protein kinase B (Akt/PKB) and glycogen synthase kinase3b (GSK3b) and of a phosphatase, calcineurin (Cn) in an experimental model of thoracic aorta constriction (TAC).

Methods – 4 week-old B6D2/F1 male, Sham-operated (Sham) and TAC mice were studied 3, 7, 15, 30 and 60 days post-TAC. Gene expression and activation of signalling pathways was studied by PCR and Western Blot.

Results – TAC-induced LVH (10 – 51% at days 3-60, respectively) was associated with: 1) fetal gene reexpression characterised by an increase in mRNA levels of BNP (1.7-3 fold) and α -SK (2-4 fold), an α - to β -MHC switch seen at day 30 only; 2) a significant increase in SERCA2a (1.7 fold), PLB, and NCX (3.6 fold) protein levels at day 7. 3) a 2 fold increase in P-Akt at day 3 and a decrease at day 15 while Akt was increased at days 7 and 15; 4) an increase in P-GSK3b at day 15 (1.5 fold), whereas no change in Akt and GSK3b protein levels were seen at days 30 and 60; 5) a significant decrease in CnAb at day 15 (2 fold).