Early Repolarization associated with Primary Ventricular Fibrillation in Patients with Acute Coronary Syndrome

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Introduction: Early Repolarization (ER) is recognized as being the main indicator of new cardiac syndrome: the Early Repolarization Syndrome (ERS). This new syndrome is the consequence of repolarization heterogeneity, which appears on healthy heart, lighting the mechanism of idiopathic Ventricular Fibrillation (VF). The presence of ER has also been detected on patients with heart disorders as Hypertrophic Obstructive Cardiomyopathy, Arrhythmogenic Right Ventricular Dysplasia, Ischemic Cardiopathy.

The Goal of this study was to determine prevalence of ER in patients who have VF during Acute Coronary Syndrome (ACS).

Methods: 53 patients, 41 men et 12 women, with a mean age of 52 years (± 10) presenting primary VF (< 48h after ACS) before revascularulation of ACS have been included. We redraw cardio-vascular risk factors, history of ACS, first measure of left ventricular fraction ejection (LVEF) at hospital admission, electrocardiogram characteristics, previous treatments, myocardial revascularization and we assessed prevalence of electrocardiographic ER.

The control group comprised 106 patients with ACS but without VF, who were matched for age and sex.

Results: ER was more common in cases than in controls (56.6% vs. 37.7%, p=0.02). Risk of primary VF during ACS was twice as important when ER was present (OR=2.37, IC [1.11-5.03]). LVEF<50% (60% vs. 27.6%, p<0.001) (OR=2.8, IC [1.25-6.31]) and QTc > 440 msec (45.3 vs. 20.8%, p=0.03) (OR=2.57, IC [1.17-5.65]), were also associated with a major risk of VF during ACS.

Conclusions: Among patients with a history of primary VF during ACS, there is an increased prevalence of ER as compared to patient with ACS without VF.

Prognostic value of 24h Blood Pressure variability in Chronic Heart Failure

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Purpose: Systolic blood pressure (SBP) level is positively correlated with survival in chronic heart failure (CHF) and negatively with arterial hypertension disease. A high level of blood pressure variability (BPV) represents, especially in arterial hypertension disease, a stronger cardiovascular risk. The aim of our study was to evaluate the prognostic impact of 24h-BPV level in CHF.

Methods: We prospectively collected ambulatory monitoring blood pressure (AMBP) of 288 patients hospitalized for CHF in the department of Cardiology of the University Hospital of Rangueil in Toulouse, France, between 1999 and 2006. Follow up was realized retrospectively using physician, patient or family phone contact during 2010. The composite outcome was defined by all causes of death, heart transplant, defibrillator shock and assistance device.

Results: Mean age was 59±12 years with xx (79%) men. Mean left ventricular ejection fraction was 28±9% and mean arterial blood pressure was 110±15/68±9 mmHg. During a mean follow up of 7 years, the composite outcome was observed for 71 (32.2%) patients. After multivariate analysis, NYHA class (II vs. III/IV) and 24h-BPV (> vs.<23 mmHg - mean median value) were found to be the two independent factors of survival with an odds ratio of 5.1 (95% IC: 3 - 8;8. p=0.01) and 1.8 (95% IC 1.1 - 2.9; p<0.02) respectively.

Conclusion: In a population of CHF, high level of 24h-BPV (>23 mmHg) is a positive prognostic value for survival.
100 controls. The mutation was found in the 2 brothers, their father but absent from all other family members.

**Conclusion:** Heterozygous missense mutation in the DSP gene may result in chest pain, fainting episodes, dilated cardiomyopathy. The association of wolly hair, palmoplantar keratoderma or oligodontia may help in establishing the diagnosis of Carvajal/Naxos disease.

0109

**Lmnad1K32 heterozygous mice develop dilated cardiomyopathy that is not worsened by stress induced by exercise**

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Lmna gene encodes lamins A/C, ubiquitous nuclear envelope proteins which play crucial role in maintaining nuclear shape and stiffness. When mutated, they lead to muscular and cardiac diseases maybe due, in part, to excessive mechanical stress sensitivity (“mechanical hypothesis”). The Emery-Dreifuss muscular dystrophy (EDMD) is a LMNA-related disorder. It associates muscular dystrophy and dilated cardiomyopathy (DCM).

To understand the pathophysiological mechanisms involved in a severe form of EDMD, we have deleted the lysine 32 in mouse Lmna gene. The aim of this study was to characterize the phenotype of the heterozygous (Het) mice LmnaK32+/- and to investigate the sensitivity of myocardium to exercise.

Het mice show a progressive cardiac contractile dysfunction, evolving in DCM which leads to death between 35 and 70 weeks of age. 17 week-old Het and Wt mice were subjected to strenuous treadmill exercise for 5 weeks, 5 days/week, 1h/day at speed ranging from 27 to 35 cm.s -1. Before the running protocol, cardiac function of Het mice was similar to Wt-littermates. After 5 weeks, Het mice (trained (T) and sedentary (S)) showed decreased cardiac function compared to Wt mice (FS: 34±6,1% vs 40±4,7%) but cardiac function of Het-T did not differ from Het-S. There was no increase in heart-to-body weight ratio and expression level of cardiac remodelling markers ANP and BNP as well as cellular and nuclear size of cardiomyocytes were similar in Het-T and Het-S mice. However, β-MHC was increased by 3-fold in Het vs Wt mice. All these parameters were not changed by training in Wt mice.

In conclusion, the Lmnad1K32+/- mouse is the first mouse model harbouring a heterozygous Lmna gene mutation which develops a phenotype affecting specifically the heart. The pathophysiological mechanisms of the DCM are still unclear but contradicting the “mechanical hypothesis”, the heart of Het mice is not more vulnerable to exercise-induced mechanical stress than their Wt-littermates.

0274

**Local disorganisations of mdx myocytes membrane and sub-membrane in dilated cardiomyopathy associated to Duchenne Muscular Dystrophy**

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Duchenne Muscular Dystrophy (DMD) is an X-linked myopathy. DMD is characterised by muscular degeneration and fibrosis, which cause progressive, and then, total loss of ambulatory activity. Dystrophin forms bridge between the cytoskeletal F-actin and the extracellular matrix via the protein complex DAPC (Dystrophin-Associated Protein Complex). Loss of proteins scaffolding, resulting of dystrophin absence, induced membrane instability involving functional alterations.

In spite of many studies and palliative treatments permitting an increased life expectancy, 90% of patients develop dilated cardiomyopathy (Frisenzer and al, 2003). Consequently, it is important to study cardiac alterations in DMD.

Our study investigates changes of membrane and sub-membrane structures induced by dystrophin-deficiency in dilated cardiomyopathy.

We performed studies on ventricular cardiomyocytes from 13 month-old mdx mice (animal model of DMD). The Scanning Ion Conductance Microscopy (Gorelik and al, 2006), which allows to observe membrane surface topography from living cells, and confocal images after staining with di-8-ANEPPS, showed surface membrane local and T-tubules disorganisation in mdx myocytes. DHPR immunolabelling corroborates these local disorganisations. Loss of dystrophin seems disrupt actin myofilaments too, contrary to BI10 ventricular myocytes.

In conclusion, our observations showed structural alterations of myocytes in dilated cardiomyopathy associated to dystrophin-deficiency.


0180

**Predictors of outcome in 369 patients with heart failure with preserved ejection fraction**

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**Introduction:** A heart failure with preserved ejection fraction (HFPEF) is present in half the patients with heart failure (HF); the prognosis in more recent studies has been shown to be essentially similar to that of systolic HF. The objective of our study is to define the clinical, biological and echocardiographic predictors of outcome in patients with HFPEF.

**Material and methods:** We included 1548 patients, admitted in Ibn Rochd Center of Cardiology from May 2006 to October 2010. HFPEF was defined as LVEF ≥ 45% and receiving a loop diuretic for breathlessness. All patients were evaluated clinically with monitoring of blood pressure (BP), 6 min walk test and electrocardiogram. Two-dimensional echocardiography and laboratory tests were performed in all patients.

**Results:** Of 1548 patients, 369 (24%) had HFPEF; the median age was 66 years (42–94) and 61.9% were men. 49.2% of the patients were hypertensive and 33% were diabete, and 61.9% were in NYHA class II, and 23.8% were in NYHA class III. The median of 6min walk test was 118m. the mean LVEF was 49% (45–74). Hypertensive (44.4%) and Ischemic heart disease (17.4%) remain the two most frequent etiologies. During a median follow up of 32 months, mortality was 16%.

**Conclusion:** As several studies, clinical and biological variables were more powerful predictors of outcome in HFPEF than echocardiographic variables which are recommended to identify diastolic function.
Background: The preclinical stage of systolic heart failure (HF), known as asymptomatic left ventricular dysfunction (ALVD), is diagnosed only by echocardiography, frequent in the general population and leads to a high risk of developing severe HF. Large scale screening for ALVD is a difficult task and represents a major unmet clinical challenge that requires the determination of ALVD biomarkers.

Methods: 294 individuals were screened by echocardiography. We identified 9 ALVD cases out of 128 subjects with cardiovascular risk factors. White blood cell gene expression profiling was performed using pangenomic microarrays. Data were analyzed using principal component analysis (PCA). To build an ALVD classifier model, we used the nearest centroid classification method (NCCM) with the ClaNC software package. Classification performance was determined using the leave-one-out cross-validation method.

Results: Blood transcriptome analysis provided a specific molecular signature for ALVD which defined a model based on 7 genes capable of discriminating ALVD cases. Analysis of an ALVD patients validation group demonstrated that these genes are accurate diagnostic predictors for ALVD with 87% accuracy and 100% precision.

Discussion: These targets could serve to enhance the ability to efficiently detect ALVD by general care practitioners to facilitate preemptive initiation of medical treatment preventing the development of HF.