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Early Identification of mutation carriers by echodoppler and TDI in familial Hypertrophic Cardiomyopathy

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Aims: Some studies suggested that abnormal diastolic dysfunction was an early manifestation of Hypertrophic Cardiomyopathy (HCM) and that Tissue Doppler Imaging (TDI) was able to correctly identify mutation carriers before the development of hypertrophy. Data are however limited and still controversial. We therefore performed a systematic analysis of Echocardiography, TDI and ECG in familial HCM to identify predictive parameters for genetic status.

Methods and Results: We recruited 120 adults spread out in three groups: HCM patients with hypertrophy (LVH+, n=48), mutation carriers without hypertrophy (LVH-/G+, n=24), normal control subjects (n=48). Several parameters were significantly different in G+/LVH- as compared to controls, including septal Ea peak velocity. Multivariate logistic regression identified three Echographic/TDI independent predictors for genetic status in LVH-free subjects: the inter-ventricular/left posterior wall (IVS/LPW) ratio, the relative wall thickness (RWT) and the septal E/Ea ratio. An Echo/TDI score determined after ROC analysis, showed 67% sensitivity and 96% specificity for the identification of mutation carriers. In comparison, sensitivity and specificity of septal Ea peak velocity (<13 cm/s) were 63% and 69% respectively. Major ECG abnormalities were not correlated with the Echo/TDI score and sensitivity of ECG was only 33%.

Conclusion: Although DTI velocities alone were not reliable enough to identify LVH-free mutation carriers in HCM, a new Echo/TDI score can achieve preclinical diagnosis with high accuracy. Abnormal LV remodeling, and not only functional abnormalities, might be an early manifestation of HCM in human.

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Heliported ECMO for cardiogenic shock expands cardiac assist surgical programs

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Objectives: ECMO is an effective technique to provide emergency mechanical circulatory assistance for patients with cardiogenic shock refractory to conventional medical therapies. For patients outside our institution we create a Heliported Remote Cardiac Assist unit to implant the ECMO. Our study was undertaken to evaluate the feasibility of the procedure and the results of our experience.

Methods: Between March 2006 and June 2008 38 consecutive patients in acute cardiogenic shock were implanted with percutaneous ECMO by our heliported team.

Results: Mean distance from our ICU was 42 miles (1-143). Maximal time limit between phone call and implantation was 90 min. Mean LVEF evaluated by TTE was 19 ± 5%. Indications were fulminant myocarditis, pharmacologic suicide attempt, acute myocardial infarction, post-partum cardiopathy, end-stage dilated cardiomyopathy. They received a percutaneous veno-arterial femoral ECMO with immediate reperfusion of the limb. Seventeen patients (45%) were successfully weaned from ECMO after 9.4 ± 8.7 days. Four patients (11%) were transplanted. One patient (3%) was switched to a left ventricular assist device and successfully transplanted. Twenty-one patients (55%) survived to hospital discharge.

Conclusions: The Heliported Cardiac Remote Assist unit allowed the emergent implant of ECMO support and could rescue 55% of otherwise lethal cardiogenic shock patients in remote institutions.

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Analysis of TAZ (tafazzin) and LDB3 (LIM domain-binding3/Cypher/ZASP) genes in Left ventricular non compaction

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Background: Left ventricular non compaction (LVNC) is a recently identified cardiomyopathy, characterized by an excessively prominent trabecular meshwork and deep intertrabecular recesses. Some genes have been described as responsible for LVNC, including TAZ and LDB3, but the precise prevalence of these genes and the impact of mutation screening in clinical practice are poorly understood.

Objective: To assess the prevalence of mutations in TAZ (tafazzin, Xq28) and LDB3 (LIM domain-binding3/Cypher/ZASP, 10q23.2) genes in a large cohort of patients with LVNC, whatever the familial context.

Methods: DNA was extracted from a population of 59 consecutive patients with a definitive diagnosis of LVNC (Echo core lab), from the French registry of LVNC. Direct sequencing of exons and intron-exon boundaries was performed with ABI Prism 3100 Genetic Analyzer (Applied Biosystems). The suspected mutations were tested in a control population (>240 chromosomes); segregation within the families were analysed when available; evolutive conservation among various species were analysed by multiple alignement.

Results: We identified two new missense mutations in the TAZ gene (Phe128Ser and Met155Val) in two index male patients. No mutation was observed in the LDB3 gene, but two new genetic polymorphisms. The prevalence of TAZ mutations was 3% (2/59) and 0% for LDB3.

Conclusion: Mutations in TAZ gene were not unfrequent in LVNC whereas no mutation was observed in LDB3 gene. These findings may have impact for LVNC mutation screening strategy in clinical practice, and also for genetic counselling as TAZ mutations are associated with X-linked inheritance.

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Chronic obstructive pulmonary disease: the new deal for b-blocker prescription in chronic heart failure

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Background: The recent European Guidelines for the treatment of CHF 2008 underlined that the majority of patient with CHF and COPD can safely tolerate β-blocker therapy.

Aims: The IMPACT-RECO program III analysed the impact of NYHA class and of comorbidities on therapeutic management of French outpatients with stable CHF and left ventricular ejection fraction (LVEF) < 40%.

Methods: This survey was carried out from March 2007 to December 2007 among randomly selected French private cardiologists. 1574 patients with CHF and LVEF < 40% were included. Key demographics including comorbidities such as asthma and COPD, as well as ongoing medical treatment of CHF were collected. Physicians were asked about reasons for not prescribing β-blockers.

Results: Mean age was 71 ± 11 years, 75% of the patients were men, 34% were in NYHA class III-IV, 54% had coronary artery disease, 30% atrial fibrillation and the mean LVEF was 34 ± 7%. 78.3% of the patients received a β-blocker, and asthma or BPCO were reported in 13.7%. 341 patients were ▶

not receiving β-blockers. The first reason for non-prescription was presumed contra-indication in 51.9% (177 pts). This contra-indication was asthma or COPD in 71%, symptomatic hypotension in 15%, bradycardia in 12% and other problems in 8% . The second reason for non prescribing β-blockers was previous side effects in 35.2% (120 pts) including heart failure decompensation in 39%, symptomatic hypotension in 36%, asthenia in 26%, bradycardia in 18%, impotence in 5% and others in 6%. Lastly, in 10.9% of patients without β-blockers, the reason for non prescription was fear of potential side effect.

Conclusion: Respiratory disease remains the main reason for not prescribing β-blockers in CHF despite the fact that selective β-blockers are now recommended in this population. Room remains for improvement in β-blockers prescription rate in CHF patients with concomitant COPD, underscoring the importance of pursuing education of cardiologists.

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Clinical and echocardiographic characteristics of multivalvular infective endocarditis

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Introduction: The multivalvular endocarditis is rare, frequently involving two valves, and is associated with bad prognosis.

Objective: To compare clinical, microbiological and in hospital prognostic of multivalvular infective endocarditis with single valve infective endocarditis.

Methods and patients: This is a retrospective study; included 225 patients admitted between 2001 and 2005 for management of infective endocarditis. Subsequently, our population was divided into two groups: Group 1: multivalvular patients (29 patients), Group 2: monovalvular patients (196 patients).

Results: Group1's patients were younger. Most of patients of two groups had underlying heart disease, essentially rheumatic heart disease.

In group1, there is more mitral insufficiency, more aortic insufficiency (p=0.002), but less aortic stenosis. Groups' 1 patients have more mechanical valves prosthesis (p=0,004). The germ most frequently involved was the staphylococcus in case of multivalvular disease (46.7% vs 37.3%) and streptococcus in case of monovalvular disease (26.7% vs 38.2%), but without a significant difference in the both cases. The localization of vegetations in multi valvular IE were: mitro aortic in 25 cases.

In the TTE, there are more vegetations in group 1 :(p=0,048). Vegetations with size between 10 and 15 mm are more frequent in the group 1(p=0,019). Valvular perforations are more frequent (p=0,070). Evolution to valvular abscess (p=0,414), and acute pericardial effusion (p=0,051) was more frequent in group 1.

During their hospital period, urgent surgical indication was more frequent in the group 1(62, 1% vs. 51, 3%; p=0,279), with more frequent hemodynamic indication (72, 2% vs. 47%; p=0,049). Hospital mortality is higher in the group 1 (21, 4% vs. 17, 2%; p=0,586), but without a statistical significance.

Conclusion: Mutivalvular endocarditis has specific characteristics: Staphylococcus is the more incriminated germ. It is associated to more complications, and necessitates more urgent surgery because of acute left heart failure.

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Additive role of beta blockade in determining positive response to cardiac resynchronization therapy

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Cardiac resynchronization therapy (CRT) and beta blockers (BB) are effective in advanced heart failure (HF). Often, due to side effects, BB are not used or dose not increased. We evaluated the titration of BB therapy with carvedilol (Carv) in CRT Responders (R) and Not Responders (NR), recruiting 65 HF outpatients (pts) with CRT indication and on optimal treatment [70% males; age 67.9±12.6 years, ys; NYHA 2.7±0.7; aetiology 44% coronary artery disease (CAD), 43% dilated cardiomyopathy (DCM)]. All underwent ECG, echocardiography, NYHA evaluation before and after 1 y of CRT. Considering NYHA response and improvement of systolic left ventricular function (EF,%), R (ΔNYHA> 1 and/or ΔEF> 5%) and NR were defined. During follow-up, Carv was titrated. Basally R and NR were similar for age, sex, HF aetiology (R 40% CAD, 42.5% DCM; NR 48% CAD, 40% DCM), QRS duration (168±32 vs 178±29 msec), end-diastolic (EDV, ml), end-systolic (ESV) volume, EF (R 25.1±7.9 NR 27.4±8.2), BB treatment (85 vs 88%) and Carv dose (16.3±18.6 vs 13.2±10.3 mg/day). Only basal NYHA (R 2.9±0.7 NR 2.4±0.6, p=0.002) was significantly different. There was no significant difference in QRS duration postCRT (R 123±32, NR 127±36 msec). After 1 y, R showed greater variation of EDV and ESV (ΔEDV -45±46 vs -2±56 p=0.01; ΔESV -46±46 vs -1±45 p=0.003) and mitral regurgitation entity (-0.5±0.7 vs 0±0.7 p=0.02). After 1 y there was an overall increase of pts on BB (92.5 vs 92%), but R achieved a greater Carv dose (25.1±20.4 vs 14.5±7.3 mg/day p=0.002, Δdose 8.7±11 vs 1.2±10.7 p=0.009). Carv dose increase and EF improvement were correlated (r=0.40, p=0.02), while dose increase and ventricular remodeling (LVR) were negatively related (ΔEDV r=0.42 p=0.02; ΔESV r=0.45 p=0.01). In both groups CRT allows to introduce and augment BB dose, but only in R dose increase is statistically significant, correlating with LVR regression. Such results suggest an addictive role of BB titration in determining CRT positive response.

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Therapeutic management of heart failure by french outhospital cardiologists is in line with ESH guidelines

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Rationale: HF treatment is often started during hospitalisation. It appeared interesting to describe the evolution of treatment after hospital discharge.

Objectives: To describe changes in HF treatment since hospital discharge after stratification on the time elapsed between discharge and beginning of the survey.

Methods: Cross sectional observational survey with retrospective collection of data at hospital discharge. Patients must have been diagnosed with HF and have been hospitalised for HF within the previous 18 months.

Results: 1452 HF patients met the inclusion criteria and started the survey. 1170 (67% males, age 72±11 years, LVEF 40%±13%) have had at least one visit by the cardiologist between hospital discharge and entry in the survey. Patients were stratified according to the time since hospital discharge (<3 months N=414, 3-6 months N=297, 6-12 months N=296, 12 to 18 months N=163). At hospital discharge, recommended betablocker, ACEI (of which perindopril) or ARB, are prescribed respectively to 826 (70,6%), 807 (69,0%) and 170 (14,5%) patients. Target doses were reached in 87 (10.5%) patients with betablocker, 411 (50.9%) patients with ACEI, 7 (4.1%) patients with ARB and 417 (43.4%) patients with either ACEI or ARB. At start of the survey, target doses were reached in 176 patients (20.4%) treated with betablockers, 470 patients (59.6%) treated with ACEI, 16 patients (7.2%) receiving ARB and 484 patients (49.7%) receiving either ACEI or ARB. Rates of patients reaching the target dose for betablockers increased significantly with time (from 19.5% to 29.8% p=0.01). No significant changes were noticed for ACEI or ARB.

Conclusion: Treatment strategies for Heart Failure started at hospital are well followed and amplified by French outhospital cardiologists after hospital discharge.

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