072

Psychological impact of predictive genetic testing in cardiomyopathies

Marie-Lise Babonneau (1), Audrey Mallet (1), Benjamin Granger (2), Pascale Richard (3), Veronique Fressart (3), Francoise Hidden-Lucet (4), Michel Komajda (4), Philippe Charron (4)
(1) Centre de référence maladies cardiaques héréditaires, Paris, France – (2) CHU Pitie-Salpétrière, Unité de biostatistiques et informatique médicale, Paris, France – (3) CHU Pitie-Salpétrière, Service de biochimie – UF cardiogénétique, Paris, France – (4) CHU Pitie-Salpétrière, Département de cardiologie, Paris, France

**Background:** Most Cardiomyopathies are inherited diseases with autosomal dominant inheritance and delayed cardiac expression. In families with a documented causal mutation, predictive genetic testing can be proposed to “healthy” relatives to appropriately manage medical follow-up. Psychological impact of predictive genetic testing is however poorly described in these diseases.

**Aim and methods:** We performed a prospective study about the psychological impact of predictive genetic testing in adults seen in our out-patient multidisciplinary consultation (cardiologist, genetic counselor, and psychologist). Self-report questionnaires were proposed during the initial consultation (Q1) and 1 to 3 month after genetic result was given (Q2). Questionnaires used validated scales to evaluate anxiety, depression, hopelessness, self-esteem, impact of announcement, quality of life (QOL), and motivations.

**Results:** Sixty-six adults completed questionnaire Q1 and 38 completed questionnaire Q2 (15 mutation carriers, 23 non carriers). Analysis of psychological tests revealed no significant modification before/after genetic results. However, genetic status influenced the level of general anxiety, depression score and QOL. The consultation process was evaluated as useful (97%) and reassuring (80%). The interview with the psychologist was useful especially for the anticipation of the result (73%). Waiting period (minimal period fixed between consultation and blood sampling) was evaluated as reassuring (38%) but unnecessary (91%).

**Conclusion:** We report on the first French evaluation of the psychological impact of predictive genetic testing in cardiomyopathies. No deleterious effect of genetic results was observed. However the study underlines the usefulness of multidisciplinary management, especially to help the relatives to better anticipate the genetic result and consequences.

073

Very long-term effects of pacing therapy in Hypertrophic Obstructive Cardiomyopathy (HOCM)

Adrien Luçon (1), Laurent Palud (2), Erwan Donal (1), Nathalie Behar (1), Raphael Martins (1), Dominique Pavin (1), Christophe Leclercq (1), Philippe Mabo (1), Jean-Claude Daubert (1)
(1) Hôpital Pitié-Salpêtrière, Département de cardiologie, Paris, France – (2) Hôpital Pitié-Salpêtrière, Cardiologie, Paris, France

The clinical value of DDD pacing as primary treatment of HOCM remains controversial. Very long-term data are lacking.

**Aims:** single-centre observational study aimed at describing the very long term effects on symptoms, clinical and echocardiographic outcomes

**Patients:** 54 patients (59±14 years) with symptomatic (NYHA Class >2) drug-refractory HOCM implanted with a DDD pacemaker with or without defibrillator between 1991 and 2007 and followed up to 20 years (mean 11.5; range 0,4-21,8).

**Main results** are summarised in table. No patient had myomectomy or septal ablation during follow-up (f/u). NYHA functional class and other symptoms were significantly improved at 1-2 years and at the end of f/u. Left ventricular outflow tract (LVOT) gradient decreased by a mean of 78% at 1-2 years and 89% at end f/u consistent with SAM resolution. LV ejection fraction decreased over time with a mean value of 56% at end f/u without evidence of cavity dilatation. The actuarial survival was 90% at 5-years and 65% at 10-years. 24 patients died, 19 from non cardiac cause and 5 cardiovascular. 2 patients had heart transplant after 8 and 13 yrs.

**Conclusion:** The clinical and echocardiographic outcome of HOCM patients treated by DDD pacing seems favourable, inviting to re-evaluate the exact value of the therapy in further controlled studies

<table>
<thead>
<tr>
<th>Table – Main results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
</tr>
<tr>
<td>Grade 2</td>
</tr>
<tr>
<td>Grade 3</td>
</tr>
<tr>
<td>Grade 4</td>
</tr>
<tr>
<td>Syncope/near-syncope (%)</td>
</tr>
<tr>
<td>NYHA functional class, (%)</td>
</tr>
<tr>
<td>LVOT gradient (mmHg)</td>
</tr>
<tr>
<td>SAM (%)</td>
</tr>
<tr>
<td>LVEF (%)</td>
</tr>
<tr>
<td>LVEDD (%)</td>
</tr>
</tbody>
</table>

074

Potential role of peptide natriuretic and troponin-T to predict cardiac echocardiographic findings in hereditary transthyretin amyloidosis patients

Thibaud Damy (1), Jean-François Deux (2), Stéphane Moutereau (3), Soulef Guendouz (4), Dania Mohiti (5), Stéphane Rappeneau (4), Sylvain Loric (3), Jean-Pascal Lefaucheur (6), Luc Hittinger (4), Violaine Plante-Bordeneuve (7)
(1) CHU Henri Mondor, Fédération de cardiologie, Créteil, France – (2) CHU Henri Mondor, Cardiologie, France – (3) CHU Henri Mondor, Service de biochimie, Créteil, France – (4) CHU Henri Mondor, UF insuffisance cardiaque 8e étage, Créteil, France – (5) Centre de référence des amyloses AL, Limoges, France – (6) CHU Henri Mondor, Service des explorations fonctionnelles, Créteil, France – (7) Réseau amylose mondorien – CHU Henri Mondor, Service de neurologie, Créteil, France

**Background:** Transthyretin (TTR) familial amyloid polyneuropathy (FAP) is a fatal autosomal dominant neurodegenerative disease characterized by deposition of transthyretin targeting mainly the peripheral nervous system and the heart. Early noninvasive detection of cardiac impairment is of importance for the therapeutic management.

**Aim:** Assess if natriuretic peptide (NT-proBNP) or troponin T (cTnT) are reliable biomarkers to predict echocardiographic left ventricle (LV) impairment in a wide variety of TTR patients.

**Methods:** 36 asymptomatic carriers and patients with proven FAP genetic mutation had clinical, biological and echocardiographic assessment of left ventricle (LV) systolic function (SD), filling pressure (FP) and hypertrophy (LHV) as marker of amyloid deposition

**Results:** In the all cohort, the median (IQR) age. NT-proBNP. LV ejection fraction were respectively 59 (41-74), 323pg/ml (58-1960) and 60% (51-66). 64% were men and 12 had an increased in cTnT. TTR gene mutations prevalence was 50% for Val30Met. 4 patients were asymptomatic, 6 had only neurologic clinical signs and 26 had echo-LV abnormalities with or without neurologic disorders. Their median NT-proBNP value were respectively: 33 (19-50), 54 (37-154) and 747 (253-2840). Using received-operator curve, NTproBNP identified significantly patients with echo-LV abnormalities (Area : 0.92(0.83-0.99), p=0.001) with a threshold above 82pg/ml and a sensitivity of 92% and specificity of 90%. Elevated cTnT (superior to 0.01ng/ml) was only observed in patients combining impairment of LHV and/or SD or LHV, SD and FP.
Cardiac safety and tolerability, and effects on cardiac function of tafamidis in patients with non-V30M TTR-FAP

Thibaud Damy (1), Daniel Judge (2), Ahmet Dogan (3), Michel Slama (4), Karine Berthet (5), Violaine Planté-Bordeneuve (6)

Objective: To evaluate cardiac safety and tolerability of tafamidis in patients with non-V30M TTR-FAP.

Methods: Patients (N=21) with TTR-FAP due to non-V30M TTR mutations and no OLT history were studied in a phase 2 open-label trial. Cardiac assessments included ECG, 24-hour Holter monitoring, echocardiogram, and cardiac biomarkers (troponin I and NT-pro-BNP) at baseline and 6 and 12 months.

Results: Of the 21 patients enrolled, mean (SD) age, LVEF, troponin I, and NT-pro-BNP at baseline were 63.1 (9.86) years, 60.3 (9.96)% LVEF, 21.7 (9.5) μg/L, and 54.4 (27.8) ng/mL, respectively. Nine patients had a history of cardiac events. Six of these 9 experienced peripheral edema or dyspnea related to heart failure while on treatment, and 3 patients were hospitalized for other cardiovascular events (AV block, coronary stenosis, TIA). Eighteen patients completed the study, with no significant changes in troponin I, LVEF, or cardiac remodeling. NT-pro-BNP, while elevated at baseline, remained stable with no clinically relevant changes. The pattern of Holter monitoring abnormalities was similar at baseline and while on treatment (eg, atrial tachycardia, 52.4% [11/21] vs 44.4% [4/9]). The percentage of patients with normal heart rate variability (HRV) increased from 21% (4/19) at baseline to 42% (8/19) at month 12.

Discussion: This study showed no deleterious effects of tafamidis on cardiac function among a cohort of treated TTR-FAP patients. The number of patients with severe cardiac disease.

Cardiac safety and tolerability, and effects on cardiac function of tafamidis in patients with non-V30M TTR-FAP

075

Cardiac safety and tolerability, and effects on cardiac function of tafamidis in patients with non-V30M TTR-FAP

Thibaud Damy (1), Daniel Judge (2), Ahmet Dogan (3), Michel Slama (4), Karine Berthet (5), Violaine Planté-Bordeneuve (6)

Background: Transthyretin familial amyloid polyneuropathy (TTR-FAP) is an autosomal dominant disease characterized by extracellular amyloid deposition in the nerves and heart. Orthotopic liver transplant (OLT) is recommended to remove the source of mutated TTR and stop amyloid deposition. However, progressive cardiomyopathy due to continuing amyloidosis has been described following OLT in patients with non-V30M mutations. Tafamidis prevents dissociation of TTR into monomers and formation of amyloid.

Objectives: To evaluate cardiac safety and tolerability of tafamidis in patients with non-V30M TTR-FAP.

Methods: Patients (N=21) with TTR-FAP due to non-V30M TTR mutations and no OLT history were studied in a phase 2 open-label trial. Cardiac assessments included ECG, 24-hour Holter monitoring, echocardiogram, and cardiac biomarkers (troponin I and NT-pro-BNP) at baseline and 6 and 12 months.

Results: Of the 21 patients enrolled, mean (SD) age, LVEF, troponin I, and NT-pro-BNP at baseline were 63.1 (9.86) years, 60.3 (9.96)% LVEF, 21.7 (9.5) μg/L, and 54.4 (27.8) ng/mL, respectively. Nine patients had a history of cardiac events. Six of these 9 experienced peripheral edema or dyspnea related to heart failure while on treatment, and 3 patients were hospitalized for other cardiovascular events (AV block, coronary stenosis, TIA). Eighteen patients completed the study, with no significant changes in troponin I, LVEF, or cardiac remodeling. NT-pro-BNP, while elevated at baseline, remained stable with no clinically relevant changes. The pattern of Holter monitoring abnormalities was similar at baseline and while on treatment (eg, atrial tachycardia, 52.4% [11/21] vs 44.4% [4/9]). The percentage of patients with normal heart rate variability (HRV) increased from 21% (4/19) at baseline to 42% (8/19) at month 12.

Discussion: This study showed no deleterious effects of tafamidis on cardiac function among a cohort of treated TTR-FAP patients. The number of patients with severe cardiac disease.

Conclusion: In TTR amyloidosis, NTproBNP and troponin T are associated with LV impairment measured by echocardiography suggesting that NTproBNP could be useful in FAP carriers to start echocardiographic follow-up whereas troponin would identify patients with severe cardiac disease.

Atrial flutter or fibrillation, the most frequent and life-threatening arrhythmia in myotonic dystrophy

Béatrice Brenhilla-Perrot (1), Jérôme Schwartz (1), Jean Marc Sellal (2), Anne Moulin-Zimsh (3), Hugues Blangy (1), Nicolas Sadoul (1), Sarah Louis (2), Mahesh Pauriah (2), Gabriel Cismaru (2), Pierre Kaminsky (4)

Purpose: Diastolic Left ventricular (LV) dysfunction is a common finding in sickle cell disease. Furthermore, left atrial (LA) size usually reflects left ventricular filling pressures. The aim of our study was to determine if LA size is an expression of left ventricular filling pressures or reflects remodelling associated with anemia and/or haemolysis in sickle cell disease.

Methods: We evaluated 127 patients with sickle cell disease in stable condition (mean age 28.8±8.5 years, 83 women) and 38 age and sex-matched healthy controls. LA size was measured with Simpson’s method in apical 4-chamber view. LV filling pressures were assessed using ratio between pulsed Doppler peak E velocity and peak Ea velocity obtained with tissue Doppler imaging of the lateral annulus (E/Ea ratio). Clinical and biologic data were collected from clinical records.

Results: Compared with the normal group, patients with sickle cell disease had a LA volume and E/Ea ratio significantly increased (48.4±11.2 ml/m² and 5.9±1.7 ; 30.5±7.6 ml/m² and 4.5±1, respectively, p=0.0001).

In multivariate analysis, LA enlargement in patients is only influenced by age and haemato logical parameters (haemoglobin and reticulocyte levels).

No correlation was found between LA volume and E/Ea ratio (figure).

Conclusion: Subjects with sickle cell disease have LA enlargement. However, in this population, LA dilatation is not an index of left ventricular filling pressures.