

## P-03

### CLINICAL AND PROGNOSTIC PROFILE OF PATIENTS WITH DILATED CARDIOMYOPATHY CAUSED BY MUTATIONS IN MYBPC3 GENE

Alexandra Sousa<sup>1</sup>, Paulo Canedo<sup>2</sup>, Brenda Moura<sup>3</sup>, Luís Lopes<sup>4</sup>, Olga Azevedo<sup>5</sup>, Sandra Amorim<sup>6</sup>, Francisco Rocha Gonçalves<sup>1</sup>, José Carlos Machado<sup>2</sup>, José Silva-Cardoso<sup>6</sup>, Elisabete Martins<sup>1</sup>

<sup>1</sup> Faculty of Medicine, University of Porto, Porto

<sup>2</sup> Institute of Molecular Pathology and Immunology, University of Porto, Porto

<sup>3</sup> Regional Military Hospital nº1, Porto

<sup>4</sup> Garcia de Orta Hospital, Lisboa

<sup>5</sup> Alto Ave Hospital Center, Guimarães

<sup>6</sup> São João Hospital, Porto

xanasousa81@gmail.com

**Background:** *MYBPC3* mutations are frequent in patients (pts) with hypertrophic cardiomyopathy (HCM), representing 40–50% of all mutations. Mutations in this gene are also found in pts with dilated cardiomyopathy (DCM), accounting for approximately 2% of the cases, where knowledge of genotype-phenotype correlations remains sparse. We aimed to describe the clinical course of pts with DCM carrying mutations in *MYBPC3* gene.

**Methods:** We evaluated 107 pts with idiopathic DCM (age ≤ 50 years) or familial DCM (irrespective of age). Detailed clinical data were obtained. Echocardiographic, ECG, Holter and CMR parameters were collected. Molecular analysis included *LMNA/C*, *MYH7*, *MYBPC3*, *TNNT2*, *ACTC1*, *TPM1*, *CSRP3*, *TCAP*, *SGCD*, *PLN*, *MYL3*, *TNNI3*, *TAZ* and *LBD3* genes. Pts with mutations in *MYBPC3* gene were comprehensively analyzed.

**Results:** Ten variants in *MYBPC3* gene were found in nine (8.4%) pts (four men, mean age 52±12 years, six cases of familial DCM). None of the variants had been previously described in association with DCM, but six were associated with HCM (Asp75Asn, Gly278Glu, Gly279Ala, Glu441Lys, Arg495Gln and Glu619Lys). Mean age at diagnosis was 44±10 years and symptoms of heart failure (HF) were the initial manifestation in 7 pts. Five pts had previous hospitalization (two from HF and three from arrhythmic causes), two received an ICD and one a CRT device. In 3 pts there was history of heart transplant in a family member and in 2 there was family history of sudden death. Mean LVEDD was 67±3 mm, LVEF 32±10% and in 3 pts there was right ventricular function impairment. Three pts had AF, 5 LBBB and episodes of nonsustained VT (NSVT) were documented in 2. LGE was present also in 2 pts.

Three pts exhibited a particular dismal clinical course: a woman with c.1226+6T>C mutation, LVEDD 71 mm and LVEF 18%, AF, LBBB and NSVT, presented 3 HF-hospitalizations, had ICD implantation and eventually died of HF; a man with Arg495Gln mutation, had LVEED 67 mm and LVEF 32%, extensive LGE, a previous hospitalization from arrhythmic cause, presented aborted cardiac arrest and subsequent ICD implantation; a woman with Ala433Gly mutation presented in NYHA class III, LVEF 15%, LVEDV 212 mL/m<sup>2</sup> and 10 previous

HF-hospitalizations. On the other hand, one pts had two *MYBPC3* variants (Glu441Lys+Gly279Ala) and another an additional mutation in *TNNT2* gene (Ser275Phe) beyond *MYBPC3* mutation (Arg44His): both were in NYHA class I and had no congestion; LVEF/LVEDD were 49%/61mm and 45%/51mm and neither had right ventricle impairment; the latter had AF and a previous arrhythmia-related hospitalization.

**Conclusions:** In our population, mutations in *MYBPC3* gene appear to be more common than in previous series. Although most of the variants found were previously associated with HCM, a causative role also in DCM seems plausible. Carriers of mutations in *MYBPC3* gene present a variable, but in general dismal, clinical course, with very severe outcome in some instances.