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ABSTRACTS

02 — Heart failure and cardiomyopathies

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Mode of death in cardiac amyloidosis

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Introduction Cardiac amyloidosis (CA) is a severe disease, often lethal. Little is known about cause of death during the natural course of CA. Identification of cause of death during CA is of particular interest to design clinical trials and identify therapeutic targets in this pathology.

We aimed to describe mode of death in CA patients during long-term follow-up, according to the type of amyloidosis.

Material and methods All patients consecutively referred to the French referral center for light-chain (AL), transthyretin hereditary (hTTR) or wild-type (WT-TTR) CA were consecutively included between 2010 and 2016 were included. Mode of death was centrally adjudicated by two blinded clinical committees, using multiple sources, and classified as cardiovascular (including worsening heart failure, sudden death, stroke) or non-cardiovascular (1).

Results From the 565 patients included, 187 patients had AL amyloidosis, 220 had hTTR and 158 had WT-TTR amyloidosis. One hundred thirty-nine patients (25%) died during a follow-up of 864 patients-years, with median follow-up in survivors 14.6 months (IQR 3.7—33.9). One-year survival was 67% in AL patients, 92% in hTTR patients and 89% in WT-TTR patients (logrank < 0.0001). Among 139 deaths during follow-up, 86 (62%) resulted from cardiovascular causes, mainly worsening heart failure (58/86, 67%) and sudden death (20/86, 23%). Thirty-four deaths were from non-cardiovascular causes (24%), mostly from infection (27/34, 79%).

Discussion and Conclusions Mortality is high during natural course of cardiac amyloidosis, significantly different according to CA type. Main causes of death were cardiovascular (mostly worsening heart failure and sudden death), opening room for optimal prevention and management.

Disclosure of interest The authors declare that they have no competing interest.

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Cardio-circulatory exercise response in AL amyloidosis and comparison with hypertrophic cardiomyopathy

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Introduction Cardiopulmonary exercise test (CPET) can help the physician in understanding mechanisms that underlie patients exercise limitation. We aimed to characterize exercise response in AL amyloidosis through CPET and to compare it with hypertrophic sarcomeric cardiomyopathy (HCM).

Methods We prospectively included 49 patients: 24 with cardiac amyloidosis (group A), 10 with amyloidosis without cardiac involvement (group B) and 15 HCM (group C). All were clinically stable and underwent clinical examination, ECG, echocardiography, cardiac MRI and CPET. CPET assessed systolic blood pressure (SBP) as well as heart rate (HR) responses, O_2 pulse response, peak VO_2, circulatory power ($SBPxVO_2$) and VE/VCO_2slope.

Results The SBP response was 25 mmHg in group A from rest to peak exercise, 19 mmHg in group B and 49 mmHg in group C

($P < 0.05$). Circulatory power was 2073 mmHg.mL^{-1}min^{-1} in group A, 2620 mmHg.mL^{-1}min^{-1} in group B and 4040 mmHg.mL^{-1}min^{-1} in group C ($P < 0.05$). A chronotropic incompetence was observed in 46% of group A and 44% in group B versus 7% in group C ($P < 0.05$). Peak VO_2 was 14 mL.min.Kg^{-1} in group A, 19 mL.min.Kg^{-1} in group B and 20 mL.min.Kg^{-1} in group C ($P < 0.05$). The increase of O_2 pulse during exercise was 2 in group A versus 3 in group B and group C ($P < 0.05$). The VE/VCO_2 slope was increased in group A compared to group B and C (respectively 40 vs. 31 and 30, $P < 0.05$).

Conclusion CPET quantifies and specifies determinants of the poor cardio-circulatory response during exercise in AL amyloidosis patients, including decrease of peak VO2 and low circulatory power suggestive of poor exercise inotropic reserve; a chronotropic incompetence that can be related to cardiac dysautonomia and an increase of VE/VCO2 slope suggestive of exercise pulmonary hypertension.

Disclosure of interest The authors declare that they have no competing interest.

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Targeted panel sequencing in adult patients with left ventricular non-compaction reveals a large genetic heterogeneity

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Introduction Left ventricular non-compaction (LVNC) is a rare cardiomyopathy that may be of genetic origin, however few data are available about the global yield of mutation screening, the spectrum of genes and allelic variations.

Purpose The aim of this prospective study was to better characterize the allelic and genetic spectrum of isolated LVNC in a cohort of 95 unrelated adult patients through the molecular investigation of a custom panel of 107 genes involved in various cardiomyopathies and cardiac arrhythmias.

Results Sixty pathogenic or probably pathogenic variants, including 47 novel ones, were identified in 44 patients (46.3%) including 31 patients (32.6%) with single variant and 13 patients with complex genotypes (13.6%). The most prevalent genes were *TTN*, then *HCN4, MYH7, RYR2, MYH6, and MYBPC3*. The genotype-phenotype correlation and the major clinical outcome enhanced the fact that mutated patients tended to have younger age of diagnosis. Interestingly the mutation yield was significantly higher in youngest patients < 65 years old (42/84, 50%) as compared to oldest patients > 65 years (2/11, 18,2%, $P = 0.02$). The LV mean ejection fraction in patient with a mutation in sarcomeric genes was lower than in patients mutated in non-sarcomeric genes (41.7% vs. 52.7%, $P = 0.05$). The distribution includes 14 genes previously reported in LVNC and 13 additional candidate genes.

Discussion Our results showed that LVNC is basically a genetic disease and support genetic counselling and cardiac screening in relatives. There is a large genetic heterogeneity, with predominant *TTN* mutations and a distribution close to the one observed in dilated cardiomyopathy but with specific genes such as *HCN4*. The prevalence of complex genotypes in these patients is important to notice in the context of genetic counselling. We also identified 13 potential new genes associated with LVNC.

Disclosure of interest The authors declare that they have no competing interest.

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