Introduction

Hereditary cardiac problems are a common reason for consultation in clinical genetics. Due to the implications for the family of a hereditary cardiac condition, a familial workup is recommended in order to offer cardiac and genetic screening to at-risk family members.

In Liège, a multidisciplinary clinic by a clinical geneticist, a cardiologist and a genetic counselor was set up in 2015 to examine index patients with their first-degree relatives. The purpose of this study is to inventory our patient population.

Methods

We performed a retrospective observational study of patients from the University Hospital of Liège who had come to the cardiological consultation between July 2015 (date of creation of the consultation) and December 2017. Each index patient with a suspicion of an hereditary cardiac problem received a complete clinical workup with 24-hour Holter, ECG, cardiac ultrasound and exercise test. We made a descriptive statistical analysis of demographic and clinical characteristics as well as the prescribed complementary. Genetic analysis was performed for each index case.

Several gene panels are available here in Belgium:

• For patients with hypertrophic cardiopathy (HCM), a panel including MYBPC3, MYH7, TNN1 and other genes
• For patients with dilated cardiopathy (DCM), a panel including LMNA, MYH7, MYH6, SNC5A, MYBPC3, TNN1 and other genes
• For patients with a cardiac arrhythmia, including Brugada syndrome, QT long syndrome and a rhythm dysplasia of the right ventricle (ARVC/D).

Table 1: Clinical characteristics of the patients seen in the cardiological consultation

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>Number of patients</th>
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<tr>
<td>Sex</td>
<td>65.5%/34.5% F (n=55)</td>
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<td>Age (years)</td>
<td>Mean±21.1 (n=55)</td>
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Cardiac condition index case

<table>
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<tr>
<th>Family 1st degree</th>
<th>HCM</th>
<th>DCM</th>
<th>Cardiac arrhythmia</th>
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<td>(n=187)</td>
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Results

From June 2015 to December 2017, we have seen 55 patients for an hereditary cardiac condition in our cardiogenetics consultation: 19 women and 36 men, with mean age of 49.1 ± 15.7 years. 23 patients were referred for HCM, 16 patients for DCM and 16 patients for a cardiac arrhythmia, including Brugada syndrome, QT long syndrome and ARVC/D. Preliminary analyses of the results of genetic analyses showed both mutation-negative and mutation-positive cases, but also a substantial proportion index patients had a variant of unknown significance (23.1%). In 16 cases, the genetic analyses is still ongoing.

A causative mutation was found in 5 patients with HCM (n=18; 27.8%), in 3 patients with DCM (n=12; 25%) and in 4 patients with cardiac arrhythmia (n=10; 40%).

A variant of unknown significance (VUS) was found in 8 patients with HCM (n=18; 44.4%), in 1 patient with DCM (n=12; 8.3%) and in 1 patient with cardiac arrhythmia (n=10; 10%).

Conclusion

Hereditary cardiac problems are not rare and these conditions are frequently autosomal dominant. Therefore, a multidisciplinary cardiological consultation including analysis of first-degree at-risk family members fulfills a need in the clinic. In our population, in 30.8% of index patient, a pathogenic mutation was identified. The identification of the pathogenic mutation facilitates screening for at-risk family members. When the presence of a causative mutation is confirmed in index case, we can propose a presymptomatic test in the first-degree family members such as parents, sisters, brothers and children.

For people with a confirmed pathogenic mutation, a follow-up at least once a year and/or a drug treatment is indicated.

When a VUS is found in an index case, we can propose a familial study including non-affected and affected to determine the pathogenicity of the variant. The best attitude would be to test the both parents of index case but often they are already deceased. In this situation, when the implication of the variant found is clear, we propose to reevaluate in 3-5 years.

In any case, when the implication of the VUS is not clear or when no mutation is found in index case, a cardiac follow-up is recommended all 3 years for the proband and his first-degree apparented and we propose to reevaluate the situation in 3-5 years.