Introduction

Each year, an estimated 1.1 million sudden cardiac arrests (350 000 out-of-hospital and 200 000 in-hospital) occur in both Europe and the USA. Most of the sudden deaths (90%) are caused by a termin-al arrhythmic event secondary to underlying coronary, valvular, congenital, or infiltrative heart disorder and cardiomyopathies. Primary arrhythmias syndromes (no identifiable structural cardiac problem) with known long QT syndrome (LQTS), Brugada syndrome (BrS), catecholaminergic polymorphic ventricular tachycardia (CPVT), short QT syndrome (SQTS) or unknown early repolarization syndrome (ERS), idiopathic ventricular fibrillation (IVF) ion-channel mutations are responsible for the remaining 10% of sudden deaths.

The diagnosis and management of patients with primary inherited arrhythmias require a specialized multidisciplinary approach, since having an arrhythmic disorder can have significant medical and psychosocial implications for patients and their families. The presence of inherited arrhythmia syndromes or a positive genetic test raises questions related to transmission of disease to children, participation in sports, employment, and insurance.

The purpose of this electrophysiology (EP) wire survey was to assess the European clinical practice in primary arrhythmia disorders including LQTS, SQTS, BrS, CPVT, ERS, and IVF. The previous survey was conducted in 2010.

Methods and results

This survey is based on an electronic questionnaire sent out to the European Heart Rhythm Association (EHRA) Research Network. Responses were received from 50 centres in 23 countries. These included 71% university hospitals and 14% private hospitals. The remaining were other type of hospitals. Ten centres (22%) manage >100 patients with inherited primary arrhythmia syndromes;
6 (13%) manage 51–100, 13 (28%) manage 21–50, and 17 (37%) manage <20 patients, annually.

**Distribution of inherited arrhythmia syndromes**

Long QT syndrome is the most commonly encountered inherited arrhythmia disorder in clinical practice (35.6%), followed by BrS (32.1%). Short QT syndrome is the least common one (1.97%) whereas CPVT, ERS, and IVF each comprises 6–9% of inherited arrhythmia syndromes in Europe.

**Initial presentation**

Half of the patients (50%) are asymptomatic at the time of first diagnosis. While 30% of them are diagnosed during health checkup, 20% are diagnosed when screened as a family member of a diseased person. Syncope (25%), aborted sudden death (16%), electrolyte disorder (2%), fever (1%), and other symptoms (4%) including ischaemic heart disease and recurrent arrhythmia are different modes of initial presentation in symptomatic individuals.

**Genetic testing**

Genetic tests are performed in 70% of patients with LQTS, 57% with Brs, 26% with ERS, 60% with CPVT, 36% with IVF, 48% with SQTS, and 25% with other inherited arrhythmia (familial heart block, hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, familial clusters of sudden death). Among the relatives of these patients, 65, 52, 24, 50, 24, 43, and 19% undergo the genetic tests, respectively.

Depending upon the arrhythmic disorder, genetic tests are available in the same centre (16–28%) or at another institute in the country (40–50%), or outside the country (in Europe: 16–31%, the USA: 4–12%). One-third of all participants in this survey discuss the results of genetic tests with their patients together with a geneticist, but the majority (64%) does not consult a geneticist. Very few (2%) prefer to communicate the results by post or electronically. While many (37–59%, depending on the disorder) refer the patient to an expert (in their hospital > another institute in the country > elsewhere in Europe) for risk analysis, a significant proportion (33–41%) does not.

**Contribution to registry**

A slightly over 50% of participants do not contribute to any type of (local institutional, national, or international) registries of LQTS and BrS. For other disorders, the lack of contribution to the registry is higher (60–65% of participants). The majority of contributors register their cases nationally (32–39%) or in European registries (up to 11%). Very few centres (2–3%) participate in North American registries.

**Diagnostic drug challenge and electrophysiological study**

To diagnose BrS, 89.74% use a sodium channel blocker. For the diagnosis of CPVT, 36% use isoproterenol, 8.33% use nor-epinephrine, and 47.22% do not perform a diagnostic drug challenge. For the diagnosis of LQTS, SQTS, and ERS, 80–92% do not undertake drug provocation. For IVF, while the majority (67%) do not use the drug challenge, 24% use a sodium channel blocker.

Electrophysiological study is not used to assess inducibility of arrhythmias in the majority (82–98%) of the centres except for BrS, where 39% of centres report performing EP study. Inducibility of ventricular tachycardia or ventricular fibrillation is the main (60–70%) endpoint of EP study. For SQTS, the ventricular refractory period is an additional important measurement. Atrioventricular conduction is determined in 8–10% studies done for BrS, ERS, and CPVT.

**Other tests**

Echocardiography is the most common investigation used by 72–84% participants followed by Holter (63–83%) and stress test (36–82%). Magnetic resonance imaging is advised for the diagnostic workup of BrS, ERS, and IVF more often than for LQTS, SQTS, and CPVT (by 27–54 vs. 11–17% participants). Participating centres prefer to include coronary angiography in the work-up of IVF (62% of the centres) and CPVT (27%). Myocardial biopsy (8%) and signal-average (27%) are included in the diagnostic workup of IVF but rarely advised otherwise.

**Patient education and management of disease-related triggers**

Almost all participants (86–93%) emphasize the importance of avoiding disease-specific triggers (including QT-prolonging and BrS-provoking drugs, electrolyte imbalance, fever, abrupt noise, and strenuous exercise) in the management of inherited arrhythmia syndromes. Patients are also educated about their disease using the appropriate websites (77%) and information booklets (56%).

**Treatment and follow-up**

The first-line therapy in LQTS is drugs (76%), drugs and implantable cardioverter-defibrillator (ICD) (19%), ablation and ICD (3%), whereas no specific treatment was reported by 3% of the centres. For SQTS, it is ICD (50%), drugs (21%), ICD and drugs (18%), or nothing (12%). In BrS, the first-line treatment is ICD (48.65%), drugs (11%), ICD and drugs (8%), ablation and ICD (3%), or nothing (30%). For ERS, it is ICD (29%), drugs (16%), ICD and drugs (3%), or none (52%). In CPVT, first-line therapy is drugs (47%), ICD (11.11%), or ICD and drugs (42%), whereas in IVF, it is ICD (67%), drugs (9%), ICD and drugs (18%), ablation and ICD (3%), or none (3%).

After initiation of therapy, the patients are followed by electrophysiologists (14%), cardiologists at university (68%) or non-university hospital (14%), or generalists (5%) (Table 1).

**Primary and secondary prevention implantable cardioverter-defibrillator therapy**

In patients with LQTS, SQTS, BrS, ERS, CPVT, and IVF, the majority of participating centres (68, 61, 58, 86, 62, and 81%, respectively) use an ICD for primary prevention in only 0–5% of cases. The use of ICD therapy for secondary prevention increases to 90–100% as reported by the majority of the centres (83, 87, 89, 86, 81, and 91%) for LQTS, SQTS, BrS, ERS, CPVT, and IVF, respectively.
Management of recurrent arrhythmias

Recurrent arrhythmias leading to multiple ICD shocks in LQTS are managed with beta-blockers (43%), reinforcement of ongoing medications (22%), cardiac sympathetic denervation (19%), isoproterenol infusion (8%), or ablation (5%). In SQTS, the recurrent arrhythmias are treated with quinidine (50%), beta-blockers (19%), isoproterenol infusion, reinforcement of ongoing drugs, or ablation (8% each). In BrS, quinidine (58%) or isoproterenol infusion (22%) is the mainstay of therapy, whereas ablation is attempted in 8%. In ERS, quinidine (36%), beta-blockers (24%), and isoproterenol (20%) are preferred over ablation (4%). In CPVT, a beta-blocker (53%) and sympathetic denervation (17%) are attempted more often than ablation (6%). In IVF, ablation (20%) is the most preferred therapy after beta-blockade (40%).

Discussion

In the European clinical practice of inherited arrhythmia syndromes, LQTS and BrS constitute more than two-thirds of cases. Syncope and aborted sudden death are the presenting features of ~40% of the inherited arrhythmia population, whereas most of these patients are diagnosed while they are asymptomatic. The diagnostic drug challenge is undertaken for most BrS and some CPVT suspects but rarely otherwise. Similarly, EP study, which remains the test of choice for inducible ventricular arrhythmias, is mostly limited to BrS patients.

Overall, about two-fifths of patients and their relatives do not undergo genetic testing. Genetic tests are available in <25% centres, although more than 90% of centres find the facility available within Europe. One-third of the centres prefer to have a geneticist to explain the test results to the patients and their relatives and two-thirds refer their patients to an expert for risk analysis.

The pharmacological and non-pharmacological (device-based or surgical) management of patients is done in agreement with the current guidelines and recommendations. At present, ablation of triggers in recurrent arrhythmias is undertaken in 5–10% cases. Importantly, >50% centres do not participate in any form of registry (local institutional, national, or international) which is probably due to lower burden of primary arrhythmic disease in comparison with other electrical disorders of heart.

Conclusion

Although the current European clinical practice (diagnosis and management) generally concurs with the established guidelines on the management of inherited arrhythmia syndromes, there appears to be a need for establishing the pan-European registry for better assessment of epidemiology of these syndromes which can help improve their diagnostics and therapeutics.

Acknowledgements

The production of this EP wire document is under the responsibility of the Scientific Initiative Committee of the European Heart Rhythm Association: Carina Blomström-Lundqvist (chairman), Maria Grazia Bongiorni (co-chair), Meleze Hocini, Jian Chen, Nikolaos Dagres, Heidi Estner, Antonio Hernandez-Madrid, Torben Bjørgaard Larsen, Laurent Pison, Tatjana Potpara, Alessandro Proclemer, Elena Sciraffa, Derick Todd. We acknowledge the EHRA Research Network centres participating in this EP wire. A list of the Research Network can be found on EHRA website.

Conflict of interest: none declared.

References


Table 1 First-line treatment and follow-up care provider (% of the participating centres)

<table>
<thead>
<tr>
<th>Treatment of first choice</th>
<th>Drugs</th>
<th>ICD</th>
<th>Drugs and ICD</th>
<th>Ablation and ICD</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>LQTS</td>
<td>76%</td>
<td>0%</td>
<td>19%</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>SQTS</td>
<td>21%</td>
<td>50%</td>
<td>18%</td>
<td>0%</td>
<td>12%</td>
</tr>
<tr>
<td>BrS</td>
<td>11%</td>
<td>49%</td>
<td>8%</td>
<td>3%</td>
<td>30%</td>
</tr>
<tr>
<td>CPVT</td>
<td>47%</td>
<td>11%</td>
<td>42%</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>ERS</td>
<td>16%</td>
<td>29%</td>
<td>3%</td>
<td>0%</td>
<td>52%</td>
</tr>
<tr>
<td>IVF</td>
<td>9%</td>
<td>67%</td>
<td>18%</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Follow-up care provider</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electrophysiologist</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>14%</td>
</tr>
<tr>
<td>Cardiologist (university hospital)</td>
<td>68%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiologist (non-university hospital)</td>
<td>14%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generalist</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3%</td>
</tr>
</tbody>
</table>


