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Screening for, and management of, possible arrhythmogenic syndromes (channelopathies/ion channel diseases)

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This survey assesses the current management strategies for individuals with electrocardiographic features, suggesting an arrhythmogenic syndrome [including long QT syndrome (LQTS), Brugada syndrome (BS), catecholaminergic polymorphic ventricular tachycardia (CPVT) or short QT syndrome] or family members of patients with a known arrhythmogenic syndrome, in 44 large European centres. The principal findings of this survey were: (i) the number of new patients with arrhythmogenic syndromes (symptomatic and asymptomatic) is relatively small; (ii) the clinical work-up of these patients consists mainly of non-invasive tests; (iii) a relatively high use of genetic testing is noted, especially in LQTS and CPVT; (iv) EP testing is commonly performed in asymptomatic BS patients and in family members of symptomatic BS patients; and (v) the majority of European electrophysiologists focus on first-degree relatives when dealing with family members of an index patient.

Keywords Channelopathies • Cardiac arrhythmia • Long QT syndrome • Brugada syndrome • Catecholaminergic polymorphic ventricular tachycardia • Short QT syndrome

Introduction

Management of symptomatic patients with arrhythmogenic syndromes (channelopathies/ion channel diseases) associated with increased risk of sudden cardiac death is well established.[1–5] Increasingly, however, cardiologists are confronted with asymptomatic putative cases and family members of index patients. Further evaluation and management of these asymptomatic individuals is not straightforward and it is unclear how heterogeneous the approach is in different practices across Europe.

The purpose of this survey was to identify the current strategies used by leading European electrophysiology practices for screening and further evaluation of these arrhythmogenic syndromes, with a focus on the management of asymptomatic individuals.

Results

Responses were received from 44 of the European Heart Rhythm Association's Network for the electronic questionnaire distributed in February 2010 regarding their clinical strategies for dealing with patients with suspected arrhythmogenic syndromes. The responding centres represented 18 countries (7 from Spain, 5 from Belgium, 4 from Germany, 3 each from Denmark, France, and Italy, 2 each from UK, the Netherlands, Iceland, Norway, and Sweden, and 7 countries were represented by one centre only). All responders represented invasive centres and the majority came from relatively high-volume centres (84% performing more than 150 catheter ablations per year and 41% performing more than 150 ICD implants per year).

In the questionnaire, we asked for information regarding their approach to four specific arrhythmogenic syndromes: the long QT syndrome (LQTS), the Brugada syndrome (BS), catecholaminergic polymorphic ventricular tachycardia (CPVT), and the short QT syndrome (SQTS). Although the respondents represented large centres, the large majority (73–84%) see only 1–10 new symptomatic patients with LQTS, BS, or CPVT each year. Similarly, the majority of centres (55–71%) see 1–10 new asymptomatic patients with LQTS, BS, or CPVT. Interestingly, SQTS indeed is a very rare entity as is reflected by the very large number of centres that do not see any newly diagnosed symptomatic (71%) or asymptomatic (73%) patients.

Concerning the clinical work-up of *asymptomatic* individuals with electrocardiographic features suggesting either LQTS, BS, or CPVT, Holter recording was a requirement in the majority of centres (68–86%), but also 50–82% of responders would perform genetic testing, especially in LQTS. As might be expected,

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an exercise test was considered of great value in the work-up of asymptomatic individuals suspected of CPVT (82%), while imaging studies and implantable loop recorders are seldom used in the evaluation of asymptomatic cases. Of note, 68% would perform EPS in asymptomatic individuals with a BS ECG pattern, although the existing literature does not unequivocally support its use. The majority of responders (57%) felt that they could not offer opinion with respect to SQTS.

Family screening of symptomatic index patients is done by all centres but seems to be confined in the majority (52–68%) to first-degree relatives, whereas 23–36% would screen the extended family. The tests used in the screening of family members of symptomatic patients involved mainly the 12-lead ECG (82–98%), but a relatively high use of genetic testing (41–59%), exercise testing/pharmacology testing (43–77%), and Holter monitoring (55–61%) was noted; 30% would perform EPS in family members of symptomatic BS patients.

The answers on family screening in family members of asymptomatic index patients were comparable with the results of screening family members of symptomatic cases, although only 14% would perform EPS in family members of asymptomatic BS index patients.

Although a relatively high use of genetic testing was reported in the evaluation of asymptomatic patients and family members of index patients, the clinical value of these tests was rated high in 67% of centres for LQTS and in only 29% of centres for BS and 36% in CPVT. Furthermore, in more than 40% of centres, it took more than 6 months before the results were available. In 57% of the countries, national guidelines on genetic testing exist, but 17% were not sure about the existence of such guidelines in their country. The biochemical work of the genetic testing was performed in the responder's own institution in 71% of cases, but in the majority of countries the testing could be performed at other sites in their home country. In 55% of sites, genetic testing is completely or partially reimbursed.

Discussion

Screening of apparently healthy asymptomatic individuals is challenging for the cardiologist and may have significant consequences for the person to be tested with respect to psychological factors ('fear of becoming a patient'), need for future follow-up and potential procedure-related risks. In addition, screening may be costly for the healthcare system.

This survey showed that the majority of European electrophysiologists would only screen first-degree relatives of both asymptomatic and symptomatic patients with arrhythmogenic syndromes. The test program was more extensive with incidentally detected abnormalities suggesting an arrhythmogenic syndrome when compared with the tests performed in family members of an index patient.

About three quarters of large European centres that responded to this questionnaire have not seen SQTS patients lending credence to the perceived rarity of this syndrome. In addition, it is interesting that the invasive EPS would be performed in about two-thirds of asymptomatic individuals with suspicion of BS, whereas this test would be performed in only 30% of family members of symptomatic index cases and 14% of family members of asymptomatic index cases.

Only about half of the responding European countries have guidelines dealing with genetic testing of these individuals. Genetic testing can be performed locally for the majority of cases and the response time is longer than 6 months for more than 40% of centres, decreasing clinical applicability of these tests. Genetic testing was considered most valuable in LQTS and CPVT whereas its value was considered low in BS.

Conclusions

The number of new patients with arrhythmogenic syndromes (symptomatic and asymptomatic) is relatively small in the 44 large EP centres that answered to the survey. The clinical work-up of these patients consists mainly of non-invasive tests, focusing on electrocardiographic manifestations and rhythm monitoring. Also, a relatively high use of genetic testing is noted, especially in LQTS and CPVT. EP testing is commonly performed in asymptomatic BS patients and in family members of symptomatic BS patients

The majority of European electrophysiologists focus on first-degree relatives when dealing with family members of an index case with an arrhythmogenic syndrome.

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