

Overview of Inherited Heart Rhythm Disorders for Patients

Introduction

Inherited heart rhythm disorders affect a small portion of the population, presenting as palpitations, fainting, heart arrest and sudden death. Many patients present as teenagers or young adults, but can present as babies, young children or when elderly. Tragically, children and adolescents are often highly publicized victims of fatal inherited heart rhythm disorders. These can be broadly divided into conditions with a primary electrical basis [Long and Short QT syndromes (LQTS, SQTS), Brugada syndrome, catecholaminergic polymorphic ventricular tachycardia (CPVT), Wolff-Parkinson White (WPW)], and disease of heart muscle that often present with arrhythmias including sudden death [hypertrophic cardiomyopathy (HCM), and arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D)]. If undetected, these disorders can lead to sudden cardiac death (SCD).

How common are these conditions?

Inherited heart rhythm disorders are considered rare conditions that are typically unfamiliar to much of the general population. Systematic evidence suggests that their prevalence is considerably higher than this perspective would support.

Table 1 Prevalence of inherited heart rhythm disorders.

Condition	Prevalence
Hypertrophic cardiomyopathy	1 in 500 ¹
Long QT syndrome	1 in 2,500 ²
Wolff Parkinson White	1 in 3,000 ³⁻⁵
Arrhythmogenic right ventricular cardiomyopathy*	1 in 1,000 to 1 in 5,000 ⁶
Brugada syndrome	1 in 5,000 ⁷
Catecholaminergic polymorphic ventricular tachycardia	1 in 10,000 ^{8,9}

* Arrhythmogenic right ventricular cardiomyopathy and arrhythmogenic right ventricular dysplasia are the same condition, and will be referred to as arrhythmogenic right ventricular cardiomyopathy (ARVC) in this document.

Clinical Presentation

The clinical presentation varies between patients and conditions, ranging from no symptoms to severe and frequently occurring symptoms¹⁰. Though palpitations may occur infrequently, the typical symptoms are syncope (fainting) and cardiac arrest. Most inherited heart rhythm disorders are caused by autosomal dominant mutations¹¹⁻¹³. This means that a single genetic defect is present that results in the clinical condition that is inherited or transmitted to 50% of offspring. Typically, an index case (termed proband) presents with fainting, cardiac arrest or sudden death, and family screening identifies other members that are affected but with little or no symptoms. Being genetically affected, however, does not necessarily mean that individuals will be symptomatic. Penetrance is the term used to describe the proportion of individuals who

possess the genetic mutation and are also symptomatic. The penetrance of inherited heart rhythm disorders is variable, ranging from 20-60%^{6, 14-17}. It is also important to note that patients who are symptomatic may experience symptoms to different degrees^{6, 10, 15, 18, 19}.

Fainting

Fainting (termed syncope) is a relatively common problem, with up to one in five individuals experiencing an episode by the time they reach 15 years of age²⁰, and a 30-50% lifetime prevalence^{21, 22}. Though it is often benign, fainting can be a sentinel sign of a more serious, underlying heart condition such as an inherited heart rhythm condition. Warning signs that are key involve unusual circumstances of fainting, such as during exercise, swimming, with loud noises or strong emotion.

While fainting is the most common symptom associated with inherited heart rhythm disorders, others symptoms may exist. These include, but are not limited to palpitations, dizziness, chest pain, and shortness of breath^{11, 23-27}.

Tragedies

A small proportion of patients who die suddenly remain unexplained after autopsy, that have presumed primary electrical disease attributed to inherited heart rhythm disorders²⁸. This type of sudden presumed electrical death is termed sudden arrhythmic death syndrome – SADS. Sudden death is a tragic but all too common manifestation of inherited heart rhythm disorders. Limited evidence suggests that fainting or other sentinel signs may precede sudden death on some occasions. Inherited heart rhythm disorders such as Long QT or Brugada Syndrome have no structural counterpart that is detectable at autopsy. Because the electrical system ceases to function at death, it is not possible to detect these conditions at autopsy. Family screening after a SADS death yielded a diagnosis in half of families, identifying family members with the whole range of inherited heart rhythm disorders, most commonly Long QT Syndrome²⁹.

Recent advances in the genetic testing for these conditions has enabled researchers to perform genetic testing on the DNA from the sudden death victim, termed “molecular autopsy”. This process has been applied to a small number of sudden death victims, and suggests that an explanation can be detected in almost half of the victims. This provides an explanation for the sudden death that would otherwise be unexplained, and permits screening of the remaining family members to prevent further tragedy³⁰⁻³⁴.

Changing the perspective to patients with a diagnosed inherited heart rhythm disorders, the risk of sudden death is highly variable. In general, the lifetime risk of sudden death in Long QT Syndrome is 4%^{25, 35-42}, but this estimate is derived from a high-risk population that is untreated. The majority of these patients had fainting before they died. Other inherited heart rhythm disorders have been less well studied, and the resultant risk of sudden death is less well established.^{11, 17, 43-45}

Risk factors for sudden death can be identified for many of these conditions, typically a combination of symptoms (most often syncope) and ECG and monitoring measures. It is crucial for inherited heart rhythm disorders to be detected as soon as possible, as death may be the first clinical presentation of the disease.

Diagnosis

Many tests are currently used for identifying and diagnosing inherited heart rhythm disorders. The key “test” is a careful account of patient symptoms and a family history. Inherited heart rhythm disorders often present with symptoms in unusual circumstances such as swimming, loud noises or during exercise. Details of fainting and sudden death are key to direct testing. After this, testing includes assessment of the structure of the heart with imaging (ultrasound of the heart (called an echocardiogram) and MRI), and the function of the electrical system with an ECG, heart monitoring, exercise testing, electrophysiologic testing and drug provocation^{50, 57}.

Genetic testing is often used for detecting the genetic basis of the condition in a patient who is affected by an inherited heart rhythm disorder, or for screening family members to help confirm a diagnosis²⁰. The yield of genetic testing is variable in the different inherited heart rhythm disorders, and is strongly influenced by the likelihood of the diagnosis based on clinical testing. Patients that undergo genetic testing should be educated in the reasons for testing, the complexity of interpretation and the implications for them.

Treatment

Depending on whether the patient is symptomatic or asymptomatic, several treatment approaches may be considered. These include lifestyle recommendations to reduce risk, medications and occasional use of an implantable cardioverter-defibrillator (ICD)⁴⁶⁻⁵⁰. More details regarding treatment of specific conditions is available under each section, and should be discussed with your doctor.

Discussion

Inherited heart rhythm disorders affect more individuals than previously appreciated. As scientific research continues to push forward, the tools and techniques for diagnosing and treating will continue to improve. In order to effectively treat these heart conditions, early recognition is crucial. Recognizing symptoms can be difficult, as individuals may not experience any, or may fail to seek medical attention because they feel their symptoms are unrelated to a heart condition. Increasing public education of the signs and symptoms of inherited heart arrhythmias will facilitate early detection and preventive therapy.

Once an individual is diagnosed with an inherited heart rhythm disorder, steps can be taken towards an effective treatment plan. With most conditions, treatment preceding the development of symptoms is virtually completely protective. As an example,

treatment in asymptomatic patients with Long QT Syndrome can help prevent a life-threatening arrhythmic event.

For those with inherited heart rhythm disorders, the future looks promising. Genetic analysis allows for family members of affected individuals to be tested. If positive, treatment can be initiated before the onset of symptoms. Early diagnosis of inherited heart rhythm disorders and initiation of treatment may prevent fatal arrhythmic events. The continued funding and support of medical research, as well as the enhancement of public awareness of inherited arrhythmias ensures that the lives of those affected will continue to improve.

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