ECRONICON OPEN ACCESS

EC CARDIOLOGY
Editorial

Cardiac Channelopathies: Which Way to Go?

Daniel B Petrov MD*

Department of Emergency Cardiology, "Pirogov" Emergency Hospital, Sofia, Bulgaria

***Corresponding Author**: Daniel B Petrov, Department of Emergency Cardiology, "Pirogov" Emergency Hospital, Sofia, Bulgaria.

Received: March 01, 2022; **Published:** March 28, 2022

DOI: 10.31080/eccy.2022.09.00867

Channelopathies are a heterogeneous group of disorders resulting from the dysfunction of ion channels located in the membranes of all cells and many cellular organelles. These include diseases of the nervous system (e.g. generalized epilepsy with febrile seizures plus, familial hemiplegic migraine, episodic ataxia, and hyperkalemic and hypokalemic periodic paralysis), the cardiovascular system (e.g. long QT syndrome, short QT syndrome, Brugada syndrome, and catecholaminergic polymorphic ventricular tachycardia), the respiratory system (e.g. cystic fibrosis), the endocrine system (e.g. neonatal diabetes mellitus, familial hyperinsulinemic hypoglycemia, thyrotoxic hypokalemic periodic paralysis, and familial hyperaldosteronism), the urinary system (e.g. Bartter syndrome, nephrogenic diabetes insipidus, autosomal-dominant polycystic kidney disease, and hypomagnesemia with secondary hypocalcemia), and the immune system (e.g. myasthenia gravis, neuromyelitis optica, Isaac syndrome, and anti-NMDA [N-methyl-D-aspartate] receptor encephalitis). The field of channelopathies is expanding rapidly, as is the utility of molecular-genetic and electrophysiological studies.

The cardiac channelopathies arise from mutation in the genes which encode for ion channels, the glycoproteins embedded in the membrane of cardiac myocytes, which allow the flux of ions in and out of the cell. Depolarising currents are mediated mainly by channels that allow the entry of sodium and calcium ions into the cell; repolarising currents are mediated by channels that allow the exit of potassium ions, with the order of activation giving rise to electrical currents that are responsible for myocyte excitability. When these channels do not work properly there is a tremendous potential to cause lethal arrhythmias. The four cardiac channelopathies - Long QT syndrome, Brugada syndrome, Short QT syndrome and Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) will be the main focus of this brief review:

1. Long QT syndrome, which takes its name from the distinctive abnormality of the electrocardiogram (ECG), results from mutations in the potassium channel and more rarely in the sodium and calcium channels. Altogether, ten different subtypes of Long QT have been defined, which are thought to affect around one in 5000 people [1-3].

2. In Brugada syndrome, first described by Pedro and Josep Brugada in 1991, a mutation in the gene encoding the sodium channel reduces inward sodium current. Brugada syndrome, which affects around one in 5000 people, is defined by a characteristic ECG pattern of right bundle branch block and persistent ST-segment elevation [4,5].

3. Short QT syndrome, identified by an extremely short QT interval, has been linked to three separate genes encoding different potassium channel proteins. Short QT syndrome is an extremely rare inherited disease. Since the condition was first identified in 2000, less than 200 cases of short QT syndrome have been reported worldwide [6]. Cardiac events usually occur in adrenergic situation (noise or exercise), although it can occur in rest. Clinical presentation included repolarization abnormalities (Ventricular Tachycardia) and syncope.

4. Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) is caused by enhanced calcium release through a defective ryanodine receptor, one of the proteins found in the potassium channel [7]. CPVT is an inherited disorder that is characterized by

emotion- and exercise- induced polymorphic ventricular arrhythmias and may lead to sudden cardiac death (SCD). CPVT plays an important role in SCD in the young and therefore recognition and adequate treatment of the disease are of vital importance [8].

Diagnosis of Long QT syndrome, Brugada and Short QT syndrome can often be made on the basis of the patients ECG. However, patients with a CPVT produce unremarkable ECG changes, only developing the typical patterns of bi-directional or polymorphic ventricular tachycardia through exercise (when the heartbeat exceeds 110 - 120 beats per minute) or through catecholamine infusion. The bottom line is when we have a patient with syncope during exercise and cannot identify any abnormalities on standard electrocardiogram, then we should always undertake an exercise ECG. Since the resting electrocardiogram is usually normal, ECG during exercise and Holter monitoring play a relevant role in the diagnosis. It is important to note that Long QT, Brugada and Short QT can all be responsible for sudden infant death syndrome. While SCD is a rare event in pediatrics it has a significant social impact, since it often presents as the first symptom in previously healthy children. In all cases of sudden infant deaths a work-up should be undertaken for family members. The ECG may be a useful tool as a part of routine neonatal screening tests for early identification of the channelopathies.

One of the major challenge in the management of channelopathies is exactly which patients require treatment. There is no doubt that anyone who has suffered a cardiac arrest, should have an implantable cardiac defibrillator (ICD). The issues, however, are much less clear for asymptomatic patients who have had an ECG or genetic diagnosis. Genetic mutations do not affect all family members in the same way. One relative may have problems, while another may be a silent carrier, so that it is not clear from the start who will develop the full disease. In this context a normal ECG does not exclude future events, and an abnormal ECG pattern does not necessarily mean that someone will suffer an event, which renders therapeutic decision making difficult in an asymptomatic individuals. The current guidelines however are helpful on this matter. Beta blockers offer the mainstay of treatment for Long QT syndrome and CPVT, where the rationale is to inhibit catecholaminergic stimulation. This, therefore, offers a good treatment option for asymptomatic patients, since the approach is largely without risk. If despite beta blocker medication, syncope occurs, an implantable cardiac defibrillator (ICD) should be considered. The subjects with Long QT and CPVT should avoid competitive sports, even if they are taking beta blockers, because SCD related to sports activity is an unexpected and rare event usually occurring in young and apparently healthy athletes. This group of patients should only practice “lazy” sports, such as walking and bike riding, that do not risk raising heartbeat above 130 per minute. An electrocardiographic early repolarization pattern (ERP) is another important aspect in competitive athletes. While ERP is a common finding among the athletic population, its discovery on the 12-lead ECG of an asymptomatic individual without family history, does not currently warrant further assessment. There remain considerable challenges in determining which athletes with ERP are at increased risk of SCD [9]. The problem for patients with Brugada and short QT, where no effective drug options are available, is that an ICD is the only proven treatment. ICDs are not without dangers - complications include a risk of infections, lead dislodgement and perforation of the heart. The situation is particularly challenging for children who require frequent lead changes as they grow older. Additionally, in some patients, the risk of the ICD treatment may be more than the risk of suffering an arrhythmia. Risk stratification of asymptomatic Brugada patients with programmed electrical stimulation (PES) introduces one of the most heated debates in arrhythmology. Supporters believe that PES can be used to distinguish - to some extent - high-risk patients from low-risk patients, who can be left alone (with advice to take certain precautions, including for example, the avoidance of fever and cocaine) and monitored annually with ECGs to ensure no deterioration in their condition. Opponents do not believe that PES can predict subsequent events. Even when an arrhythmia can be induced in a PES study, there is still controversy over whether the risk of an event is high enough to warrant both the complications and cost of ICD treatment. Future research should focus on the identification of genes associated with the disease, other risk factors, improved risk stratification to better screen, recognize and tailor management of these potential lethal cardiac channelopathies.

Bibliography

1. Moss AJ. "Prolonged QT-interval syndromes". *Journal of the American Medical Association* 256.21 (1986): 2985-2987.

2. Algra A., *et al.* "QTc prolongation measured by standard 12-lead electrocardiography is an independent risk factor for sudden death due to cardiac arrest". *Circulation* 83.6 (1991): 1888-1894.

3. Al-Khatib SM., *et al.* "What clinicians should know about the QT interval". *Journal of the American Medical Association* 289.16 (2003): 2120-2127.

4. Brugada P and Brugada J. "Right bundle branch block, persistent ST-segment elevation and sudden deaths: a disting clinical and electrocardiographic report". *Journal of the American College of Cardiology* 20.6 (1992): 1391-1396.

5. Antzelevitch C., *et al.* "Brugada syndrome: 1992-2002: a historical perspective". *Journal of the American College of Cardiology* 41.10 (2003): 1665-1671.

6. Bjerregaard P and Gussak I. "Short QT syndrome". *Annals of Noninvasive Electrocardiology* 10.4 (2005): 436-440.

7. Leenhardt A., *et al.* "Catecholaminergic Polymorphic Ventricular Tachycardia". *Circulation: Arrhythmia and Electrophysiology* 5.5 (2012): 1044-1052.

8. Lieve KV., *et al.* "Catecholaminergic Polymorphic Ventricular Tachycardia". *Circulation Journal* 80.6 (2016): 1225-1291.

9. Petrov DB and Petrova YD. "An electrocardiographic early repolarization pattern in a competitive athlete: is it a sign of danger". *International Journal of Clinical Cardiology* 8 (2021): 236.

Volume 9 Issue 2 April 2022