Arrhythmias in the Muscular Dystrophies

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KEYWORDS

• Muscular dystrophy • Arrhythmia • Sudden cardiac death • Genetics • Pacemaker
• Implantable cardioverter-defibrillator

KEY POINTS

- Duchenne, Becker, and limb-girdle 2C-2F and 2I muscular dystrophies frequently develop a dilated cardiomyopathy, which precedes arrhythmia and conduction disturbance. Decision for prophylactic device implant is based on current guidelines for nonischemic cardiomyopathy.
- Myotonic dystrophy, Emery-Dreifuss, and limb-girdle type 1B muscular dystrophies are variably associated with cardiomyopathy and frequently develop conduction disturbances requiring pacing. Recent studies support use of cardioverter-defibrillator rather than pacemakers.
- Fascioscapulohumeral is a common muscular dystrophy, only variably associated with cardiac involvement and arrhythmias.

INTRODUCTION

The muscular dystrophies are a group of inherited disorders affecting skeletal muscle diseases and to variable degree, cardiac muscle, with manifestations including heart failure, conduction disease and heart block, atrial and ventricular arrhythmias, and sudden death. With improved multidisciplinary care and increase in the life span, the prevalence of later-onset cardiac involvement is increasingly being recognized. Electrophysiologists are typically part of the care team involved in the management of patients with muscular dystrophies due to associated atrial and ventricular arrhythmias and the risk of sudden cardiac death. The aim of this article is to familiarize the reader with the nature, prevalence, treatment, and outcome of arrhythmias in muscular dystrophies and present the recent advances in this arena.

Classification of the muscular dystrophies is shown in **Box 1**.

DUCHENNE AND BECKER MUSCULAR DYSTROPHIES

Genetics and Cardiac Pathology

Duchenne and Becker muscular dystrophy are X-linked recessive disorders caused by mutations in the dystrophin gene. Abnormalities in dystrophin and in dystrophin-associated glycoproteins underlie the degeneration of cardiac and skeletal muscle in several inherited myopathies, including X-linked dilated cardiomyopathy. In Duchenne muscular dystrophy (DMD), dystrophin is nearly absent, whereas in Becker muscular dystrophy (BMD), dystrophin is present but reduced in size or amount. This leads to the characteristic rapidly progressive skeletal muscle disease in DMD and the more benign course in BMD. Cardiac involvement is seen in both disorders, and the severity is not correlated with the severity of skeletal muscle involvement. Mutations in specific domains of the large dystrophin gene are

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Box 1
Classification of the muscular dystrophies

- Duchenne and Becker muscular dystrophies
- Type 1 and type 2 myotonic dystrophies
- Emery-Dreifuss muscular dystrophies and associated disorders
- Limb-girdle muscular dystrophies
- Facioscapulohumeral muscular dystrophy

associated with a higher risk for cardiomyopathy.[1] Most patients with DMD develop a cardiomyopathy with a predilection for involvement in the inferobasal and lateral left ventricle. In BMD, cardiac disease can be even more pronounced than skeletal muscle weakness.[2]

Electrocardiography

Most patients with DMD have an abnormal electrocardiogram (ECG) with the classically described electrocardiographic pattern of distinctive tall R waves and increased R/S amplitude in V1[3] and deep narrow Q waves in the left precordial leads, possibly related to the posterolateral left ventricular involvement.[4] Other common findings include short PR interval and right ventricular hypertrophy. No association between the presence of a dilated cardiomyopathy and ECG abnormalities has been established.[5] Left bundle branch block may be seen in patients with a dilated cardiomyopathy.

Arrhythmias

In patients with DMD, persistent or labile sinus tachycardia is the most common arrhythmia recognized. Atrial arrhythmias, including atrial fibrillation and atrial flutter, can occur, often in the setting of respiratory dysfunction with cor pulmonale and in those with a dilated cardiomyopathy. Abnormalities in atrioventricular conduction have been observed with both short and prolonged PR intervals recognized. Ventricular arrhythmias occur on monitoring in 30%, primarily as ventricular premature beats. Complex ventricular arrhythmias have been reported, more commonly in patients with severe skeletal muscle disease. The presence of systolic dysfunction was a powerful predictor of mortality but ECG abnormalities, late potentials, or ventricular arrhythmias were not predictive.[6] In a cohort of patients with DMD, QT dispersion was an independent risk factor for the occurrence of ventricular tachycardia.[7] Sudden death occurs in DMD, typically in patients with end-stage muscular disease. Whether the sudden death is caused by arrhythmias is unclear. Several follow-up studies have shown a correlation between sudden death and the presence of complex ventricular arrhythmias.[8] The presence of ventricular arrhythmias was not a predictor for all-cause mortality. Arrhythmia manifestations in BMD typically relate to the severity of the associated structural cardiomyopathy. Distal conduction system diseases with complete heart block and bundle branch reentry ventricular tachycardia have been observed.

Screening, Treatment, and Prognosis

Clinical care guidelines recommend screening echocardiography at diagnosis or by the age of 6 years and subsequently every 2 years; until the age of 10 and annually thereafter in boys with DMD.[9] In patients with DMD, with improvement in respiratory support, age at death has increased so that most patients survive into their 30s.[10] Decision of implantation of an implantable cardioverter-defibrillator (ICD) should be considered individually based on patient status and wishes. Advanced heart failure therapy, including primary prevention ICDs, is appropriately considered in patients with cardiomyopathy. Patients with BMD often develop cardiac complications and death from congestive heart failure and arrhythmias are estimated to occur in up to 50% of cases.[9] BMD has a high heart transplantation rate in the first year after diagnosis of cardiomyopathy.[11] Female carriers of DMD and BMD do not develop a cardiomyopathy during childhood, but it can occur later in life. Screening echocardiography should be done in adults or with symptoms.

MYOTONIC DYSTROPHIES

Genetics and Cardiac Pathology

The myotonic dystrophies are autosomal dominant disorders characterized by myotonia (delayed muscle relaxation after contraction), weakness and atrophy of skeletal muscles, and systemic manifestations. Two distinct mutations are responsible for the myotonic dystrophies. In myotonic dystrophy type 1 (DM1), the mutation is an amplified trinucleotide cytosine-thymine-guanine (CTG) repeat found on chromosome 19.[12] It is typical for the CTG repeat to expand as it is passed from parents to offspring, resulting in the characteristic worsening clinical manifestations in subsequent generations, termed anticipation.[13] Myotonic dystrophy type 2 (DM2), also called proximal myotonic myopathy, has generally less severe skeletal muscle and cardiac involvement than in DM1 and is a tetranucleotide, CCTG repeat expansion occurs on chromosome 3. A recent study suggests that cardiac pathology in both DM1 and DM2 is related