Letter to the Editor

Cardiac Resynchronization Therapy in Becker Muscular Dystrophy: For Which Patients?

Abdallah Fayssoil[1], Soumeth Abasse[2]

[1]University of Medicine and Dentistry of New Jersey, Camden, New Jersey, USA; [2]Reims University Hospital, Reims, France

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Address:
Abdallah Fayssoil

University of Medicine and Dentistry of New Jersey,
401, Haddon Avenue
Camden, New Jersey, USA
e-mail: fayssoil2000@yahoo.fr

Becker muscular dystrophy (BMD) is a benign form of neuromuscular dystrophy with an incidence of 1 in 30,000 male births.[1] This disease is caused by an X-linked recessive mutation causing an abnormal or absent dystrophin protein.[2] Dystrophin is a sarcolemmal protein that is considered to strengthen the cytoskeleton linked with the dystrophin-associated glycoprotein complex. Dystrophin deficiency leads to a disruption of the dystrophin-associated protein complex, which leads to a loss of the integrity of the sarcolemma and to fiber necrosis. The symptomatology in BMD is usually milder with a slower progression. BMD is associated with a near normal life expectancy.

The heart can be involved in 15% of patients younger than 16 years and in 75% of patients older than 40 years.[3] Myocardial involvement in BMD seems to be unrelated to the clinical severity of skeletal muscle involvement. Histopathologic studies disclosed focal subendocardial fibrosis and fatty replacement of the myocardium.[4] Initially, the left ventricular (LV) posterobasal and lateral walls are affected.[4] The evolution of the disease may be marked by LV dilatation and mitral regurgitation.[5] In an echocardiographic study[1] that included 19 BMD patients (age range 16-41 years), the authors found a left ventricular dilatation in 7 patients (37%) and global hypokinesia in 12 patients (63%). Because cardiac involvement is an important determinant of functional capacity and survival in BMD, heart management must be optimal. Pharmacologically, this management relies mainly on angiotensin converting enzyme (ACE) inhibitors and beta-blockers. Given the lesser neuromuscular limitations and the longevity of patients, cardiac transplantation may be the effective treatment for patients with cardiac failure refractory to medical treatment.

Between medical therapy and heart transplantation, cardiac resynchronization therapy (CRT) can be discussed in the resynchronization therapy era. CRT is an adjuvant treatment for patients with symptomatic, drug refractory heart failure, providing both acute and long term hemodynamic and functional improvements. Recent studies have noticed markers of reverse remodeling, including reduction of left ventricular volumes, increase of LV ejection fraction (LVEF) and reduction of mitral regurgitation.[6,7]

Two trials, COMPANION (Comparison of Medical Therapy, Pacing, and defibrillation in Heart Failure) and CARE-HF (Cardiac Resynchronization–Heart Failure), have evaluated the effect of CRT on survival.[8,9] Enrolment criteria included sinus rhythm, NYHA class III or IV, an LVEF of 35% or less, and a QRS interval of at least 120 ms. In the two trials, the risk of death from any cause was reduced

by CRT as compared with no pacing. The difference was significant in the CARE-HF study (hazard ratio 0.64; $p<0.002$) but not in the COMPANION trial. According to the European Society of Cardiology guidelines,[10] CRT can be considered in patients with a reduced LVEF (<35%) and ventricular dyssynchrony (QRS ≥120 ms), and who remain symptomatic (NYHA III-IV) despite optimal medical therapy to improve symptoms (Class of recommendation I, level of evidence A), hospitalizations (Class of recommendation I, level of evidence A) and mortality (Class of recommendation I, level of evidence B).

Two randomized clinical trials assessed the effect of CRT on remodeling and disease progression in NYHA class I-II congestive heart failure patients.[11,12] The REVERSE (REsynchronization reVErses Remodeling in Systolic left vEntricular dysfunction) study[11] included 610 patients with asymptomatic left ventricular dysfunction (NYHA I) or mild systolic heart failure (NYHA II) with a QRS duration >120 ms and LVEF ≤40% for a 12-month follow up. In this study, left ventricular remodeling was found in the CRT- ON group.

The MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy)[12] study included 1820 patients with ischemic cardiomyopathy (NYHA I-II) or non-ischemic cardiomyopathy (NYHA II), EF <30%, and QRS duration >130 ms for 2.4 years' follow up. This study reported significant reduction in left ventricular volumes and improvement in LV ejection fraction in patients treated with CRT.

Few data are available about resynchronization therapy in BMD patients. Stollberger C et al[13] reported a case of a 40-year-old BMD patient with severe heart failure (LVEF 25%) who benefited from CRT. But no amelioration was found regarding the LVEF 3 months after the CRT therapy and the patient died 16 weeks after implantation.[13]

Indications for CRT might be discussed in selected BMD patients with heart failure.[10] Patients with neuromuscular disorders are at risk for respiratory insufficiency because of diaphragm involvement and chest deformities. Moreover, pacemaker implantation is problematic because of possible and serious mechanical and infective complications. Further studies may contribute to evaluating the place for CRT in this neuromuscular dystrophy.

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