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Cardiomyopathy in Muscular Dystrophy: When to treat?

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Duchenne Muscular Dystrophy (DMD) is a rare, X linked condition with progressive muscle weakness and accompanying cardiomyopathy. Cardiac MRI has proved particularly useful for monitoring the earliest signs of cardiac involvement in DMD including left ventricular (LV) strain defects and myocardial fibrosis, which appear prior to onset of LV systolic function. Most DMD males develop cardiomyopathic features between 10 and 15 years of age. Because of this tight timeline during which heart dysfunction appears, DMD offers a unique opportunity to assess strategies to limit cardiomyopathy progression. Becker Muscular Dystrophy, like DMD, is caused by dystrophin mutations and often also includes dilated cardiomyopathy but with variable progression.

In this issue of JAMA Cardiology, Conceição Silva and colleagues evaluated a cohort of 76 DMD/BMD patients (mean age 13.1 years) using MRI[1]. Myocardial fibrosis was most commonly seen mid- and subepicardially and tended to occur in inferior and lateral walls. Myocardial fibrosis correlated with systolic function, and those with poor outcomes had greater myocardial fibrosis. Forty-two individuals had myocardial fibrosis but preserved function (LVEF >50%) and were randomized to treatment with enalapril or not. After two years, the treated group had slower progression of myocardial fibrosis by MRI. The findings provide support for the concept of pre-treating cardiomyopathy prior to the onset of LV dysfunction.

Early treatment of cardiomyopathy in DMD has been advocated based on nuclear imaging of a distinct but similar age DMD population[2]. In addition to ACE inhibitor, eplerenone has also been shown to reduce LV strain defects in DMD[3]. Together these studies provide sound evidence for early intervention to prevent or slow cardiomyopathy progression with medical management. Moreover, this recommendation was the consensus from a working group meeting convened by the NHLBI and Parent Project Muscular Dystrophy on the cardiac management of DMD[4].

Clinical trials in rare diseases have the advantage of using well-defined homogenous populations but are often limited by small sample size. Nonetheless, in some settings it may be reasonable to extrapolate from these smaller studies to other groups. With the increasing availability of genetic testing for dilated cardiomyopathy, there is now emerging a group of younger, gene mutation-positive individuals who are prone to developing cardiomyopathy and ultimately heart failure. These gene mutation-positive individuals are most often discovered through cascade genetic testing of a family member with cardiomyopathy. Data is lacking on whether early treatment would similarly benefit this group, but the current investigation indicates this question should be addressed. As we move closer to using

genetic signatures to identify those at risk and applying tailored therapy, we realize a goal of personalized medicine.

References

1. Conceição Silva M, Magalhães TO, Zilda MA, et al. Myocardial Fibrosis Progression in Duchenne and Becker Muscular Dystrophy – ACE Inhibitor Therapy Randomized Trial. JAMA Cardiology. 2016
2. Duboc D, Meune C, Lerebours G, Devaux JY, Vaksmann G, Becane HM. Effect of perindopril on the onset and progression of left ventricular dysfunction in Duchenne muscular dystrophy. Journal of the American College of Cardiology. 2005; 45(6):855–857. [PubMed: 15766818]
3. Raman SV, Hor KN, Mazur W, et al. Eplerenone for early cardiomyopathy in Duchenne muscular dystrophy: a randomised, double-blind, placebo-controlled trial. The Lancet Neurology. 2015; 14(2):153–161. [PubMed: 25554404]
4. McNally EM, Kaltman JR, Benson DW, et al. Contemporary cardiac issues in Duchenne muscular dystrophy. Working Group of the National Heart, Lung, and Blood Institute in collaboration with Parent Project Muscular Dystrophy. Circulation. 2015; 131(18):1590–1598. [PubMed: 25940966]