Duchenne Muscular Dystrophy Cardiomyopathy: Early Diagnosis and Treatment

Authors:

Bryan D Siegel, MD[1]

E-mail: Bsiegel@cnmc.org

Christopher F Spurney, MD[1,2]

E-mail: Cspurney@cnmc.org

Affiliation

[1]Children's National Heart Institute

[2]Center for Genetic Medicine Research

Children's National Health System

Washington, DC 20010 USA

Abstract:

Duchenne muscular dystrophy (DMD) is an X-linked genetic disorder affecting approximately 1 in every 5000 live male births. DMD cardiomyopathy universally affects patients as they age into adulthood and is the leading cause of death. This review focuses on diagnosis and treatment of DMD cardiomyopathy with an emphasis on emerging imaging modalities that allow for early diagnosis. These include the expanded use of cardiac magnetic resonance imaging (CMR) and both echocardiographic and CMR myocardial strain measurements. Evidence has accumulated for the use of angiotensin converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARB) in the treatment of early myocardial disease in DMD cardiomyopathy while newer medications with different therapeutic targets are under development. Appropriate surveillance with echo-cardiography and CMR and early initiation of treatment are becoming standard of care to prevent the progressive fibrosis and dysfunction that is characteristic of DMD cardiomyopathy and improve the quality and duration of life in DMD.

Background:

Duchenne muscular dystrophy (DMD) is an X-linked genetic disorder affecting approximately 1 in every 5000 live male births. It is the most severe form of muscular dystrophy and is caused by a variety of different mutations in the dystrophin gene, a 2.5- Mb gene on chromosome Xp21.1, resulting in the absence of a functional dystrophin protein. Dystrophin acts to stabilize the plasma membrane from the muscle contractile forces[1]. The absence of dystrophin leads to cell membrane damage and the progressive loss of muscle function. Historically, respiratory issues would be the primary cause of mortality in DMD patients. However, as skeletal and respiratory muscle treatments, including non-invasive positive pressure ventilation, have advanced, patients with DMD are living into their 20's and 30's and require transition to adult care providers. During these adult years, DMD cardiomyopathy is the leading cause of death[2]. This review focuses on the current and future diagnostic and treatment options for DMD cardiomyopathy.

The pathogenesis of DMD cardiomyopathy is similar to the process by which skeletal muscle damage occurs in DMD. The absence of dystrophin causes instability in the myocyte cell membrane, leading to increased susceptibility to damage from muscle contractions. This manifests as an increase in the influx of calcium into the cell which activates proteases in the cell, causing a cascade of inflammation, cell death, and fibrosis[1]. In cardiomyocytes, the loss of dystrophin also affects L-type calcium channels and mechanical stretch-activated receptors which further exacerbate the influx of calcium and resultant inflammatory pathway[3]. This results in the loss of cardiomyocytes and remodeling leading to myocardial fibrosis and loss of function.

The cardiomyopathy associated with DMD universally affects patients as they age into adulthood[4]. A natural history study of 174 DMD patients demonstrated the rates of diagnosis of cardiomyopathy by echocardiogram increase steadily throughout childhood. Only 5% of those under 5 years, while 38% of those aged 14-17 and 61% of those aged ≥18 years had an echocardiographic diagnosis of cardiomyopathy[5]. Using cardiac Magnetic Resonance (CMR), Hor et al found that by age 16, 59% of patients had evidence of late gadolinium enhancement (LGE), a marker of the fibrosis found in DMD cardiomyopathy[6]. Likely due to the limitations in activity from skeletal muscle disease, it is more common for these patients to be asymptomatic at the time of diagnosis as compared to other forms of cardiomyopathy[5,7]. Duboc et al. (2005) demonstrated that 20% of patients who were asymptomatic at age 10 had evidence of an abnormal ejection fraction[8]. Patients with DMD cardiomyopathy are also less likely to have left ventricular enlargement at diagnosis and have a higher mortality than other dilated cardiomyopathies[7].

Despite cardiomyopathy becoming the leading cause of death in DMD patients, there is concern that it is underdiagnosed and undertreated. Guidelines from 2010 recommended initial cardiac screening at diagnosis followed by every 2 years until age 10, and yearly thereafter[9]. However, data showed that a third of patients with a DMD diagnosis had never had an echocardiogram and over half of patients with a DMD cardiomyopathy diagnosis were on no cardiac medications[5]. This reinforces the need for increased awareness among medical providers and updated guidelines incorporating new imaging modalities and treatment options for these patients.

Diagnosis:

Early diagnosis is essential for the treatment of cardiomyopathy to prevent progression to more severe heart failure symptoms and diminished quality of life. Patients often remain asymptomatic from a cardiac perspective due to reliance on motorized wheelchairs and use of respiratory assistance while sleeping in the late teenage to early adult years. However, this is a critical period to recognize and treat DMD cardiomyopathy in young adults.

Physical exam may provide initial clues to diagnosis including S3/S4 heart sounds or a murmur of mitral regurgitation, but these are usually associated with later stages of cardiomyopathy after loss of systolic function and ventricular dilation. The cardiac exam in the late teenage and early adult years is often not sensitive or specific enough to be relied upon and further testing is recommended for an appropriate cardiac evaluation. What further testing is most appropriate?

Electrocardiogram (ECG) in DMD cardiomyopathy may demonstrate resting tachycardia, Q waves in left precordial leads, a tall R wave in V1, and a short PR interval. These findings are related to the development of myocardial fibrosis starting in the lateral wall of the left ventricle. Yet despite the high prevalence of these abnormalities in DMD patients, ECG was very poor at differentiating between those patients with and without cardiomyopathy as defined by decreased systolic function[10]. Screening ECG's can demonstrate evidence of myocardial damage and the presence of any arrhythmias during recording, but the test is a poor predictor of cardiomyopathy.

DMD patients are consistently shown to have a resting tachycardia on ECG and Holter monitoring. A recent cohort documented resting tachycardia in 75% of patients with DMD[11]. There is also a high rate of reduced heart rate variability and loss of circadian rhythm demonstrated on Holter monitoring[12]. Chiang et al. (2016) found that Holter monitors demonstrated clinically significant arrhythmias in 10% of DMD patients, yet these were overwhelmingly only found in those with moderate to severe cardiac dysfunction[13]. This suggests that routine Holter monitor use has limited utility prior to the development of cardiac dysfunction and at this point, the use of Holter monitors for arrhythmia monitoring would follow similar guidelines as an adult heart failure patient.

Laboratory diagnostics have been examined for relevance in the DMD cardiomyopathy population, specifically beta-natriuretic peptide (BNP), a commonly used laboratory marker in other cardiomyopathies. However, previous studies have shown that BNP levels in DMD cardiomyopathy are lower when compared with other forms of dilated cardiomyopathy regardless of the systolic dysfunction present[14]. More recently, in a population of DMD patients, the sensitivity of BNP for identifying cardiomyopathy was 85% with a very low specificity of 23%, indicating that it is likely not very useful as a screening tool or for diagnosis[15]. There may be some role in the future for trending BNP in the DMD cardiomyopathy patient but it will likely remain secondary to imaging techniques. Troponin, a surrogate marker of myocardial cell death, is used commonly in acute chest pain syndromes yet has not found a place in routine clinical care for DMD cardiomyopathy. It has been shown to be elevated in some DMD patients with cardiomyopathy and absent in others, but with moderate ability to predict LGE in DMD patients[16]. Further research is needed in interpreting troponin values and trends in DMD cardiomyopathy.

There are additional serum biomarkers that may demonstrate future importance in monitoring DMD cardiomyopathy.

Interleukin 1 receptor-like 1 protein (ST2), a protein involved in CD4+ T Cell activation and stimulates production of Th2 cytokines, is related to cardiac fibrosis and shown to be increased in DMD cardiomyopathy (Anderson et al., in review). Osteopontin,a matricellular protein with cytokine-like properties, was shown to be involved in inflammatory pathways implicated in the fibrotic remodeling of cardiac myocytes[17]. In DMD patients, it has been reported to change in association with LGE[18]. Becker et al. (2016) investigated the use of circulating microRNA's (miRNA) in reflecting LGE and cardiac dysfunction in DMD patients. They found significant upregulation of three miRNAs in DMD patients with LGE compared to those without LGE and a similar ability in predicting LGE as troponin[16]. Laboratory biomarkers hold some future promise in non-invasively evaluating and monitoring early cardiomyopathy but currently lag behind imaging modalities in its utility.

Diagnostic imaging is the most important tool for cardiomyopathy screening in DMD. Echocardiography and cardiac Magnetic Resonance (CMR) are the two main techniques used and echocardiography historically has been the most commonly used imaging technique in DMD cardiomyopathy. Echocardiography is easily accessible, often at a local cardiologist office or hospital, and cost effective. However, echocardiography is limited by acoustic windows and these become more limited in DMD due to scoliosis, chest wall adiposity, barrel chest abnormalities and difficulties with positioning. All of these worsen with age and echocardiography imaging quickly becomes very limited in the young adult with DMD.

As previously discussed, the 2010 Care Consideration guidelines included an echocardiogram beginning at 6 years of age and then subsequent studies every 1 to 2 years with annual echocardiograms recommended after age 10[9]. Due to this frequent reliance for monitoring, several studies have examined the utility of echocardiographic measures in diagnosing decreased cardiac systolic function in DMD cardiomyopathy. Soslow et al. (2016) recently studied inter-observer reliability of echocardiographic measures in DMD patients and concluded that the two best measures in both reliability and correlation with CMR derived ejection fraction (EF) were two-dimensional fractional shortening (FS) and 5/6 area-length left ventricular EF. However, the correlations were not excellent (r=0.75) and were unable to be measured in all patients (80% in FS and 50% for 5/6 area-length EF)[19]. A previous study undertaken by Spurney et al. (2015) showed similar results in the inter-observer reproducibility (ICC) of echocardiographic measures and inability to measure EF in all subjects. In that study cohort, the ICC for FS was 0.63 and the ICC for EF was lower (r=0.49). Both studies demonstrated that FS was the most reproducible measure of systolic function commonly obtained but has limitations, especially as patients become older[20].

Newer echocardiography techniques focus on early changes in DMD myocardial function prior to the loss of global systolic function. Myocardial strain imaging measures the change in length of a segment of myocardium during the cardiac cycle in the longitudinal, circumferential and radial directions. As a decrease in diastolic function precedes loss of systolic function in DMD cardiomyopathy, previous studies measured myocardial strain in DMD patients with normal systolic function. Spurney et al. (2015) found significant differences in speckle-tracking echocardiography (STE) myocardial strain measures amongst DMD patients while Soslow et al. (2016) found a moderate correlation between STE measures and CMR derived EF (r=-0.66). Differences in STE circumferential strain measures between

DMD patients and controls have also been confirmed by Ryan et al. (2013) and Ha Jo et al. (2016)[21,22]. Other measures of diastolic dysfunction including E and A wave velocities, tissue Doppler imaging, and myocardial performance indices (MPI) were found to be reproducible and show differences between DMD patients and controls[22,23]. These results emphasize that diastolic dysfunction precedes systolic dysfunction in DMD cardiomyopathy and can monitor subclinical progression of myocardial disease and effectiveness of early therapies.

Recently, a novel echocardiographic measure termed tonic contraction was suggested for monitoring of early cardiac dysfunction in DMD cardiomyopathy. Su et al. (2016) proposed that calcium dysregulation due to the loss of membrane stability leads to a period of left ventricular underfilling due to tonic contraction that pre-dates the development of left ventricular dilation seen in later stages of cardiomyopathy. They define tonic contraction as a left ventricular internal dimension in diastole (LVIDd) Z-score below -1. They showed this was a consistent phenomenon in DMD patients occurring before the loss of systolic function. This corresponds with the previous work showing diastolic dysfunction preceding systolic dysfunction in DMD cardiomyopathy and may become an easy echocardiographic measure to assist in the early diagnosis and monitoring of DMD patients[24].

Due to limits in echocardiography from the mentioned challenges of the body habitus especially in older DMD patients, CMR has become increasingly utilized in the assessment of cardiac function in DMD[5,7,19].CMR has become the gold standard for assessment of ventricular function due to improved volume measurements, a more accurate ejection fraction calculation and the ability to detect the presence of myocardial fibrosis[25]. The limitations of CMR are more procedural related including possible sedation requirements in young children, expense and availability; but not imaging quality. The breadth of data that can be obtained has made it a more preferable choice for evaluating DMD cardiomyopathy in teenage and young adults and newer clinical trial treatment protocols.

One important technique in CMR is late gadolinium enhancement (LGE). LGE is the retention of contrast in the interstitial space of myocardium that is associated with the presence of fibrosis. LGE initially was demonstrated in DMD patients by Silva et al. (2007)[26]. LGE occurs in a predictable pattern in DMD cardiomyopathy with the primary areas affected being inferolateral, anterolateral, inferior, and other left ventricular free wall segments[27]. Only those with very advanced disease have LGE in septal segments[6]. It has since been shown to be associated with decreases in EF and increases in mortality[6,28]. Florian et al. (2014) have shown that extent of LGE, in particular whether it is transmural, predicts occurrence of adverse events[29]. Tandon et al. (2015) showed that LGE develops prior to losses in systolic function and that the extent of LGE correlates strongly with the development of LV dysfunction[30]. LGE has also been shown to be associated with increased arrhythmia risk[31]. Therefore, the presence and extent of LGE can provide additional data to direct therapy and clinical monitoring.

Native T1 and extracellular volume (ECV) mapping are also techniques in CMR that hold promise for quantifying myocardial fibrosis. They can be used to measure the extracellular volume expansion seen in fibrosis and edema which are hallmarks of DMD cardiomyopathy. Recently two groups evaluated the use of ECV and native T1 mapping in DMD patients. Olivieri et al. (2016) demonstrated that ECV and T1 measures are different in DMD patients

compared to age-matched controls and that in LGE-negative myocardium; also, the degree of changes seen in native T1 levels are proportional to the degree of cardiac disease[32]. Soslow et al. (2016) showed similarly that DMD patients have abnormal ECV and native T1 values in patients both with and without LGE[33]. ECV and native T1 mapping measures are non-invasive outcome measures that can be monitored for response to clinical therapies and in research.

CMR also has the ability to assess myocardial strain measures similar to echocardiography. Tagged cine imaging along with harmonic phase processing allows for the measurement of cardiac strain and does not require gadolinium administration. Hor et al. (2009) showed that tagged strain imaging identified abnormalities prior to the development of any alteration in the EF. They were also able to demonstrate that these abnormalities increased with age[34]. Tagged imaging strain measures also correlated with severity of cardiac disease and the greatest changes were seen in the lateral segments where LGE evidence of fibrosis was detected[35]. Feature tracking is a CMR measure of strain that does not require additional tagged images and can be performed on standard steady state free procession images. Hor et al. (2010) showed that it correlates well with the tagged harmonic phase strain measures[36]. Siegel et al. presented data showing that feature tracking strain measures are superior to echocardiographic STE measures in identifying abnormalities in DMD patients and that abnormalities in feature tracking strain are present prior to the development of LGE[37]. As imaging modalities continue to improve, our ability to assess myocardial changes earlier becomes better. Figure 1 demonstrates some of the multiple forms of cardiac imaging utilized in DMD cardiomyopathy. Improvements in imaging will hopefully lead to earlier initiation of therapies that can delay the onset of irreversible cardiac dysfunction.

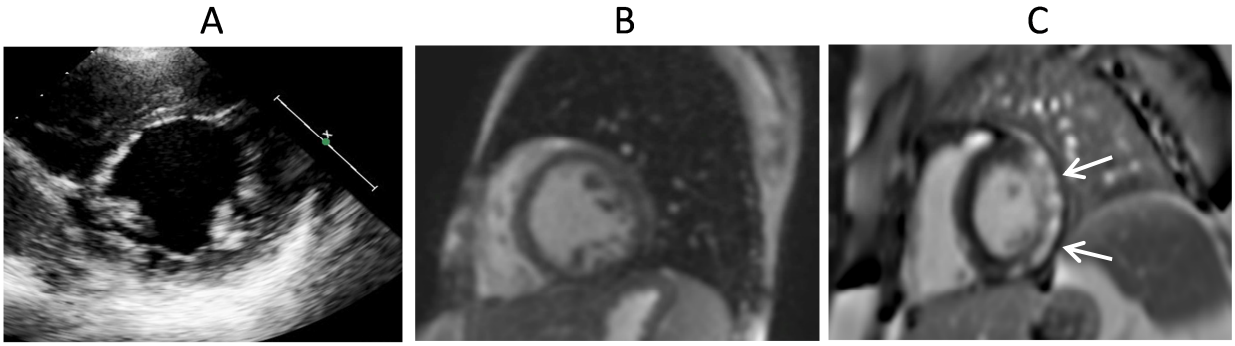

Figure 1: Three short axis images of the same patient with Duchenne muscular dystrophy. A) Echocardiographic image of mid-papillary short axis which is unable to show LGE but would be adequate for STE measures. B) CMR short axis steady state free processing image without contrast which cannot show LGE but is able to be used for FT strain measures. C) CMR short axis imaging post gadolinium contrast administration showing LGE (bright white) in the posterior and lateral segments (arrows).

Treatment:

Glucocorticosteroids have been standard of care for the skeletal muscle disease associated with DMD and a 2016 Cochrane review found moderate quality evidence for steroids as a treatment for improving symptoms. The highest quality evidence suggests prednisone at 0.75 mg/kg/day with uncertainty still existing as to intermittent versus daily dosing[38]. Multiple studies have shown the beneficial effects of steroids on the development of cardiomyopathy in DMD. Silversides et al. (2003) demonstrated a difference in the rates of reduced EF from 58% to 5% incidence in children treated with steroids > 3 years[39]. Houde et al. (2008) showed patients treated with steroids had increased EF, FS, and less incidence of cardiomyopathy[40]. A cohort study of 86 patients by Schram et al. (2013) found a 76% lower mortality rate in those treated with steroids compared to those without. The reduction in mortality was almost entirely driven by fewer heart failure deaths[41]. Markham et al. (2008) found freedom from ventricular dysfunction to be 93% in steroid treated groups and 53% in untreated groups over 12 years of follow-up[42]. Clinical research has overwhelmingly supported that steroids are effective treatment for both skeletal and cardiac muscle dysfunction in DMD. However, side effects, most commonly the reduction in growth potential and osteoporosis, can be severe and prevent many from taking corticosteroids altogether. Also, once patients become non-ambulatory, steroids are often stopped to prevent further side effects associated with little gains in skeletal muscle function[41]. Therefore, many older DMD patients will have completed their steroid course and there are no specific cardiac indications to continue steroids at this time.

Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) are mainstays of treatment in multiple forms of heart failure. They are used as both medical management and prophylaxis for left ventricular dysfunction. The most recent DMD Working Group guidelines recommended initiation of ACEi or ARB by 10 years of age with a recommendation to consider starting earlier if no contraindications[7]. These recommendations were based on studies evaluating these classes of medications effectiveness in slowing the progression of left ventricular dysfunction. Duboc et al. (2005; 2007) found in a double-blinded study that ACEIs given prophylactically reduce incidence of cardiomyopathy and mortality at 10 years of treatment[8,43]. Allen et al. (2013) found significant improvements in EF in DMD patients treated with either lisinopril or losartan[44]. Other non-randomized studies found either stable or improvement in EF in children on ACEI with or without concomitant beta-blocker therapy[45–47]. Recently in a randomized trial, Silva et al. (2016) demonstrated that patients treated with ACEI had slower progression of myocardial fibrosis over a 2-year period[28]. It is our practice to place children on ACEi after discussion with the family at around 10 years of age.

Beta-blockers (BB) are another mainstay of heart failure management investigated in DMD cardiomyopathy. In a prospective study of 54 DMD patients, Matsumara et al. (2010) showed a benefit in survival free from cardiac events in DMD patients on BB[48]. The majority of trials evaluating BB were in conjunction with ACEi therapy and make interpreting the true effect of BBs difficult. Kajimoto et al. (2006) showed an increase in left ventricular size and function in 13 DMD patients on ACEi and carvedilol compared to ACEi alone[49]. However, as previously noted in the study by Viollet et al. (2012), there was no difference in the improvement in EF between ACEi plus beta-blocker and ACEi

alone. However, a beta-blocker in this case was only added for heart rates above 100 beats per minute[47].

Mineralocorticoid receptor antagonists (MRA) are a standard of care in heart failure regimens. Mineralocorticoid receptors have been implicated in the pathways leading to fibrosis. The proposed anti-fibrotic mechanisms make them important candidates for slowing of the progression of the fibrosis that is characteristic of DMD cardiomyopathy. Initiation of an ACEi and aldosterone in a mouse model of DMD cardiomyopathy was shown to preserve left ventricular function greater than previously described studies, although different treatment regimens were not directly compared[50].

Recently, a double blinded, randomized, placebo trial of eplerenone in DMD subjects with normal CMR derived EF demonstrated a significant improvement in the rate of decline in CMR circumferential strain[18]. With a small side effect profile, the addition of MRA to early prophylactic therapy in DMD is recommended in DMD patients with evidence of fibrosis on CMR (LGE positive). Future studies should focus on longer-term outcomes such as mortality and delay in developing LGE. Figure 2 illustrates our proposed mechanism for monitoring and treatment utilizing the most common imaging modalities and treatment options.

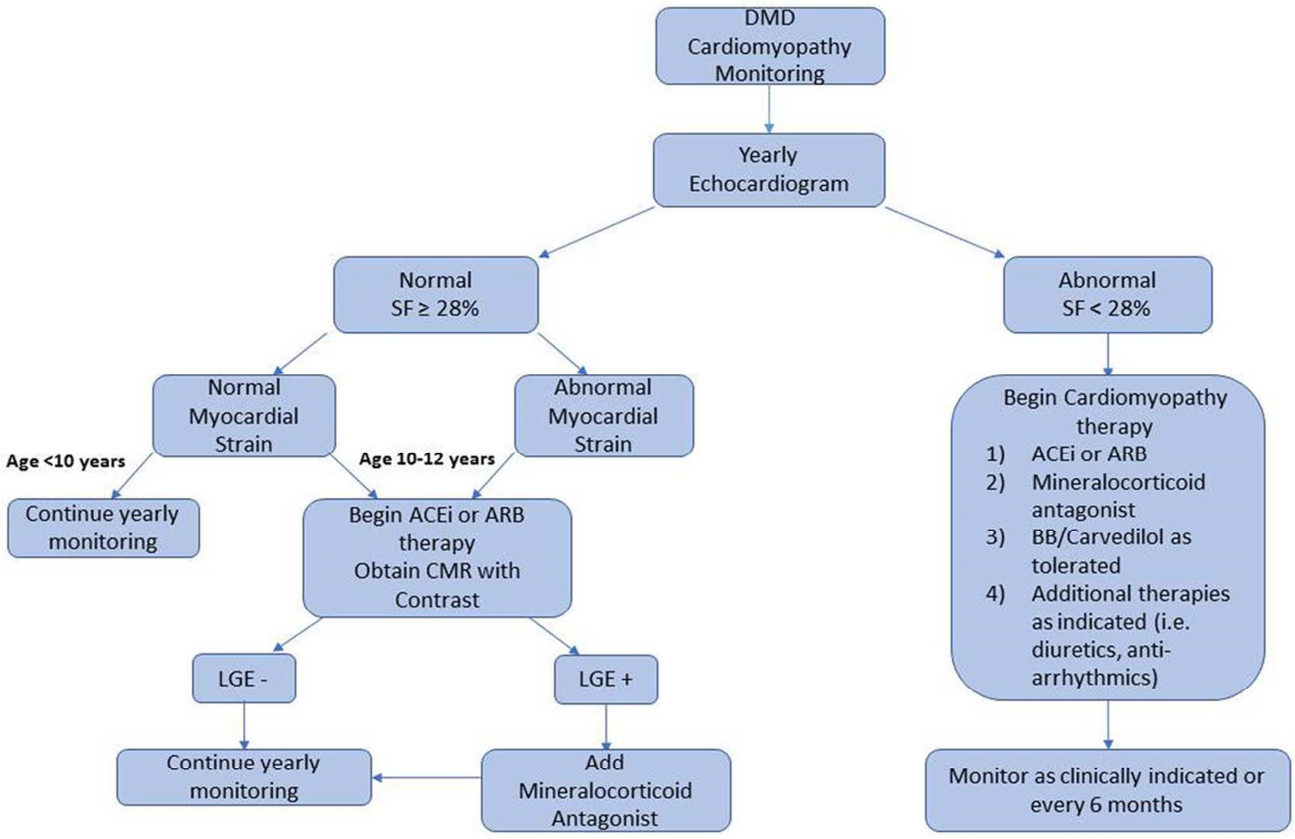

Figure 2: Proposed flow chart for incorporating new imaging modalities into monitoring and treatment of DMD Cardiomyopathy

As DMD cardiomyopathy progresses and the myocardium becomes more fibrotic, arrhythmias become an increasing cause of morbidity and mortality[31,51]. DMD cardiomyopathy is associated with both atrial and ventricular arrhythmias, particularly as cardiac function decreases. Anti-arrhythmic therapy should be instituted based on the appropriate diagnoses. Pacemakers or implantable cardiac defibrillators (ICD) have not been extensively studied in the DMD cardiomyopathy population. Currently, the standard of practice is to use the adult heart failure guidelines for ICD placement which includes patients with an EF under 35%[7]. This correlates well with the increase in incidence of arrhythmias seen with increasing cardiac dysfunction but does not take into account the risks of ICD placement in this specific patient population nor the life expectancy that may be shorter due to other sequelae of DMD. A study of hospitalized DMD patients showed that mortality was significantly increased in DMD patient with ventricular tachycardia, yet ICD placement remained low suggesting that this therapy may be underutilized[51]. The decision to proceed with ICD placement should be made on an individual basis at this time taking into consideration personal goals for care since there is no evidence to support improved outcomes or quality of life until further research is completed.

As cardiomyopathy has become the leading cause of death in DMD patients and advanced mechanical therapies have improved, ethical dilemmas present themselves regarding the use of mechanical therapies and transplant in this patient population. Left ventricular assist devices (LVAD) in pediatrics have increased utilization and shown excellent results, comparable to that seen in young adults[52,53]. There are a few case reports describing implantation of LVADs in DMD patients showing acceptable results[54,55]. The majority of these were placed for destination therapy since these patients are not suitable transplantation candidates. Cardiac transplantation is described in DMD patients[56] but it is not common practice due to the shortened life expectancy and multiple co-morbidities faced by these patients. With improved respiratory support, the used of ventricular assist devices is likely to increase in the young adult population and will require clear discussions of quality and end of life goals.

As our understanding of the pathogenesis behind DMD cardiomyopathy improves, multiple other targets for medical therapies will be investigated. PDE5 inhibitors are interesting due to the evidence that cGMP may have a role in modifying the development of cardiomyopathy due to downstream signaling. Inhibition of PDE5 was shown to slow the rate of and possibly reverse cardiac dysfunction in mdx mice[57]. Tadalafil has also been shown to delay the onset of cardiomyopathy in the canine model of muscular dystrophy[58]. However, in humans, a double-blinded randomized, placebo study using sildenafil had to be stopped due to the worsening of LV end-systolic volume in the treatment group[59] and a recently completed trial using tadalafil demonstrated no improvement in the 6-minute walk test[60]. Currently the role of PDE5 inhibitors is unclear, and will require further clinical trials to determine if there is a potential therapeutic role in DMD cardiomyopathy.

Eteplirsen is an exon skipping phosphorodiamidate morpholino oligomer (PMO) that can bind to the pre-mRNA of exon 51 of the dystrophin gene. This binding can restore the open reading frame and result in the production of a truncated version of dystrophin. This protein has partial function and produces a less severe phenotype closer to Becker muscular dystrophy. Randomized double blind placebo-controlled clinical trials demonstrated improved strength, improved

muscle fibers histologically, and improved ambulation[61]. Three years later, the treated groups showed a slower decline in their ambulatory status compared to historical controls[62].Unfortunately, cardiac muscle was not studied in these trials and preclinical trials in animal models showed less cardiac muscle dystrophin expression after treatment than seen in skeletal muscle[63]. Only 13% of patients with DMD have a mutation in exon 51 but this proof of gene-directed therapy is encouraging for the future. Hopefully exon skipping will benefit the myocardium, but it will be important to monitor these patients closely for any changes in cardiac status during therapy.

And the latest advances involve dystrophin gene editing that is primarily undertaken using clustered regularly interspaced short palindromic repeats (CRISPR) which have the ability to break DNA at a target gene, where it can be replaced by a new gene. This technology has already been shown to be able to replace a dystrophin mutation in the mdx mouse model of DMD and even in isolated human DMD cells[64,65]. Currently these therapies will be limited by the inability to transfer affected myoblasts into hosts, but further applications using stem cells may help advance the field.

DMD Carriers:

A particularly underserved population is DMD carriers. Due to skewed X inactivation, cardiomyopathy is found in DMD carriers with some estimates suggesting 10% of female carriers. LGE was demonstrated on CMR in carriers, which as shown in a 6 minute walk test, correlates with worse clinical signs of heart failure[66]. The risk of developing cardiomyopathy in DMD carriers appears to be under-reported as a survey of known DMD carriers has shown that only 63% were aware of the risk and 64% having undergone a cardiac evaluation[67]. This demonstrates a need for increased awareness and education for both families and providers of DMD patients. All carriers should receive screening echocardiograms and CMR as available to aid in early diagnosis and treatment of cardiomyopathy.

Conclusion:

As cardiomyopathy becomes the leading cause of death in Duchenne muscular dystrophy, there exists a large area for improvement in the way these patients are diagnosed and treated. As techniques improve in echocardiography and CMR, it is becoming easier to diagnose subtle changes in the myocardium at a younger age and provide data to direct early diagnosis and therapies. As these children transition to young adults, recognition of cardiomyopathy by adult practitioners is imperative to improve quality of life and outcomes. This review highlights the importance of diagnostic imaging and early treatment of DMD cardiomyopathy. Further information regarding available clinical protocols and innovative therapies is available from an extremely supportive community including the Muscular Dystrophy Association and Parent Project Muscular Dystrophy among others.

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