CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187

Avalable online at: http://www.iajps.com *Research Article*

CARDIOMYOPATHY AND LEFT VENTRICULAR STRUCTURAL REMODELING IN DUCHENNE MUSCULAR DYSTROPHY CARRIERS

[1]Amel Basheer Mohammed Saad,' [2]Monia Turbosh Hamood Naji Alhadad, [3]MOHAMMAD Nadhir Abbas AL-ANSARI, [4]Khalid Mohamed Ahmed Ali, [5]Sara Mohamed osman abdelrahaman

[1]University of bahri
[2]Taiz university Faculty of medicine and health sciences
[3]University of Baghdad / College of Medicine
[4]University of Khartoum
[5]Gezira university

Article Received: January 2020 **Accepted:** January 2021 **Published:** February 2021

Abstract:
Duchenne muscle dystrophy (DMD) accounts for over 80 percent of muscle dystrophies due to x-linked muscle diseases. A common event not necessarily linked to skeletal myopathy is a heart disease; the predominant manifestation can be muscle disease with or without any other evidence. Usually, death comes from ventricular dysfunction, blockage of the heart, or malignancy. For DMD patients, it may be not only cardiac involvement but also for female carriers. Clinical open heart failure in dystrophinopathy may or may not be delayed due to relative physical inactivity. Conduction defects, arrhythms (supraventricular or ventricular), hypertrophy and evidence of myocardial necrosis are commonly found in electrocardiography. Significant variability of left ventricular dysfunction may be assessed by echocardiography, irrespective of the age of onset or the mutation group. Cardiovascular Magnetic Resonance (CMR) has been documented in both patients and carriers of dystrophinopathy to observe a pattern of epicardial fibrosis, even if there is no apparent muscular disease. New CMR techniques for the detection of diffuse myocardial fibrosis have recently been applied in Duchenne muscle dystrophy, such as postcontrast myocardial T1 mapping. Combined medical and CMR evaluations can motivate early cardioprotective therapy and retard the development of serious heart complications in patients and asymptomatic carriers.

Keywords: *duchenne muscular dystrophy, Muscular dystrophies, dilated cardiomyopathy, Echocardiography, Heart failure.*

Corresponding author:
Amel Basheer Mohammed Saad,
University of bahri

QR code

Please cite this article in press Amel Basheer Mohammed Saad et al, ***Cardiomyopathy and left ventricular structural remodeling in duchenne Muscular dystrophy carriers.,*** *Indo Am. J. P. Sci, 2021; 08(02).*

INTRODUCTION:

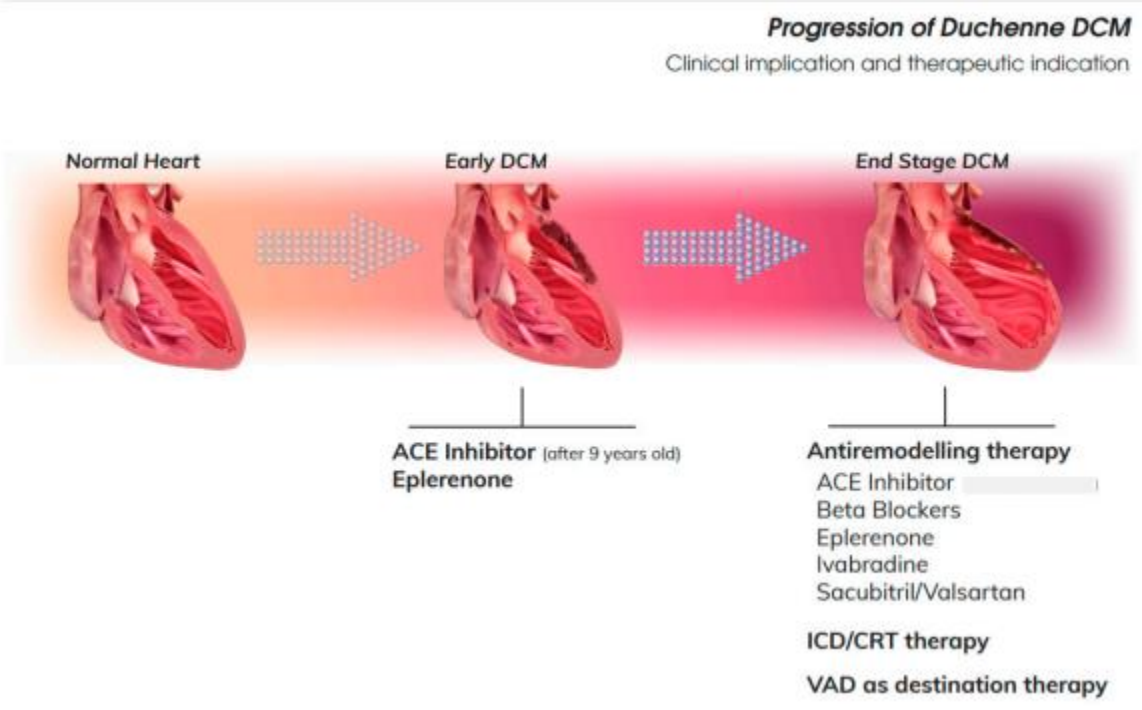
Duchenne muscular dystrophy (DMD) is a group of x-related muscle diseases that accounts for more than 80 percent of muscular dystrophy cases. DMD 1 is characterized by a weakness in early childhood leg, pelvic, and shoulder girdles in 3,500 male neonates, with a prevalence of 6,000 in 100,000 males.

In DMD, children are diagnosed as infants and, at 15 years of age, most are wheelchair-bound. Death generally takes place due to respiratory or cardiomyopathic complications at the age of 20. Due to homemade ventilation and corticosteroids that can extend the risk of scoliosis to ambulatory patients by 2-3 years and postpone pulmonary and heart failure at an old age of 20, more patients have survived up to 30 years. More than 25% of DMD boys, despite this documented efficacy, do not have side effects or an inadequate reaction to corticosteroids. In BMD, the disease is milder and more heterogeneous than DMD. Muscle weakness in teens or young adulthood is often noticed for the first time. Cardiac participation in BMD may precede muscle skeleton decline, with cardiomyopathy deaths often before 60.

The most significant life-limiting conditions in Duchenne muscular dystrophy (DMD) are expanded cardiomyopathy (DCM), rhythms, and congestive cardiac failure (HF). In the current 2018, DMD Care Study sponsored by the Centers for Disease Control and Prevention, routine cardiovascular assessment including echocardiography is recommended. Furthermore, HF treatments have changed greatly since the 1980s and have been enriched by using new drugs and devices by an adult HF weapons expert before heart transplants (i.e., cardiac resynchronization therapy, intracardiac defibrillator device, and ventricular assistance device). In general, DMD patients are not candidates for cardiovascular transplants due to progressive skeletal myopathy, limited functionality, and donor availability. This review presents a view of the cardiologist on current data on the clinical management of DMD patients.

Pathophysiology of DMD:

DMD is a recessive, X-linked disorder in one in 3,500 male births. It is caused by dystrophin gene mutations, which cause significant decreases or lack of sarcolemmal protein dystrophin. DMD is part of the dystrophinopathy group, characterized by various pathogenic conditions and muscle impairment levels of the skeleton and heart. DMD is usually the most severe, whereas Becker MMD and XL-DCM and DMD are the most benign forms. Initially, several pathologies involve cellular damage to the skeletal and cardiac muscles because of the lack of dystrophin. The myocyte and sarcolemmal membrane are generally structured by linking actin to the amino terminus C to the complex dystrophin-related protein and sarcolemma to the carboxyl terminus extracellular muscle matrix.

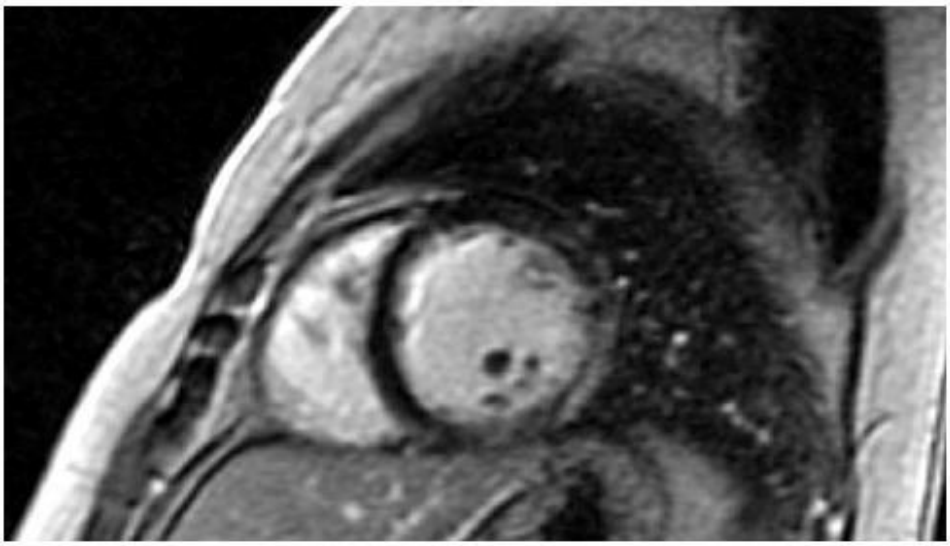


Progression of DMD-DCM. According to the clinical stage of the DMD-DCM, different strategies might be considered. ACE: Angiotensin Converting Enzyme; CRT: Cardiac Resynchronization Therapy; ICD: IntraCardiac Defibrillator; VAD: Ventricular Assist Device

Dystrophin is also present in cardiac myocyte T-tubular membranes. Therefore, it helps maintain the membrane's stability and transfers mechanical strength to the sarcomas' extracellular matrix. The absence of dystrophin causes outer cell membranes' extreme vulnerability; cellular stress might be mediated directly by the absence of dystrophin and indirectly by intracellular or oxidative stress of Ca2+. Dystrophic DCM can be triggered by these damaging cellular pathways and signaling pathways for Ca2+. Necrosis and repair mechanisms of the skeletal and cardiac myocytes are not adequate as muscle disease progresses, and fibrofatty tissue substitution is, therefore, ongoing. The DMD-DCM is typical of a thinner left ventricle (LV) wall and gradual LV dilatation due to ongoing myocyte loss. In particular, Fig.1 repetitive mechanical stress results in apoptosis and fibrotic replacement and scarring, usually in the region behind the rear and mitral valve systems, starting from the epicardium to endocardium. This cavity spreads gradually down to the apex and around the heart and finally into DCM.

CARDIAC DISEASE IN DMD:

DMD is a progressive cardiac condition that ultimately leads to ventricular dysfunction, usually ventricular dilation. The cardiomyocyte late-stage pathology test shows hypertrophy, atrophy, and fibrosis. The left ventricle fibrosis in DMD carriers was observed during autopsy and late improvement in gadolinium after cardiovascular magnetic resonance (CMR) evaluation (LGE).



Fibrosis of the left ventricle in a mother Duchenne muscular dystrophy carrier, presented as late gadolinium enhancement in the lateral wall of left ventricular

After the third decade of their age, the majority of DMDs developed cardiomyopathy. Although relatively physical inactivity clinically open heart failure may delay or absent, before the left ventricular systolic function declines, cardiomyopathy is the main cause of DMD death and myocardial damage. No correlation was found between the mutation type and age at which cardiomyopathy was first introduced or serious. Eplerenone was recently documented in DMD with a pre-served expulsion fraction to add background ACE inhibitors to the left systolic ventricular function.

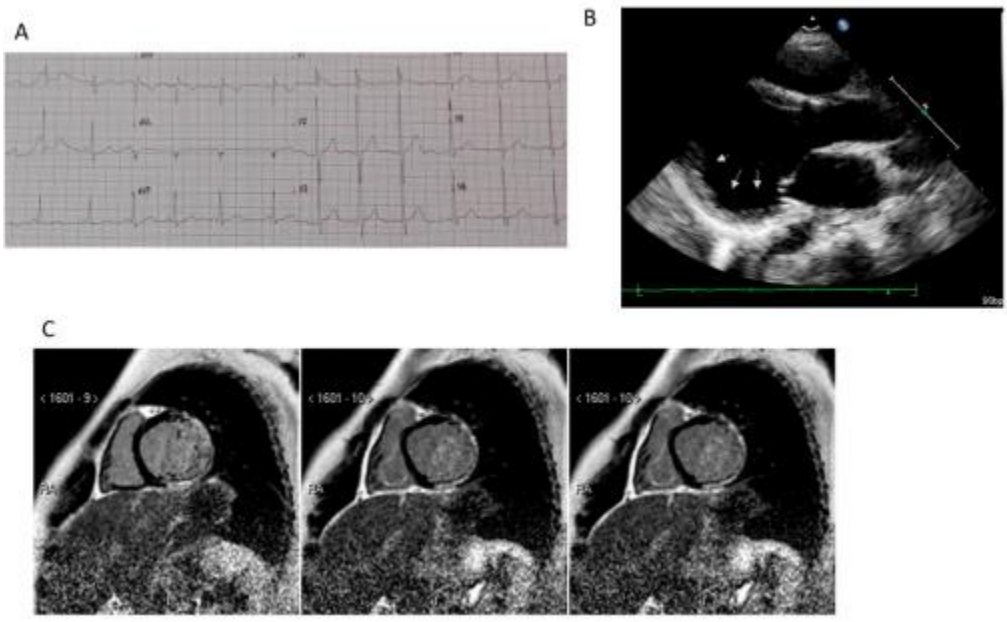
The primary clinical complication is cardiomyopathy in patients with subclinical or mild BMD. Early right ventricular dysfunction is usually clinically present and is then linked to the left ventricular disorder. Myocardial damage can develop in light BMD because patients unaware of potential heart disease still exercise their muscles and induce mechanical stress detrimental to myocardial dystrophin-deficient cells through overloading pressures or volumes.

Hypertrophy, arrhythmia, and dilated cardiomyopathy may be present in female carriers of dystrophinopathy. The percentage of clinically open-ended heart disease

significantly increases at age, from 15% in carriers <16 to 45% in carriers > 16. In contrast, it is unlikely that significant heart disease will occur in women carriers < 16 years of age. A cross-section study of 85 DMD and 44 BMD ventricular dilatation and dilated cardiomyopathy evaluated 18% and 8% of patients 18 to 58 years of age. In only 47 percent of this population, electrocardiography (ECG) abnormalities were discovered. An additional 56 female carriers had no ECG abnormalities, but 14% ventricular dilatation or hypertrophy and 7% dilated cardiomyopathy was reported. However, in some women who require heart transplantation to survive, severe heart failure may develop. A systematic ventricular left (LV) dysfunction may be unmasked. In a study carried out by our group, CMR documented myocardial fibrosis in most mother carriers of DMD and BMD, although the clinical submission and the regular non-invasive assessment were somewhat abnormal. For this reason, a detailed cardiac assessment of all-female carriers should be recommended at least once after adolescence in order to begin early treatment.

The DMD is linked to increased R/S in the right precordial pathways, high Q waves in the side paths, lead abnormalities, and rhythms (mainly supraventricular but also ventricular). ECG in a 131 DMD study was abnormal at 78.6 percent. All of them Fig.2 were found in the sinus rhythm and were found to show abnormal Q waves in V6 = 21,3%; abnormal VR repolarisation = 64,9%; abnormal QS waves in lower and upper lateral walls = 37,4%; leading disturbance in the right bundle The two of these variables were found in the rhythm and were identified as following for the major studied variables: Early DMO cardiomyopathy can also be detected through a serial clinical assessment, including routine electrocardiogram monitoring, even if left ventricular function is maintained.

LV functional differences in DMD patients, regardless of the age of onset or mutation groups, have already been documented in echocardiography. LV dysfunction has also been very common with frequent, systematic ventricular asynchrony in DMD, especially in EF patients < 35 percent. New echocardiographic techniques can detect subclinical LV dysfunction by traditional echocardiography in DMD patients without wall movement abnormalities using a transmural strain profile (TMSP). The use of myocardial strain imaging in DMD patients was characterized by decreased systolic peak strain from the posterior wall despite normal echocardiographic results. However, these studies were not universally accepted for the routine assessment of DMD.



Clinical features of Duchenne muscular distrophy cardiomyopathy (DMD-DCM). Panel (A): typical EKG with sinus tachycardia and tall R waves. Panel (B): parasternal long axis view of left ventricle (LV). Arrows indicate the presence of posterior wall aneurysm. Panel (C): cardiac magnetic resonance: short axis view of the LV. Presence of a transmural late gadolinium enhancement pattern located at the infero-lateral wall (Courtesy of Dr. A. Secinaro).

The most robust detection method of premature myocardial fibrosis in DMD and female carriers with a late improvement in gadolinium is a non-invasive non-radiating (CMR) (LGE). In the inferolateral wall, cardiomyopathy involves subepicardial fibrosis, similar to viral myocarditis in dystrophinopathy. CMR applications are very valuable in addition to standard monitoring for DMD and women's carriers as follows: (1) the early onset of therapy for heart failure can retard progression of LV dysfunction; (2) myocardial fibrosis measured with LGE may be seen even if the echo cars are normal and can be used as a sensitive early-onset star index. The simple and visually-accessible 'Transmural LGE' parameter has a predictor additive value in DMD patients with relatively conserved DVE-FE; (4) the transmitter carriers have revealed a fibrosis pattern that is similar to DMD but without any correlation with the genotype-phänotype, and even when there was no open muscle disease; (5) new CMR methods, s. 4. Compared to controls, T1 from Look-Locker sequences (T1LL) has been documented to be abnormally shortened to DMD, even in DMD patients with normally conducted CMR studies. Applying more aggressive T1LL therapy on DMD can improve cardiomyopathy morbidity and mortality.

Female DMD Carriers:

DMD is X-linked and usually affects men, with most women mutating alone in an asymptomatic carrier. Mutations cause approximately one-third of all DMD cases in de novo and another two thirds by mother heritage. This means that every mother can carry a single male DMD case for two-thirds. Due to a second alone, most women with a pathogenic DMD variant are present as asymptomatic carriers, which normally work. However, there may also be muscle weakness, abnormal gait, fatigue, and heart involvement in some female carriers. In female DMD carriers, the "skewed inactivation of normal x-chromosome" explains the mosaic pattern of dystrophin expression in the skeleton and cardiac muscles. According to this hypothesis, higher percentages of normal X-chromosome skewed inactivation were responsible for cardiomyopathy in some MD women's carriers. However, there is no relation between the dystrophic muscle phenotype and either the X-inactivation pattern or the transcriptional comportment of dystrophin in the Brioschi et al.' study, which indicates that the manifestation of the disease results simply in the total amount of dystrophin. In a female carrier, every male child has a 50 percent chance of having DMD clinically. Carrier tests may show that a woman is at risk of infection.

While women with DMD are generally free of skeletal muscle symptoms, approximately 8% of this population are affected by cardiac symptoms. They may develop cardiomyopathy, including asymptomatic forms of progressive HF, including heart transplantation, with mild abnormalities. The onset of clinical events in women with symptoms varies from early childhood to late adulthood. Cardiomyopathy increases even in patients with normal electrocardiograms and no age muscle skeleton symptoms. Adult carriers of dystrophinopathy in Europe and the United States are therefore recommended to undergo echocardiography under the clinical guidelines every five years. Other heart events include behavioral defects and rhythm, but long-term DCM effects may occur. The initial presentations in late adulthood, although not as common, have been acute HF and nonsustained ventricular tachycardia. The disease's severity is variable, and genotype phenotypic correlations are not well established in this patient group, and cardiac involvement can occur without simultaneous skeletal muscle manifestations. Cardiac manifestations in normal physiological conditions can be subclinical in female carriers. During major events such as pregnancy, they can become worse and more symptomatic. About two-thirds of all patients with Muscle Dystrophy limb experience muscle weakness during pregnancy, which is probably associated with increased weight and increased diaphragm. In addition to heart events, DMD carriers have different systemic features: weakness of the limb-girdle, troubled grunting, intolerance to exercise, calf hypertrophy, and scoliosis. Elevated serum creatinine kinase (CK) serum is frequently found in skeletal muscle patients. Neurocognitive problems can also be identified in this patient population as learning disabilities or behavioral problems.

CONCLUSION:

In conclusion, it is common for both DMD and female carriers to have heart involvement. The early cardiac involvement assessment with ACE inhibitors and the b-blockers should be encouraged to postpone serious cardiac complications for this population, including medical, ECG, echocardiographic, and CMR monitoring.

REFERENCES:

1. Bushby K, Finkel R, Birnkrant DJ, Case LE, Clemens PR, Cripe L, Kaul A, Kinnett K, McDonald C, Pandya S, et al. Diagnosis and management of Duchenne muscular dystrophy, part 2: implementation of multidisciplinary care.

Lancet Neurol. 2010;9:177–189. [PubMed] [Google Scholar]
2. Hoffman EP, Brown RH, Kunkel LM. Dystrophin: the protein product of the Duchenne muscular dystrophy locus. Cell. 1987;51:919–928. [PubMed] [Google Scholar]
3. Bushby KM, Thambyayah M, Gardner-Medwin D. Prevalence and incidence of Becker muscular dystrophy. Lancet. 1991;337:1022–1024. [PubMed] [Google Scholar]
4. Emery AE, Skinner R. Clinical studies in benign (Becker type) X-linked muscular dystrophy. Clin Genet. 1976;10:189–201. [PubMed] [Google Scholar]
5. Bradley WG, Jones MZ, Mussini JM, Fawcett PR. Becker-type muscular dystrophy. Muscle Nerve. 1978;1:111–132. [PubMed] [Google Scholar]
6. Bushby KM, Gardner-Medwin D. The clinical, genetic and dystrophin characteristics of Becker muscular dystrophy. I. Natural history. J Neurol. 1993;240:98–104. [PubMed] [Google Scholar]
7. Hoogerwaard EM, de Voogt WG, Wilde AA, van der Wouw PA, Bakker E, van Ommen GJ, de Visser M. Evolution of cardiac abnormalities in Becker muscular dystrophy over a 13-year period. J Neurol. 1997;244:657–663. [PubMed] [Google Scholar]
8. Monaco AP, Neve RL, Colletti-Feener C, Bertelson CJ, Kurnit DM, Kunkel LM. Isolation of candidate cDNAs for portions of the Duchenne muscular dystrophy gene. Nature. 1986;323:646–650. [PubMed] [Google Scholar]
9. Koenig M, Hoffman EP, Bertelson CJ, Monaco AP, Feener C, Kunkel LM. Complete cloning of the Duchenne muscular dystrophy (DMD) cDNA and preliminary genomic organization of the DMD gene in normal and affected individuals. Cell. 1987;50:509–517. [PubMed] [Google Scholar]
10. Blake DJ, Weir A, Newey SE, Davies KE. Function and genetics of dystrophin and dystrophin-related proteins in muscle. Physiol Rev. 2002;82:291–329. [PubMed] [Google Scholar]
11. Petrof BJ, Shrager JB, Stedman HH, Kelly AM, Sweeney HL. Dystrophin protects the sarcolemma from stresses developed during muscle contraction. Proc Natl Acad Sci USA. 1993;90:3710–3714. [PMC free article] [PubMed] [Google Scholar]
12. Mazur W, Hor KN, Germann JT, Fleck RJ, Al-Khalidi HR, Wansapura JP, Chung ES, Taylor MD, Jefferies JL, Benson DW, et al. Patterns of left ventricular remodeling in patients with Duchenne Muscular Dystrophy: a cardiac MRI study of ventricular geometry, global function, and strain. Int J Cardiovasc Imaging. 2012;28:99–107. [PubMed] [Google Scholar]
13. Moriuchi T, Kagawa N, Mukoyama M, Hizawa K. Autopsy analyses of the muscular dystrophies. Tokushima J Exp Med. 1993;40:83–93. [PubMed] [Google Scholar]
14. Perloff JK, Henze E, Schelbert HR. Alterations in regional myocardial metabolism, perfusion, and wall motion in Duchenne muscular dystrophy studied by radionuclide imaging. Circulation. 1984;69:33–42. [PubMed] [Google Scholar]
15. Frankel KA, Rosser RJ. The pathology of the heart in progressive muscular dystrophy: epimyocardial fibrosis. Hum Pathol. 1976;7:375–386. [PubMed] [Google Scholar]
16. Silva MC, Meira ZM, Gurgel Giannetti J, da Silva MM, Campos AF, Barbosa Mde M, Starling Filho GM, Ferreira Rde A, Zatz M, Rochitte CE. Myocardial delayed enhancement by magnetic resonance imaging in patients with muscular dystrophy. J Am Coll Cardiol. 2007;49:1874–1879. [PubMed] [Google Scholar]
17. Puchalski MD, Williams RV, Askovich B, Sower CT, Hor KH, Su JT, Pack N, Dibella E, Gottliebson WM. Late gadolinium enhancement: precursor to cardiomyopathy in Duchenne muscular dystrophy? Int J Cardiovasc Imaging. 2009;25:57–63. [PMC free article] [PubMed] [Google Scholar]
18. Hor KN, Taylor MD, Al-Khalidi HR, Cripe LH, Raman SV, Jefferies JL, O'Donnell R, Benson DW, Mazur W. Prevalence and distribution of late gadolinium enhancement in a large population of patients with Duchenne muscular dystrophy: effect of age and left ventricular systolic function. J Cardiovasc Magn Reson. 2013;15:107. [PMC free article] [PubMed] [Google Scholar]
19. Mavrogeni S, Bratis K, Papavasiliou A, Skouteli E, Karanasios E, Georgakopoulos D, Kolovou G, Papadopoulos G. CMR detects subclinical cardiomyopathy in mother-carriers of Duchenne and Becker muscular dystrophy. JACC Cardiovasc Imaging. 2013;6:526–528. [PubMed] [Google Scholar]
20. McNally EM. New approaches in the therapy of cardiomyopathy in muscular dystrophy. Annu Rev Med. 2007;58:75–88. [PubMed] [Google Scholar]
21. Ashwath ML, Jacobs IB, Crowe CA, Ashwath RC, Super DM, Bahler RC. Left ventricular dysfunction in duchenne muscular dystrophy and genotype. Am J Cardiol. 2014;114:284–289. [PMC free article] [PubMed] [Google Scholar]
22. Raman SV, Hor KN, Mazur W, Halnon NJ, Kissel JT, He X, Tran T, Smart S, McCarthy B, Taylor

MD, et al. Eplerenone for early cardiomyopathy in Duchenne muscular dystrophy: a randomised, double-blind, placebo-controlled trial. Lancet Neurol. 2015;14:153–161. [PMC free article] [PubMed] [Google Scholar]
23. Melacini P, Fanin M, Danieli GA, Villanova C, Martinello F, Miorin M, Freda MP, Miorelli M, Mostacciuolo ML, Fasoli G, et al. Myocardial involvement is very frequent among patients affected with subclinical Becker's muscular dystrophy. Circulation. 1996;94:3168–3175. [PubMed] [Google Scholar]
24. Politano L, Nigro V, Nigro G, Petretta VR, Passamano L, Papparella S, Di Somma S, Comi LI. Development of cardiomyopathy in female carriers of Duchenne and Becker muscular dystrophies. JAMA. 1996;275:1335–1338. [PubMed] [Google Scholar]
25. Nolan MA, Jones OD, Pedersen RL, Johnston HM. Cardiac assessment in childhood carriers of Duchenne and Becker muscular dystrophies. Neuromuscul Disord. 2003;13:129–132. [PubMed] [Google Scholar]
26. Hoogerwaard EM, Bakker E, Ippel PF, Oosterwijk JC, Majoor-Krakauer DF, Leschot NJ, Van Essen AJ, Brunner HG, van der Wouw PA, Wilde AA, et al. Signs and symptoms of Duchenne muscular dystrophy and Becker muscular dystrophy among carriers in The Netherlands: a cohort study. Lancet. 1999;353:2116–2119. [PubMed] [Google Scholar]
27. Hoogerwaard EM, van der Wouw PA, Wilde AA, Bakker E, Ippel PF, Oosterwijk JC, Majoor-Krakauer DF, van Essen AJ, Leschot NJ, de Visser M. Cardiac involvement in carriers of Duchenne and Becker muscular dystrophy. Neuromuscul Disord. 1999;9:347–351. [PubMed] [Google Scholar]
28. Grain L, Cortina-Borja M, Forfar C, Hilton-Jones D, Hopkin J, Burch M. Cardiac abnormalities and skeletal muscle weakness in carriers of Duchenne and Becker muscular dystrophies and controls. Neuromuscul Disord. 2001;11:186–191. [PubMed] [Google Scholar]
29. Melacini P, Fanin M, Angelini A, Pegoraro E, Livi U, Danieli GA, Hoffman EP, Thiene G, Dalla Volta S, Angelini C. Cardiac transplantation in a Duchenne muscular dystrophy carrier. Neuromuscul Disord. 1998;8:585–590. [PubMed] [Google Scholar]
30. Davies JE, Winokur TS, Aaron MF, Benza RL, Foley BA, Holman WL. Cardiomyopathy in a carrier of Duchenne's muscular dystrophy. J Heart Lung Transplant. 2001;20:781–784. [PubMed] [Google Scholar]
31. Weiss RM, Kerber RE, Jones JK, Stephan CM, Trout CJ, Lindower PD, Staffey KS, Campbell KP, Mathews KD. Exercise-induced left ventricular systolic dysfunction in women heterozygous for dystrophinopathy. J Am Soc Echocardiogr. 2010;23:848–853. [PMC free article] [PubMed] [Google Scholar]
32. Darras BT, Miller DT, Urion DK. Dystrophinopathies. In: Pagon RA, Adam MP, Bird TD, Dolan CR, Fong CT, et al., editors. GeneReviews [Internet] Seattle (WA): University of Washington, Seattle, 1993-; 2014. [Google Scholar]
33. Santos MA, Costa Fde A, Travessa AF, Bombig MT, Fonseca FH, Luna Filho B, Mussi A, Souza Dd, Oliveira Ad, Povoa R. [Duchenne muscular dystrophy: electrocardiographic analysis of 131 patients] Arq Bras Cardiol. 2010;94:620–624. [PubMed] [Google Scholar]
34. Petri H, Sveen ML, Thune JJ, Vissing C, Dahlqvist JR, Witting N, Bundgaard H, Køber L, Vissing J. Progression of cardiac involvement in patients with limb-girdle type 2 and Becker muscular dystrophies: a 9-year follow-up study. Int J Cardiol. 2015;182:403–411. [PubMed] [Google Scholar]
35. Thomas TO, Jefferies JL, Lorts A, Anderson JB, Gao Z, Benson DW, Hor KN, Cripe LH, Urbina EM. Autonomic dysfunction: a driving force for myocardial fibrosis in young Duchenne muscular dystrophy patients? Pediatr Cardiol. 2015;36:561–568. [PubMed] [Google Scholar]
36. Fayssoil A, Nardi O, Orlikowski D, Annane D. Cardiac asynchrony in Duchenne muscular dystrophy. J Clin Monit Comput. 2013;27:587–589. [PubMed] [Google Scholar]
37. Yamamoto T, Tanaka H, Matsumoto K, Lee T, Awano H, Yagi M, Imanishi T, Hayashi N, Takeshima Y, Kawai H, et al. Utility of transmural myocardial strain profile for prediction of early left ventricular dysfunction in patients with Duchenne muscular dystrophy. Am J Cardiol. 2013;111:902–907. [PubMed] [Google Scholar]
38. Mori K, Hayabuchi Y, Inoue M, Suzuki M, Sakata M, Nakagawa R, Kagami S, Tatara K, Hirayama Y, Abe Y. Myocardial strain imaging for early detection of cardiac involvement in patients with Duchenne's progressive muscular dystrophy. Echocardiography. 2007;24:598–608. [PubMed] [Google Scholar]
39. Mavrogeni S, Papavasiliou A, Skouteli E, Magoutas A, Dangas G. Cardiovascular magnetic resonance imaging evaluation of two families with Becker muscular dystrophy. Neuromuscul

Disord. 2010;20:717–719. [PubMed] [Google Scholar]
40. Duboc D, Meune C, Lerebours G, Devaux JY, Vaksmann G, Bécane HM. Effect of perindopril on the onset and progression of left ventricular dysfunction in Duchenne muscular dystrophy. J Am Coll Cardiol. 2005;45:855–857. [PubMed] [Google Scholar]
41. Menon SC, Etheridge SP, Liesemer KN, Williams RV, Bardsley T, Heywood MC, Puchalski MD. Predictive value of myocardial delayed enhancement in Duchenne muscular dystrophy. Pediatr Cardiol. 2014;35:1279–1285. [PubMed] [Google Scholar]
42. Florian A, Ludwig A, Engelen M, Waltenberger J, Rösch S, Sechtem U, Yilmaz A. Left ventricular systolic function and the pattern of late-gadolinium-enhancement independently and additively predict adverse cardiac events in muscular dystrophy patients. J Cardiovasc Magn Reson. 2014;16:81. [PMC free article] [PubMed] [Google Scholar]
43. Giglio V, Puddu PE, Camastra G, Sbarbati S, Della Sala SW, Ferlini A, Gualandi F, Ricci E, Sciarra F, Ansalone G, et al. Patterns of late gadolinium enhancement in Duchenne muscular dystrophy carriers. J Cardiovasc Magn Reson. 2014;16:45. [PMC free article] [PubMed] [Google Scholar]
44. Turkbey EB, Gai N, Lima JA, van der Geest RJ, Wagner KR, Tomaselli GF, Bluemke DA, Nazarian S. Assessment of cardiac involvement in myotonic muscular dystrophy by T1 mapping on magnetic resonance imaging. Heart Rhythm. 2012;9:1691–1697. [PMC free article] [PubMed] [Google Scholar]
45. Kamdar, F.; Garry, D.J. Dystrophin-Deficient Cardiomyopathy. J. Am. Coll. Cardiol. 2016, 67, 2533–2546. [CrossRef]
46. McNally, E.M.; Wyatt, E.J. Mutation-Based Therapy for Duchenne Muscular Dystrophy: Antisense Treatment Arrives in the Clinic. Circulation 2017, 136, 979–981. [CrossRef]
47. Buddhe, S.; Cripe, L.H.; Friedland-Little, J.; Kertesz, N.; Eghtesady, P.; Finder, J.; Hor, K.N.; Judge, D.P.; Kinnett, K.; McNally, E.M.; et al. Cardiac Management of the Patient With Duchenne Muscular Dystrophy. Pediatrics 2018, 142, S72–S81. [CrossRef]
48. Birnkrant, D.J.; Bushby, K.; Bann, C.M.; Alman, B.; Apkon, S.D.; Blackwell, A.; Case, L.; Cripe, L.; Hadjiyannakis, S.; Olson, A.K.; et al. Diagnosis and management of Duchenne muscular dystrophy, part 2: Respiratory, cardiac, bone health, and orthopaedic management. Lancet Neurol. 2018, 17, 347–361. [CrossRef]
49. Connuck, D.M.; Sleeper, L.A.; Colan, S.D.; Cox, G.F.; Towbin, J.A.; Lowe, A.M.; Wilkinson, J.D.; Orav, E.J.; Cuniberti, L.; Salbert, B.A.; et al. Characteristics and outcomes of cardiomyopathy in children with Duchenne or Becker muscular dystrophy: A comparative study from the Pediatric Cardiomyopathy Registry. Am. Heart J. 2008, 155, 998–1005. [CrossRef]
50. Muntoni, F.; Torelli, S.; Ferlini, A. Dystrophin and mutations: One gene, several proteins, multiple phenotypes. Lancet Neurol. 2003, 2, 731–740. [CrossRef]
51. Nigro, G.; Comi, L.I.; Palladino, A.; Petretta, V.R.; Politano, L. Cardiomyopathies: Diagnosis of types and stages. Acta Myol. 2004, 23, 97–102. [PubMed]
52. Politano, L.; Nigro, V.; Petretta, V.R.; Passamano, L.; Papparella, S.; Di Somma, S.; Comi, L.I. Development of Cardiomyopathy in Female Carriers of Duchenne and Becker Muscular Dystrophies. JAMA 1996, 275, 1335. [CrossRef]
53. Hoffman, E.P.; Brown, R.H.; Kunkel, L.M. Dystrophin: The protein product of the duchenne muscular dystrophy locus. Cell 1987, 51, 919–928. [CrossRef]
54. Campbell, K.P. Three muscular dystrophies: Loss of cytoskeleton-extracellular matrix linkage. Cell 1995, 80, 675–679. [CrossRef]
55. Shirokova, N.; Niggli, E. Cardiac phenotype of Duchenne Muscular Dystrophy: Insights from cellular studies. J. Mol. Cell. Cardiol. 2013, 58, 217–224. [CrossRef]
56. Wallace, G.Q.; McNally, E.M. Mechanisms of Muscle Degeneration, Regeneration, and Repair in the Muscular Dystrophies. Annu. Rev. Physiol. 2009, 71, 37–57. [CrossRef]
57. Yilmaz, A.; Gdynia, H.-J.; Baccouche, H.; Mahrholdt, H.; Meinhardt, G.; Basso, C.; Thiene, G.; Sperfeld, A.-D.; Ludolph, A.C.; Sechtem, U. Cardiac involvement in patients with Becker muscular dystrophy: New diagnostic and pathophysiological insights by a CMR approach. J. Cardiovasc. Magn. Reson. 2008, 10, 50. [CrossRef]
58. Frankel, K.A.; Rosser, R.J. The pathology of the heart in progressive muscular dystrophy: Epimyocardial fibrosis. Hum. Pathol. 1976, 7, 375–386. [CrossRef]
59. Bushby, K.; Finkel, R.; Birnkrant, D.J.; Case, L.; Clemens, P.R.; Cripe, L.; Kaul, A.; Kinnett, K.; McDonald, C.M.; Pandya, S.; et al. Diagnosis and management of Duchenne muscular dystrophy, part 2: Implementation of multidisciplinary care. Lancet Neurol. 2010, 9, 177–189. [CrossRef]

60. Florian, A.-R.; Rösch, S.; Bietenbeck, M.; Engelen, M.; Sechtem, U.; Stypmann, J.; Waltenberger, J.; Yilmaz, A. Cardiac involvement in female Duchenne and Becker muscular dystrophy carriers in comparison to their first-degree male relatives: A comparative cardiovascular magnetic resonance study. Eur. Heart J. Cardiovasc. Imaging 2015, 17, 326–333. [CrossRef]
61. Lim, K.R.Q.; Sheri, N.; Nguyen, Q.; Yokota, T. Cardiac Involvement in Dystrophin-Deficient Females: Current Understanding and Implications for the Treatment of Dystrophinopathies. Genes 2020, 11, 765. [CrossRef]
62. Brioschi, S.; Gualandi, F.; Scotton, C.; Armaroli, A.; Bovolenta, M.; Falzarano, M.S.; Sabatelli, P.; Selvatici, R.; D'Amico, A.; Pane, M.; et al. Genetic characterization in symptomatic female DMD carriers: Lack of relationship between X-inactivation, transcriptional DMD allele balancing and phenotype. BMC Med. Genet. 2012, 13, 73. [CrossRef]
63. Finsterer, J.; Stöllberger, C. Muscle, cardiac, and cerebral manifestations in female carriers of dystrophin variants. J. Neurol. Sci. 2018, 388, 107–108. [CrossRef] [PubMed]
64. . Ishizaki, M.; Kobayashi, M.; Adachi, K.; Matsumura, T.; Kimura, E. Female dystrophinopathy: Review of current literature. Neuromuscul. Disord. 2018, 28, 572–581. [CrossRef] [PubMed]
65. Kamakura, K. Cardiac involvement of female carrier of Duchenne muscular dystrophy. Intern. Med. 2000, 39, 2–3. [CrossRef] [PubMed]