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A cardiac perspective for management of dystrophinopathies

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ABSTRACT

Cardiac disease is a leading cause of death in Duchenne and Becker muscular dystrophy, with dilated cardiomyopathy and arrhythmias nearly ubiquitous by adulthood. Guideline-directed surveillance with echocardiography, cardiac MRI, and rhythm monitoring enables early initiation of ACE inhibitors, beta-blockers, and mineralocorticoid receptor antagonists, which delay progression and improve survival. Multidisciplinary cardio-neuromuscular clinics further enhance outcomes by integrating surveillance, timely device therapy, and advanced interventions. Proactive interdisciplinary care is thus essential to preserving function and extending survival in dystrophinopathies.

Introduction

This review aims to synthesize current evidence on the recognition, surveillance, and management of cardiac disease in Duchenne muscular dystrophy (DMD) and Becker muscular dystrophy (BMD). The scope is focused on BMD and DMD because of their high cardiac morbidity and mortality, the availability of disease-specific guidelines, and recent advances in pharmacologic and device-based therapies. In addition, we attempt to highlight the emerging role of multidisciplinary cardio-neuromuscular clinics as a model of care delivery and discuss how lessons from dystrophinopathies may apply to other neuromuscular diseases.

Duchenne muscular dystrophy (DMD) and Becker muscular dystrophy (BMD) are progressive X-linked disorders caused by mutations in the dystrophin gene; patients typically develop skeletal muscle weakness in early childhood (DMD) or later childhood to adolescence (BMD), with loss of ambulation and increasing disability over time. The heart is almost inevitably involved, but cardiac dysfunction is often an under-recognized component of dystrophinopathies, contributing substantially to their morbidity and mortality[1,2]. While advances in respiratory care and other supportive therapies have extended the life expectancy of patients with certain muscular disorders, they have unmasked cardiac complications as major causes of death in these populations.[1] For example, Duchenne muscular dystrophy (DMD) now has a median survival into the late 20s, at which point dilated cardiomyopathy and heart failure become leading causes of mortality[1]. This example underscores that early recognition of cardiac involvement is crucial, as timely intervention can significantly improve outcomes[3].

Many neuromuscular conditions have specific cardiac surveillance and treatment recommendations emerging from recent research and guidelines[4]. For instance, DMD care guidelines call for at least annual cardiology evaluations from the time of diagnosis, with early initiation of heart failure therapies (e.g. ACE inhibitors or beta-blockers) once asymptomatic ventricular dysfunction is detected[5]. Novel disease-specific treatments are also becoming available, such as gene therapies in certain muscular dystrophies, making the timely recognition of cardiac involvement even more impactful.

General clinicians should be aware that patients with muscular dystrophies may develop insidious cardiac symptoms or exercise intolerance that can easily be mistaken for purely neuromuscular fatigue. A high index of suspicion, regular cardiac screening (ECGs, echocardiography, and MRI when appropriate), and interdisciplinary care are therefore warranted.

Because early intervention in these patients – whether by heart failure therapy, arrhythmia control, or supportive care – has been shown to prolong survival and improve quality of life[1,4]. recognizing cardiac involvement as "the other half" of neuromuscular disease is crucial to providing comprehensive care to this patient population.

Duchenne Muscular Dystrophy (DMD)

Duchenne muscular dystrophy (DMD) is an X-linked recessive neuromuscular disease characterized by progressive degeneration of skeletal and cardiac muscle due to mutations in the dystrophin gene[23]. While advances in respiratory care and early pharmacological interventions have extended survival, cardiac complications have emerged as a major cause of morbidity and mortality in DMD.[23] Pathologic cardiac involvement is nearly universal – dilated cardiomyopathy (DCM) develops in almost all patients by adulthood and is now the leading cause of death in DMD[23].

CARDIAC MANIFESTATIONS IN DUCHENNE MUSCULAR DYSTROPHY

Dilated Cardiomyopathy: The DMD heart typically undergoes a prolonged subclinical phase of myocardial damage and fibrosis, eventually progressing to DCM. Fibrosis often begins early, even before overt dysfunction: Late gadolinium enhancement cardiac MRI studies show fibrotic lesions in ~17% of DMD patients under 10 years old (even with normal ejection fraction on echocardiography), 34% of those[6,7,8,9,10,11], and nearly 60% of those over[11]. Fibrosis usually starts in the posterobasal left ventricular wall and gradually extends to involve much of the myocardium. Importantly, myocardial fibrosis precedes detectable systolic dysfunction, making early changes hard to detect clinically. As fibrosis accumulates, ventricular walls become thin and scarred, leading to DCM and heart failure. DMD-associated DCM typically presents in the second decade of life (teens), though cases as early as age 6 have been reported. Clinically, DCM in DMD manifests with enlarged left ventricular (LV)

dimensions, reduced ejection fraction (EF) and fractional shortening, and often mitral regurgitation. Because respiratory muscle weakness limits exercise tolerance, classic heart failure symptoms may be subtle; nevertheless, DCM progression accounts for heart failure and roughly 44–57% of DMD deaths[23].

Arrhythmias and Conduction Defects: Dystrophin deficiency also disrupts the cardiac electrical system. Sinus tachycardia at rest is often an early finding and can appear by age 5 in DMD. Progressive fibrosis and ion channel dysfunction contribute to conduction abnormalities, such as increased QRS duration and intraventricular conduction delay, observable by age[6]. On electrocardiogram (ECG), DMD patients frequently develop a shortened PR interval, deep Q waves in inferolateral leads (reflecting posterobasal fibrosis), tall R waves in right precordial leads, and right axis deviation. As cardiomyopathy advances, serious arrhythmias become more prevalent. Both atrial and ventricular arrhythmias occur: atrial fibrillation /flutter and even high-grade atrioventricular (AV) block have been reported in advanced disease, alongside ventricular tachycardia (VT) and ventricular fibrillation (VF). In one cohort, about 44% of DMD patients had some form of arrhythmia, most commonly premature ventricular contractions (~22%) and ventricular couplets (~32%); clinically significant supraventricular tachycardia (~9%) or VT (~13%) tended to appear in older patients with advanced fibrosis. Notably, arrhythmia risk correlates with declining systolic function, and patients over ~17 years old are significantly more likely to develop sustained tachyarrhythmias. Conduction system disease (bundle branch block or AV conduction delay) can also occur as the fibrotic process involves the conduction pathways. These electrical complications put patients at risk for syncope and sudden cardiac death, though the exact proportion of DMD deaths attributable to arrhythmias remains unclear. Routine ECG surveillance is therefore recommended, but standard surface ECG often fails to predict early cardiomyopathy; hence, periodic Holter monitoring is advised once cardiac involvement is established[23].

Thromboembolic Events: Thromboembolism is a recognized but relatively infrequent complication of DMD's cardiac disease. Case reports document systemic and pulmonary embolic events in DMD patients – including left ventricular mural thrombi with systemic embolization, deep vein thrombosis (DVT) with pulmonary embolism (PE), and ischemic stroke – particularly in those with advanced heart failure and immobility[24]. In a 2020 patient registry survey (351 DMD patients), however, only 2 individuals (0.6%) had a history of any thromboembolic event[24]. This low incidence suggests that DMD itself does not confer a unique hypercoagulable risk beyond the usual risk factors of chronic immobilization and severe cardiomyopathy[24]. Nonetheless, vigilance for thromboembolism is warranted in later disease stages.

Modifier Factors: Chronic glucocorticoid standard in DMD care, appears to delay the onset and slow the progression of cardiomyopathy. Long-term steroid-treated boys experience later development of LV dysfunction compared to steroid-naïve peers[25]. For example, one multicenter study found 93% of steroid-treated patients were free of DCM at age 18 versus only 53% of untreated patients[26]. Steroids likely mitigate myocardial damage via reduced inflammation and fibrosis, paralleling their benefits in skeletal muscle[27]. Nevertheless, cardiomyopathy is only postponed, not prevented: as DMD patients enter their 20s and 30s (ages increasingly attainable with modern care), cardiomyopathy and heart failure become nearly inevitable if other causes of death are averted[23]. Thus, the critical period for cardiac decompensation in DMD is the second to third decade of life, though the pathological groundwork is laid much earlier.

Screening and Management for Cardiac Involvement

SCREENING AND SURVEILLANCE

Early and regular cardiac surveillance is crucial in Duchenne muscular dystrophy (DMD) due to the high incidence of cardiomyopathy by adolescence. Guidelines recommend initiating cardiac evaluations at the time of DMD diagnosis (often in early childhood) and continuing lifelong follow-up[12]. Key screening practices include:

Baseline and Childhood Monitoring: Perform a comprehensive cardiology evaluation (including ECG and echocardiogram) at diagnosis or by age, then at least annual cardiac assessments through childhood[13]. This allows detection of subclinical

myocardial changes that typically begin in boys <10 years old.

Adolescent Surveillance: After about 10 years of age, when the risk of left ventricular (LV) dysfunction accelerates, continue cardiac screening at least yearly (many centers increase to every 6 months in high-risk patients). Even asymptomatic DMD patients can show a decline in ejection fraction (EF) below 50% as early as age[14,6], so frequent surveillance is warranted as they enter their teens[28].

Imaging Modalities: Use transthoracic echocardiography (echo) as the primary tool to track ventricular function and chamber size. In addition, incorporate cardiac MRI (CMR) in the surveillance plan by early adolescence to detect myocardial fibrosis via late gadolinium enhancement (LGE)[28]. CMR can reveal fibrotic scars (often in the inferolateral wall) even before EF falls, with LGE changes appearing in some patients before age 10 and in most by mid-teen years[28]. Current expert recommendations are to obtain CMR every 1–2 years in DMD, as this aligns with care guidelines and can sensitively index cardiomyopathy progression[28,29].

Electrocardiography: Perform a standard 12-lead electrocardiogram (ECG) at least annually. Sinus tachycardia and conduction abnormalities (e.g. tall R waves in V_1[2], Q waves inferolaterally) are common in DMD and may precede overt cardiomyopathy. Baseline and serial ECGs help identify arrhythmias or conduction block that might necessitate further intervention[28].

Escalation of Screening: If any abnormalities are detected – such as a drop in EF, significant ventricular dilation, or arrhythmias – intensify surveillance frequency (e.g. every 6 months or as clinically indicated). Additionally, once patients become non-ambulatory (typically by early teens in DMD), many experts advocate semiannual cardiac evaluations, given the association of loss of ambulation with more rapid cardiac deterioration. This proactive monitoring allows for timely initiation or adjustment of therapies as cardiac involvement progresses[28].

All surveillance should be performed in collaboration with a cardiologist experienced in heart failure. Importantly, routine screening of female DMD carriers (mothers or sisters) is also recommended (e.g. baseline echo in early adulthood with periodic follow-up), as up to 10%–20% of carriers can develop cardiomyopathy. Early detection through these surveillance strategies enables intervention before DMD patients become symptomatic, which is critical to improving long-term cardiac outcomes[12].

THERAPY GUIDELINES

ACE Inhibitors/ARBs: Start an angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) by ≈10 years of age regardless of baseline EF, or earlier if any cardiac dysfunction is noted[28,30]. This recommendation is based on clinical trials showing that boys who began an ACEI in late childhood had delayed onset of systolic dysfunction[30]. For example, a National Institutes of Health working group advised that all DMD patients should begin ACEI/ARB by age 10 (barring contraindications) to attenuate early myocardial remodeling[28]. An ACEI (such as perindopril, lisinopril, or enalapril) is typically first-line; ARBs (like losartan) are alternatives for those who cannot tolerate ACEIs. Early ACEI/ARB therapy, even in asymptomatic or normotensive patients, has been associated with slowed progression of dystrophinopathic cardiomyopathy[30].

Beta-Blockers: Add a beta-adrenergic blocker once there is any clear evidence of LV systolic dysfunction or as soon as mild dilated cardiomyopathy is present. While prophylactic beta-blockade in completely asymptomatic DMD patients (normal EF) has not yet shown proven benefit[30], guideline-directed medical therapy for heart failure in DMD generally follows standard HF management, meaning a beta-blocker (e.g. carvedilol or extended-release metoprolol succinate) should be initiated as soon as EF declines below the normal range or if resting sinus tachycardia and ventricular dilation are observed[30]. In practice, many DMD clinics introduce a beta-blocker when EF falls to ~50% or if the patient has frequent ventricular ectopy or autonomic symptoms, aiming to reduce myocardial oxygen demand and arrhythmic risk. Beta-blockers are titrated cautiously to avoid hypotension (especially important if the patient is on ACEIs and perhaps steroids). Despite some conflicting data on prophylactic use, once cardiomyopathy is present, beta-blockers are a cornerstone of therapy for their well-demonstrated mortality benefit in systolic heart failure[30].

Mineralocorticoid Receptor Antagonists: Incorporate a mineralocorticoid receptor antagonist (MRA) such as eplerenone or spironolactone in patients with DMD cardiomyopathy who have any reduction in EF or myocardial fibrosis on MRI. MRAs are part of the standard therapy for heart failure with reduced EF and have been shown to benefit DMD-related cardiomyopathy. Notably, a randomized trial (PROMISE-DMD) demonstrated that adding eplerenone to background ACEI slowed the decline in left ventricular strain in DMD boys with early fibrosis on MRI[28]. Consequently, many experts start eplerenone by early adolescence in DMD patients, especially if late gadolinium enhancement is detected, even if EF is still preserved. MRAs help counteract deleterious aldosterone effects on the heart – an important consideration given the fibrosis-driven nature of DMD cardiomyopathy[28]. (Eplerenone is often preferred over spironolactone in teenage males to minimize anti-androgen side effects, though both are effective.

Advanced Therapies: In advanced DMD cardiomyopathy (EF continuing to deteriorate <~30% despite GDMT, or advanced NYHA class III–IV heart failure), refer to a heart failure specialist to discuss advanced therapies. Options may include angiotensin receptor-neprilysin inhibitor (ARNI) therapy (e.g. sacubitril/valsartan) in place of the ACEI – early reports suggest ARNI can improve EF in DMD patients similar to other non-ischemic cardiomyopathies[31]. Additionally, SGLT2 inhibitors (like empagliflozin) have recently been shown to improve outcomes in heart failure and could be considered off-label in DMD cardiomyopathy, although pediatric experience is limited. If heart failure remains refractory, heart transplant evaluation might be appropriate for select cases. Historically, transplantation in DMD was often deemed contraindicated due to the systemic nature of the disease, but emerging data indicate transplants can be successful in carefully chosen DMD patients who have adequate pulmonary function and family support. These decisions are complex and require multidisciplinary input, including neuromuscular and palliative care teams[31].

Early and aggressive medical therapy is the cornerstone of managing DMD cardiomyopathy. Instituting ACE inhibitors (or ARBs) by age ~10 and adding other heart failure medications as soon as indicated has become standard. This proactive approach – treating before overt heart failure develops – is evidence-based and aimed at slowing disease progression and prolonging survival in DMD[28,30]. Close adherence to these therapy guidelines has significantly improved cardiac outcomes in DMD over the past decade, helping many patients reach adulthood with better preserved cardiac function[28].

DEVICE THERAPY

ICD for Primary Prevention: DMD patients with severe LV systolic dysfunction (LVEF ≤ 35%) despite optimal medical therapy should be evaluated for an ICD for primary prevention of sudden cardiac death, in line with general heart failure guidelines[32]. If the patient is ambulatory or has a reasonable expected survival >1 year (considering respiratory status and overall condition), an ICD is indicated to guard against life-threatening ventricular arrhythmias[33]. This is typically relevant in the late teens or adult DMD patients who often develop end-stage dilated cardiomyopathy. The decision should be individualized through shared decision-making with the patient and family, acknowledging the potential benefits (prevention of sudden death) against the context of DMD's progressive course[33]. Many centers use the same EF threshold of ~35% used in other cardiomyopathies for recommending ICD, as studies show a higher incidence of ventricular tachyarrhythmias once EF is severely reduced in DMD. An ICD is also indicated for secondary prevention (e.g. if a patient survives a cardiac arrest or sustained VT episode) absent a reversible cause.

Cardiac Resynchronization Therapy: For DMD patients with EF ≤ 35% who also have electrical dyssynchrony (usually evidenced by a prolonged QRS duration ≥120–150 ms, often left bundle branch block pattern on ECG), cardiac resynchronization therapy (CRT) should be considered[9,34]. CRT (biventricular pacing) can improve heart failure symptoms and LV function by resynchronizing ventricular contraction. Guidelines for CRT in neuromuscular cardiomyopathy mirror general heart failure: a CRT device (usually combined with a defibrillator as CRT-D) is recommended in patients with LVEF ≤ 35%, NYHA class II–IV heart failure symptoms, and a widened QRS (especially LBBB ≥150 ms) despite GDMT[34]. In

practice, some DMD patients develop conduction system disease or dyssynchrony as part of their cardiomyopathy (though complete LBBB is less common than in ischemic HF). If a DMD patient meets criteria, CRT can yield symptomatic benefit and reverse remodeling similar to other non-ischemic cardiomyopathies.

Pacemakers: Bradyarrhythmias are less frequent in DMD than in some other dystrophies (such as Emery-Dreifuss or myotonic dystrophy), but they can occur. If a DMD patient develops a high-grade atrioventricular (AV) block or significant sinus node dysfunction (for example, due to fibrotic infiltration of the conduction system), a permanent pacemaker is indicated. This scenario might arise in older DMD patients or those with long-standing disease. In particular, any symptomatic bradycardia or pauses should prompt evaluation for pacemaker placement, as chronotropic support may also aid cardiac output. In practice, pure AV block is rare in DMD; however, some individuals exhibit junctional rhythm or sinus pauses that require pacing support. The pacemaker mode can be tailored (often DDD/R) to also provide rate responsiveness if needed for chronotropic incompetence[12].

Device Selection and Considerations: Transvenous ICD/CRT systems are standard, but in young DMD patients with scoliosis or those who may not tolerate the implant procedure well, alternatives like a subcutaneous ICD could be considered (if pacing is not needed). Mechanical limitations (contractures, wheelchairs) should be considered when planning lead placement and device location. Also, the overall goals of care should guide device decisions; in patients with very advanced DMD (for example, on continuous ventilation with end-stage heart failure), the role of an ICD may be re-evaluated in favor of comfort measures. When devices are implanted, coordinate perioperative management (steroids stress dosing if needed, careful anesthesia planning due to DMD risks). Post-implant, periodic device interrogations are necessary and should be done with awareness of DMD patients' activity levels (or lack thereof, which can affect algorithms like rate response).

ARRHYTHMIA MANAGEMENT

Rhythm Monitoring: Regular rhythm surveillance is recommended. In addition to annual ECGs, many experts advise periodic ambulatory ECG monitoring (Holter or event monitor) in DMD patients, especially if LVEF is declining or myocardial fibrosis is present[35]. For example, one center conducts screening 24-hour Holter monitors in DMD boys who have late gadolinium enhancement on MRI or any ventricular dysfunction[36,35]. Holter monitoring every 1–3 years (frequency based on the patient's age, EF, and symptoms) can uncover silent arrhythmias[12]. Sinus tachycardia is the most common rhythm disturbance in DMD – often persistent resting tachycardia due to sympathetic overactivity or myocardial fibrosis affecting the conduction system[28]. While sinus tachycardia itself may not require antiarrhythmic drugs, it is a marker of cardiac involvement; ensuring the patient is on adequate beta-blockade (if indicated) and optimizing heart failure therapy can help mitigate excessive tachycardia[28].

Atrial Arrhythmias: As DMD patients live longer, atrial arrhythmias such as atrial flutter, atrial fibrillation (AF), or other supraventricular tachycardias may occur. Atrial flutter and AF can be poorly tolerated in DMD (due to limited cardiac reserve and risk of rapid rates causing decompensation). Standard management applies: control the ventricular rate (typically with beta-blockers; calcium channel blockers like diltiazem are less often used in DMD due to already low blood pressure and presence of HF), and consider antiarrhythmic therapy for rhythm control if episodes are frequent or symptomatic. For example, amiodarone can be used for refractory atrial arrhythmias in DMD, though long-term use must be weighed against side effects. Catheter ablation is an option for certain supraventricular arrhythmias (e.g. typical atrial flutter), provided the patient's status allows for the procedure. Anticoagulation should be initiated if a patient is in atrial fibrillation/flutter for more than a short duration or has risk factors, since stroke prevention is as important in DMD as in other AF patients (bearing in mind mobility is limited, they often have additional risk like cardiomyopathy, so an agent like warfarin or a DOAC may be indicated unless contraindicated).

Ventricular Arrhythmias: Ventricular arrhythmias are a major concern as cardiomyopathy progresses. Non-sustained ventricular tachycardia (NSVT) is not uncommon on Holter monitoring in adolescent and

adult DMD patients, and its presence usually correlates with underlying myocardial fibrosis/scar. NSVT (runs of 3+ beats of VT that self-terminate) in DMD should prompt optimization of medical therapy and consideration of an ICD, especially if NSVT is frequent or longer in duration. Although there is no specific DMD threshold for ICD based on NSVT alone, it is generally viewed as a warning arrhythmia in the context of a vulnerable myocardium. Risk stratification for sudden death in DMD relies heavily on the degree of LV dysfunction; LVEF ≤ 35% is associated with high arrhythmic risk[12]. Even moderate dysfunction (EF <50%) combined with a rapid decline in EF or extensive scar on MRI may portend elevated risk[12]. Therefore, the presence of significant ventricular arrhythmias plus a low EF should strongly bias toward ICD therapy for prevention of sudden cardiac death. If a patient has sustained VT or survives a VF arrest, an ICD is mandatory (secondary prevention) unless contraindicated by patient preference. For acute management of sustained VT in DMD, antiarrhythmic drugs such as amiodarone or lidocaine can be used (e.g. during a storm or while awaiting ICD), in addition to correcting any precipitating factors (electrolyte imbalances, ischemia, etc.). Some cases of refractory VT in DMD have been managed with catheter ablation of scar-related circuits, but the success can be limited if diffuse fibrosis is present.

Conduction System Disease: DMD can infrequently present with conduction issues like atrioventricular block (more so in advanced disease). Any high-grade AV block should be managed with a pacemaker as noted earlier. Even lesser degrees of conduction disease (e.g. bifascicular block on ECG) warrant closer follow-up, as progression can occur. The Heart Rhythm Society consensus recommends a low threshold for pacing in neuromuscular dystrophy patients if advanced conduction delay is documented, to preempt Stokes-Adams syncope.

IMPORTANCE OF PROACTIVE CARDIAC CARE

With improved DMD care enabling longer survival, proactive cardiac management has become critical for extending life and enhancing its quality. Historically, cardiology referral in DMD often occurred only after overt heart failure developed, by which time irreversible damage had accrued[37]. This reactive approach contributed to poor outcomes. Contemporary consensus stresses early and regular cardiac evaluation and preemptive therapy – in other words, treating the DMD heart *before* symptoms or significant dysfunction materialize[37]. The rationale is clear: a "heart-preservation" strategy can delay the progression of cardiomyopathy and prevent sudden deaths, complementing motor and respiratory interventions in a multidisciplinary care model[37]. Evidence from recent studies supports this approach. For instance, a 2023 longitudinal study found that starting ACE inhibitors (and other heart medications) before onset of LV dysfunction halved the risk of death compared to initiating therapy after cardiomyopathy was evident[38]. In that cohort, prophylactic cardiac therapy was associated with a significantly prolonged survival time, even after adjusting for corticosteroid use and baseline disease severity[38]. Similarly, patients receiving early cardiac prophylaxis had fewer heart-failure hospitalizations in follow-up, without any increase in respiratory-related hospitalizations[38]. These data underscore that preserving cardiac function translates into tangible survival benefits in DMD.

Equally important, maintaining better cardiac output has downstream effects on quality of life – improving exercise tolerance (within the limits of neuromuscular impairment), stabilizing energy levels, and reducing symptomatic orthopnea or fatigue that can compound the burdens of DMD. Proactive management (including scheduled cardiac imaging, timely initiation of ACEi/ARB, beta-blockers, and defibrillator therapy when appropriate) is now considered an integral part of DMD care standards[37].

In summary, as DMD patients live longer, vigilant cardiac surveillance and early intervention have proven essential in maximizing both lifespan and life quality[37]. By detecting cardiomyopathy in its subclinical stages and treating aggressively, clinicians can significantly delay heart failure progression and reduce cardiac mortality in DMD[37,38]. This proactive cardiac care, coordinated within a multidisciplinary DMD team, offers the best chance for patients to achieve their optimal functional status and longevity.

Becker Muscular Dystrophy (BMD)

Becker muscular dystrophy (BMD) is an allelic, milder form of dystrophinopathy that also leads to significant cardiac involvement. Because dystrophin is partially functional in BMD, disease

progression is slower and more variable than in Duchenne MD[39]. Many BMD patients survive into their 40s and 50s, but cardiomyopathy remains the leading cause of death[40]. Cardiac involvement is nearly as prevalent as in DMD – studies indicate roughly 60–75% of BMD patients develop dilated cardiomyopathy (DCM) by adulthood[40]. However, the onset of heart disease in BMD typically lags a decade or more behind DMD. Approximately 70% of BMD patients eventually develop DCM, most often in the third decade of life or later, and it is *rare* for a Becker patient to experience severe cardiomyopathy in childhood[39]. Historically, cardiac mortality appeared higher in BMD than DMD (likely because BMD patients lived long enough to reach advanced heart failure, whereas many DMD patients succumbed to respiratory failure earlier)[41]. With modern respiratory support extending dystrophinopathy lifespans, both disorders now demand equally proactive cardiac care.

CARDIAC MANIFESTATIONS IN BECKER MUSCULAR DYSTROPHY

The cardiomyopathy of BMD closely resembles that in DMD, with progressive myocardial fibrosis leading to a *dilated cardiomyopathy*. Fibrosis in BMD often begins in the inferolateral (posterobasal) left ventricular wall – the same region preferentially affected in DMD hearts[40]. Over time, diffuse fibrosis and muscle degeneration thin the ventricular walls and impair contraction. The cardiac trajectory in BMD typically unfolds on a slower, more variable timeline compared to DMD. During childhood and early adolescence, most BMD patients have normal cardiac function. Myocardial fibrosis often begins silently in the teen years or early twenties[39], with subtle functional impairment detectable by advanced imaging before symptoms arise. By the mid-20s to 30s (third decade of life), a substantial proportion of BMD patients will show signs of cardiomyopathy, such as reduced ejection fraction or regional wall motion abnormalities[39]. Nearly 70% of BMD patients in their late 20s and beyond have some degree of DCM, though the severity ranges widely[39]. Crucially, BMD's cardiac course is heterogeneous. Some individuals experience an *acute progressive* decline (for example, a subset develop rapidly worsening DCM in their teens or 20s despite mild muscle disease), whereas others have a *chronic persistent* mild dysfunction or even *latent* subclinical involvement well into mid-adulthood[41].

Genotype is one factor influencing this timeline: certain dystrophin mutations in BMD (especially those disrupting critical protein domains) are associated with earlier or more severe cardiomyopathy[39]. For instance, BMD patients with deletions in exons linked to the cardiac isoform of dystrophin can show earlier onset DCM in their 20s[40]. On the other hand, mutations yielding a near-intact dystrophin rod domain may spare the heart until much later. Unlike DMD, the use of long-term systemic steroids in BMD is not routine, so BMD hearts may not receive the same anti-fibrotic benefit that corticosteroids confer in DMD[40]. The absence of this intervention could partly explain why some BMD patients develop cardiomyopathy in early adulthood despite relatively mild muscle symptoms. Arrhythmias in BMD usually coincide with structural disease: frequent premature beats or non-sustained arrhythmias start appearing once fibrosis is established (often in the late teens or beyond), and life-threatening arrhythmias (sustained VT or AF with RVR) tend to manifest in the third-to-fourth decade alongside advanced DCM. Because BMD patients often reach ages that DMD patients historically did not, they can live long enough to develop end-stage heart failure complications (e.g. progressive pump failure, arrhythmic sudden death) if not aggressively managed. The critical period for BMD cardiac decompensation generally falls in the 30s–40s, although there is considerable individual variation.

Arrhythmias and Conduction Defects: Dystrophin abnormalities in BMD also disrupt the heart's electrical stability, though serious arrhythmias usually emerge later than in DMD. Common electrocardiographic changes in BMD mirror those seen in DMD. As ventricular scarring progresses, the risk of arrhythmias increases. Older BMD patients can develop atrial fibrillation or flutter and ventricular tachyarrhythmias (VT/VF), particularly once left ventricular ejection fraction declines significantly[40]. In one review, arrhythmia incidence in BMD was proportional to the degree of LV dysfunction, similar to DMD[40].

Thromboembolic Events: BMD does not appear to confer a unique predisposition to thrombosis; any thromboembolic complications usually stem from advanced heart failure or prolonged immobility. The standard precautions therefore apply.

CARDIAC SCREENING AND MANAGEMENT GUIDELINES

Care guidelines for BMD emphasize proactive surveillance and early therapy, analogous to DMD recommendations but adjusted for BMD's later onset. Key screening practices include:

Regular Cardiac Evaluations: Perform a baseline cardiac workup (ECG plus imaging) at the time of BMD diagnosis[40]. Because BMD is often diagnosed later than DMD (sometimes in adolescence or even adulthood), the initial cardiac assessment may occur in the early teen years. If the initial exam is normal, follow-up cardiac screenings should occur at least every 2 years[40]. (Older practices of spacing cardiac visits every 5 years in asymptomatic BMD have been updated in favor of more frequent monitoring.) Annual exams are advisable as patients reach adulthood or if any abnormalities begin to appear[41]. The preferred modality in teenage and adult BMD patients is cardiac MRI with gadolinium, given its sensitivity for early fibrosis, though echocardiography is used for routine functional assessment[40]. Any new symptoms or concerning findings (e.g. drop in ejection fraction, new wall motion defect, arrhythmias) should prompt immediate re-evaluation rather than waiting for the next scheduled visit. Importantly, a cardiology review is recommended prior to major surgeries (such as scoliosis correction or orthopedic procedures), since anesthesia and perioperative stress can pose risks if cardiomyopathy is present[40].

Pharmacological Therapy: Initiating heart failure medications early can delay progression of BMD cardiomyopathy. There is no strict rule for the timing of therapy in BMD, but many experts recommend starting an ACE inhibitor (or angiotensin receptor blocker) as soon as any LV systolic dysfunction is noted – commonly when LVEF falls below ~55%, even if the patient has no symptoms[40]. Some clinicians will introduce an ACEi in late adolescence as a preventative measure if fibrosis is seen on MRI, mirroring DMD practice, though formal evidence in BMD is limited. Beta-blockers are added once clear cardiomyopathy is present (e.g. reduced EF or dilated LV)[40]. A combination of ACEi + β-blocker has been shown to improve cardiac function in dystrophinopathy patients more than ACEi alone[40], so a two-drug regimen is favored for any BMD patient with moderate LV dysfunction (provided blood pressure tolerates it). If heart failure progresses (EF continues dropping or clinical HF symptoms develop), additional therapies are employed: mineralocorticoid receptor antagonists like eplerenone or spironolactone are often added. Notably, adding eplerenone has shown benefit in slowing the decline of heart function in DMD/BMD – presumably by reducing fibrosis and inflammation[40]. Diuretics (and sometimes digoxin) are used for symptomatic relief of congestive symptoms such as pulmonary edema or edema in advanced cases, though they don't improve mortality[40]. Ivabradine, an SA-node inhibitor to slow heart rate without lowering blood pressure, has been tried in BMD cardiomyopathy with some success in case reports (improving exercise tolerance and remodeling), but data are very limited and the drug is not widely available in the US[40]. Overall, the medical management of BMD-associated heart failure aligns with standard guidelines for non-ischemic DCM, with the understanding that *younger* BMD patients may tolerate medications differently.

Arrhythmia Monitoring and Treatment: Given the arrhythmic risk in cardiomyopathic BMD patients, routine rhythm monitoring is recommended. Once myocardial fibrosis or any LV dysfunction is identified, annual 24-hour Holter monitoring (or equivalent telemetry) is prudent to screen for occult arrhythmias[40]. Patient-reported palpitations or syncope, of course, warrant immediate investigation with extended monitoring. If a BMD patient develops sustained ventricular tachycardia or survives a cardiac arrest, an ICD for secondary prevention is indicated. For primary prevention, an ICD may be considered when EF is below ~35% or if there are frequent non-sustained VTs plus severe dysfunction, mirroring general DCM guidelines[40]. Device implantation in muscular dystrophy patients can be challenging due to scoliosis or respiratory issues, but several BMD patients have been successfully implanted and even undergo cardiac resynchronization therapy (biventricular pacing) if needed for dyssynchrony and heart failure[40]. Atrial fibrillation in BMD should be managed with anticoagulation (to mitigate stroke risk, especially if EF is low) and rate control medications or ablation as appropriate. In summary, arrhythmia care in BMD is individualized but follows the same

principles as in other cardiomyopathies, with close attention to device therapy criteria and stroke prevention.

Advanced Heart Failure Interventions: Unlike DMD patients (who often have contraindications), BMD patients with end-stage heart failure are increasingly being evaluated for advanced therapies like *ventricular assist devices* (VADs) or heart transplantation. Because BMD patients typically have milder skeletal muscle weakness and better-preserved pulmonary function than age-matched DMD patients, they can be better candidates for transplant when needed[41]. There have been multiple reports of successful heart transplants in BMD patients with end-stage cardiomyopathy[40]. Outcomes post-transplant in muscular dystrophy patients (mostly BMD cases) have been similar to non-dystrophic cardiomyopathy patients in terms of survival and complication rates, especially when the patient's respiratory muscle status is good[41]. Thus, current practice is to not automatically exclude BMD patients from transplant consideration solely due to their neuromuscular disease – each case is assessed on its own merits. If transplant is too high-risk or not available, palliative inotropes or hospice care may be considered, but the trend is toward aggressive management in suitable BMD patients, including mechanical circulatory support as a bridge to transplant or destination therapy in some cases.

IMPORTANCE OF PROACTIVE CARDIAC CARE

Proactive cardiac management in BMD is vital to improve survival and quality of life – even though BMD is "milder" than DMD, its cardiac complications can be equally life-threatening if untreated. Early detection of cardiomyopathy allows clinicians to start ACE inhibitors and other therapies before irreversible damage accumulates, thereby extending the period of compensated heart function. The value of vigilance is illustrated by outcomes data: in a comparative registry study, children with DMD and cardiomyopathy had significantly worse five-year survival than those with BMD, largely because 25% of BMD patients received timely heart transplants (within months of cardiomyopathy diagnosis) whereas DMD patients often could not[41]. All BMD patients in that cohort were alive five years after developing cardiomyopathy (many aided by transplant), compared to only 57% of the DMD group[41]. This striking difference underscores how aggressive intervention – whether pharmacologic or surgical – can save lives in BMD cardiomyopathy. It also highlights that BMD cardiomyopathy may be detected at a later stage (since skeletal symptoms are less pronounced), meaning some patients present in acute heart failure that progresses rapidly[41].

Discussion

THE NEED FOR CARDIO-NEUROMUSCULAR CLINICS

The complexity of managing heart disease in NMD patients – who often have concurrent skeletal muscle weakness, respiratory insufficiency, and other system involvement – makes a compelling case for interdisciplinary care models. Integrating cardiology and neuromuscular expertise is critical for early cardiac diagnosis, tailored treatment, and prevention of sudden cardiac death or advanced heart failure in this population.

EMERGENCE AND GROWTH OF CARDIO-NEUROMUSCULAR CENTERS

Recognizing these needs, the past decade has seen the establishment of dedicated cardio-neuromuscular clinics in the United States, *bridging neurology and cardiology for NMD patient*. These emerging programs illustrate how integrating cardiology expertise directly into neuromuscular care can facilitate earlier interventions (e.g. timely heart failure therapy or defibrillator placement) and vigilant surveillance for cardiomyopathy or arrhythmias in high-risk patients.

A pioneering example is the Cardio-Neuromuscular Center (CNC) at Washington University/Barnes-Jewish in St. Louis, created in 2013 as a multidisciplinary clinic for patients with genetic neuromuscular disorders that affect the heart[13]. The CNC brings together cardiologists (with heart failure and genetics expertise), neurologists (pediatric and adult neuromuscular specialists), specialized nurses, physical therapists, and orthotics and respiratory therapists to provide coordinated care. This model provides uniform care pathways and routine cardiac follow-ups explicitly aimed at improving patient quality of life[13]. Notably, the clinic also emphasizes proactive screening of at-risk family members.

Similarly, in 2019 the University of South Florida launched a Neurocardiogenetics Clinic to serve patients with hereditary neuromuscular disorders

at risk for cardiac complications[15]. This clinic, directed collaboratively by cardiologists and neurologists, offers combined cardiac evaluations and genetic assessments in one visit, aiming to personalize treatment plans for neuromuscular conditions like Friedreich's ataxia where over half of patients develop cardiomyopathy[15]. Major neuromuscular centers across the country have increasingly adopted such models. For example, Certified Duchenne Care Centers (CDCCs), a program by Parent Project Muscular Dystrophy (PPMD), now require robust cardiac care as part of their standards and in line with published guidelines[16]. Pediatric hospitals have long integrated cardiology into muscular dystrophy clinics, and more recently adult hospitals are building similar multidisciplinary teams to improve the transition of Duchenne and other NMD patients into adult cardiac care[14]. For instance, adult DMD clinics have been developed (e.g. in Southampton UK, and mirrored in U.S. centers) where cardiologists, pulmonologists, neurologists, and palliative care providers see the patient together in one setting, smoothing the transition from pediatric care and ensuring no aspect of cardiac management is lost during adolescence[14].

Overall, the trend in the U.S. is growth of these interdisciplinary "cardio-neuromuscular" centers, driven by advocacy groups and emerging consensus that coordinated care can improve quality of life. Many are embedded in academic hospitals (e.g. neuromuscular divisions working jointly with cardiovascular genetics or heart failure teams), and new programs continue to appear. This growth is underscored by professional guidelines: a 2022 Heart Rhythm Society consensus explicitly frames the care of hereditary cardio-neuromuscular disorders as a "model for the multidisciplinary care of complex genetic disorders," encouraging centers to develop specialized teams for these patients[9].

IMPROVED OUTCOMES WITH MULTIDISCIPLINARY CARE MODELS

Evidence is accumulating that these multidisciplinary cardio-neuromuscular clinics are not just convenient, but actually improve clinical outcomes for patients. A landmark prospective study (Nikhanj et al., JAMA Heart Assoc. 2020) followed 145 muscular dystrophy patients (DMD/BMD, limb-girdle MD, DM, facioscapulohumeral MD) managed in an integrated neuromuscular-cardiac clinic, and demonstrated striking benefits[12,10]. Over a 3-year period, proactive cardiac intervention within the multidisciplinary clinic led to reversal of systolic dysfunction – median left ventricular ejection fraction improved from 43% at baseline to 50% after 3 years[10]. Patients received earlier initiation and uptitration of heart-failure medications (ACE inhibitors, beta-blockers, etc.) and timely device implantations (ICDs/CRT for those with arrhythmias or conduction block) as part of the clinic's standardized care path[10]. Notably, healthcare utilization dropped substantially: unplanned cardiology visits fell by about half (from ~ Notably, healthcare utilization dropped substantially: unplanned cardiology visits fell by about half (from ~3.0 to 12.5 per year), hospitalization duration plummeted from an average 2 days/year to 2 days/year to 0.9 days/year, and cardiac-related hospitalizations decreased to near-zero[10]. This was accompanied by very low cardiac mortality over the study period (in the MD cohort, ~2% per year, which is remarkably low for advanced dystrophic cardiomyopathy)[10]. The authors conclude that comprehensive cardiac care "as part of a multidisciplinary care approach" led to sustained improvement in outcomes for MD patients[10].

Similar outcome trends are reported elsewhere. For example, centers have observed that DMD patients in coordinated care live longer and maintain better heart function due to earlier intervention (aligning with data that starting ACE inhibitors by age ~10 or at first sign of cardiac fibrosis improves long-term cardiac function)[16]. One analysis of heart transplant outcomes in muscular dystrophy – historically a controversial option – found selected MD patients can have transplant survival comparable to non-MD patients, when managed in expert centers that carefully select and prepare them[11]. In a multicenter review of 31 MD patients who underwent cardiac transplantation (mostly Becker MD cases), 5-year survival was ~83%, statistically no different from controls with other cardiomyopathies[11]. This suggests that comprehensive management (including timely referral for advanced therapies like transplant or ventricular assist devices) can indeed translate to better survival for end-stage patients who decades ago might simply have been deemed "untreatable." Advanced heart failure therapies are now considered feasible and safe in several neuromuscular conditions – as a 2024

review notes, durable LVADs and transplant "have proven to be feasible and safe treatment options" in appropriately chosen NMD patients, especially when a multidisciplinary team monitors them closely for extra-cardiac issues[17]. In sum, the data – though still limited – point to earlier diagnosis, optimized medical therapy, fewer emergencies, and extended life when cardiac care is integrated with neuromuscular care. This has led experts to deem multidisciplinary management the standard of care for many NMDs[18]. Indeed, multidisciplinary clinics are now considered "the best models" for neuromuscular disease management and are being implemented alongside research protocols to continue measuring outcomes[19].

GLOBAL PROGRAMS AND MODELS

While the United States has seen significant growth of cardio-neuromuscular centers, similar multidisciplinary approaches are emerging globally. In Italy, for example, an initiative known as the Italian Neuro-Cardiology Network (INCN) was formed to bridge neurology and cardiology for NMD patients. This network explicitly "facilitates the creation of integrated neuro-cardiac teams in Neuromuscular Disease Centers" for managing cardiovascular aspects of disorders like myotonic dystrophy type[20]. The INCN's collaborative model (neurologists working hand-in-hand with arrhythmia specialists and heart failure cardiologists) is reported to be a unique and successful experience in coordinating care for myotonic dystrophy patients across multiple Italian clinics[20]. In the United Kingdom, specialized pathways are being developed for adult NMD care, recognizing a historical gap once patients aged out of pediatric centers. A consensus guideline for adult DMD care was published in late 2020 (Adult North Star Network guidelines), and centers like the Wessex Cardiac Centre (Southampton) have piloted dedicated adult DMD clinics with integrated teams[14]. Early feedback from these UK clinics is positive – patients prefer seeing all their specialists in one day at a single site, and providers report more streamlined decision-making (for instance, a cardiologist can adjust medications the same day a neurologist identifies a change in functional status)[14]. Other countries have analogous programs: Canada's Alberta multidisciplinary clinic (source of the 2020 outcomes study) is one example in North America outside the U.S., and in France and elsewhere in Europe, neuromuscular reference centers often include cardiologists as part of routine care for muscular dystrophies[10]. Moreover, international collaborations and consensus statements (AHA 2017, HRS 2022, etc.) have raised awareness worldwide that cardio-neuromuscular care models are crucial. Notably, European Reference Networks for rare diseases (such as EURO-NMD) explicitly promote cross-disciplinary care and sharing of expertise across borders, which has led to more clinics adopting a team approach. Even in regions with fewer resources, there is movement toward at least virtual multidisciplinary consults or periodic combined clinics to manage these complex patients. In summary, the concept of the "cardio-neuromuscular clinic" is gaining traction globally as a best-practice model – although the scale and integration level vary by country.

DISPARITIES AND REMAINING GAPS IN ACCESS

Despite clear benefits, not all patients with neuromuscular diseases have access to interdisciplinary cardiac care – leading to disparities by disease, age, and geography. Some Duchenne and Becker's muscular dystrophy patients might live far from academic centers and receive only fragmented care – for instance, a patient might get a pacemaker from a cardiologist who isn't in communication with the neuromuscular specialist, potentially overlooking other aspects of care or family screening[13]. Geography plays a role: in the U.S., large multidisciplinary clinics are typically found in major cities/teaching hospitals, whereas those in rural areas or without means to travel may have difficulty accessing such comprehensive care. There are also age-related gaps; pediatric patients with Duchenne often receive excellent coordinated care at children's hospitals, but upon transitioning to adulthood, they may find few adult clinics prepared to handle their complex needs (though this is improving with programs specifically for adult Duchenne)[14]. Even among DMD care centers, variability existed before standardization – PPMD acknowledged that "cardiac care is variable across the country and around the world," which was a major driver for its certification program to ensure every center adheres to cardiac surveillance and management guidelines[16].

There are disparities in awareness: some adult cardiologists might not be familiar with

neuromuscular disorders and their unique cardiac issues (for instance, differentiating a DMD cardiomyopathy from other dilated cardiomyopathies, or recognizing when an arrhythmia in a young person suggests an underlying myopathy). This can lead to delayed diagnoses. The 2017 AHA Statement highlighted the challenge that conventional heart failure guidelines don't always directly apply to NMD patients due to their multi-system issues – without specialized knowledge, clinicians might under-treat or over-treat certain NMD cardiac problems.

In terms of insurance and resources, multidisciplinary clinics can be resource-intensive (involving multiple specialists in one visit). Patients with limited insurance coverage or those in health systems without an established clinic model might not get the same level of coordinated care. Telemedicine is being explored to mitigate geographic barriers, and patient advocacy groups are pushing for broader implementation of care standards. Nevertheless, significant gaps remain: for example, many neuromuscular patients still rely on their primary care or general cardiologists who may not conduct the recommended yearly ECG or Holter monitoring for arrhythmia risk. And while transplant and ventricular assist devices are now possible for end-stage NMD cardiomyopathy, not all transplant centers are willing to list these patients – some may consider advanced NMD a contraindication, even though recent evidence shows selected cases do well[21,11]. Smaller hospitals may lack transplant clinics altogether. This reflects an ongoing disparity in access to advanced therapies; often only the most experienced centers (frequently those with multidisciplinary teams that can manage the peri-transplant care) will consider NMD patients for heart transplant or LVAD.

The rise of interdisciplinary cardio-neuromuscular clinics represents a significant advance in the care of patients with neuromuscular diseases. These programs – particularly flourishing in the U.S. – have shown the ability to detect cardiac issues earlier, initiate therapies that preserve heart function, reduce hospitalizations, and even facilitate lifesaving interventions like transplants, thereby improving survival[10]. However, not all patients reap these benefits yet. Disparities persist based on disease type, age, and location; for example, adult and less-common NMDs lag behind in specialized care access compared to pediatric Duchenne programs[16,22]. Ongoing efforts by advocacy organizations, professional societies, and healthcare systems are crucial to expand the reach of multidisciplinary care. The goal moving forward is to ensure that every patient with an NMD and cardiac involvement can receive coordinated, expert care that optimizes both their muscular and cardiac health. This will likely entail continued growth of dedicated centers, development of telehealth networks connecting local doctors with specialty teams, and education to standardize cardiac surveillance in all neuromuscular clinics. By addressing these gaps, the improved outcomes observed in specialized programs can become a reality for a broader NMD population, closing the disparity and truly fulfilling the promise of interdisciplinary care models.

Conclusion

Cardiac disease is the leading cause of death in Duchenne and Becker muscular dystrophies, with dilated cardiomyopathy and arrhythmias representing near-universal complications by adulthood[23,41]. Early and regular surveillance with echocardiography, cardiac MRI, and rhythm monitoring, coupled with initiation of ACE inhibitors, beta-blockers, and mineralocorticoid receptor antagonists, has been shown to delay progression of cardiomyopathy and improve survival[28,30,39]. Multidisciplinary cardio-neuromuscular clinics further enhance outcomes by enabling earlier initiation of therapies, reducing unplanned hospitalizations, and facilitating advanced interventions such as device therapy and transplantation[10,11,14]. However, disparities persist in access to specialized care, particularly for adults and patients outside academic centers[14,16]. Expanding multidisciplinary programs and standardizing cardiac surveillance across neuromuscular populations are essential next steps to optimize both survival and quality of life in dystrophinopathies[9,12].

As we move forward, the landscape of care is shifting. Novel pharmacologic agents such as angiotensin receptor–neprilysin inhibitors and SGLT2 inhibitors are being explored in dystrophinopathic cardiomyopathy[31], and gene-targeted therapies hold the potential to alter the trajectory of these diseases at their root[23,28]. As

DMD and BMD patients live longer due to improvements in respiratory and supportive care, cardiology will increasingly define long-term outcomes[37,38]. Moreover, the multidisciplinary frameworks developed for dystrophinopathies are now being adapted for other neuromuscular diseases—including limb-girdle muscular dystrophies, myotonic dystrophy, and Friedreich's ataxia—where cardiac involvement is also a critical determinant of prognosis[12,20,22]. Together, these advances point toward a future in which proactive, integrated, and disease-specific cardiac care not only prolongs life but also redefines what it means to live with neuromuscular disease.

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References:

1. Study confirms cardiomyopathy as leading cause of death in DMD. Rare Disease Advisor. Published September 22, 2023. Accessed August 1, 2025. https://www.rarediseaseadvisor.com/news/study-confirms-cardiomyopathy-leading-cause-death-dmd/

2. Nigro G, Papa AA, Politano L. The heart and cardiac pacing in Steinert disease. *Acta Myol.* 2012;31(2):110-116.

3. Becker Muscular Dystrophy: Practice essentials, pathophysiology, epidemiology. *Medscape*. Updated June 26, 2021. Accessed August 1, 2025. https://emedicine.medscape.com/article/313417-overview

4. Cardiac complications of neuromuscular disorders. Clinical Tree. Published March 4, 2024. Accessed August 1, 2025. https://clinicalpub.com/cardiac-complications-of-neuromuscular-disorders/

5. Giuliani L, Di Toro A, Urtis M, et al. Hereditary muscle diseases and the heart: the cardiologist's perspective. *Eur Heart J Suppl.* 2020;22(Suppl E):E13-E19. doi:10.1093/eurheartj/suaa051

6. Myotonic Dystrophy (MDA) Clinic. Houston Methodist. Published 2021. Accessed August 1, 2025. https://www.houstonmethodist.org/neurology/centers-and-programs/myotonic-dystrophy-clinic/

7. Myotonic dystrophy (DM). University of Iowa Health Care. Published 2025. Accessed August 1, 2025. https://uihc.org/services/myotonic-dystrophy-dm

8. Friedreich's ataxia clinic: overview. Mayo Clinic. Published 2025. Accessed August 1, 2025. https://www.mayoclinic.org/departments-centers/friedreichs-ataxia-clinic/overview/ovc-20567704

9. Groh WJ, Bhakta D, Tomaselli GF, et al. 2022 HRS expert consensus statement on evaluation and management of arrhythmic risk in neuromuscular disorders. *Heart Rhythm.* 2022;19(10):e61-e120. doi:10.1016/j.hrthm.2022.04.022

10. Nikhanj A, Yogasundaram H, Nichols BM, et al. Cardiac intervention improves heart disease and clinical outcomes in patients with muscular dystrophy in a multidisciplinary care setting. *J Am Heart Assoc.* 2020;9(2):e014004. doi:10.1161/JAHA.119.014004

11. Wu RS, Gupta S, Brown RS, et al. Clinical outcomes after cardiac transplantation in muscular dystrophy patients. *J Heart Lung Transplant.* 2007;26(4):432-438. doi:10.1016/j.healun.2006.12.004

12. Feingold B, Mahle WT, Auerbach S, et al. Management of cardiac involvement associated with neuromuscular diseases: a scientific statement from the American Heart Association. *Circulation.* 2017;136(13):e200-e231. doi:10.1161/CIR.0000000000000526

13. Washington University School of Medicine. Cardio-neuromuscular disorders – cardiovascular division. Published April 12, 2024. Accessed August 1, 2025. https://cardiology.wustl.edu/patient-care/cardio-neuromuscular-disorders/

14. Haydock P. Developing an integrated, multidisciplinary clinic for Duchenne muscular dystrophy patients and their carers from across the Wessex region. Poster presented at: British Cardiovascular Society Annual Conference; February 2025; London, UK. Accessed August 1, 2025. https://britishcardiovascularsociety.org.uk/wp-content/uploads/2025/02/Paul-Haydock-Poster.pdf

15. Clinic integrates care and genetic research for patients with neuromuscular disorders. *USF Health News.* Baier AD. Published November 15, 2019. Accessed August 1, 2025. https://hscweb3.hsc.usf.edu/blog/2019/11/15/clinic-integrates-care-and-genetic-research-for-patients-with-neuromuscular-disorders/

16. PPMD's Certified Duchenne Care Center program – 2021 impact & progress. Parent Project Muscular Dystrophy. Published March 9, 2022. Accessed August 1, 2025. https://www.parentprojectmd.org/ppmds-certified-duchenne-care-center-program-2021-impact-progress/

17. Agdamag AC, Nandar PP, Tang WHW. Advanced heart failure therapies in neuromuscular diseases. *Curr Treat Options Cardiovasc Med.* 2024;26(8):255-310. doi:10.1007/s11936-024-01046-2

18. Paganoni S, Nicholson K, Leigh F, et al. Developing multidisciplinary clinics for neuromuscular care and research. *Muscle Nerve.* 2017;56(5):848-858. doi:10.1002/mus.25725

19. Enhancing multidisciplinary care for neuromuscular disorders. Peltier A. *Neurology Live.* Published March 25, 2024. Accessed August 1, 2025. https://www.neurologylive.com/view/enhancing-multidisciplinary-care-neuromuscular-disorders-amanda-peltier

20. Russo V, Antonini G, Massa R, et al. Comprehensive cardiovascular management of myotonic

dystrophy type 1 patients: a report from the Italian Neuro-Cardiology Network. *J Cardiovasc Dev Dis.* 2024;11(2):63. doi:10.3390/jcdd11020063

21. Politano L. Is cardiac transplantation still a contraindication in patients with muscular dystrophy-related end-stage dilated cardiomyopathy? A systematic review. *Int J Mol Sci.* 2024;25(10):5309. doi:10.3390/ijms25105309

22. Ashizawa T, Gagnon C, Groh WJ, et al. Consensus-based care recommendations for adults with myotonic dystrophy type 1. *Neurol Clin Pract.* 2018;8(6):507-520. doi:10.1212/CPJ.0000000000000531

23. Gandhi S, Sweeney HL, Hart CC, Han R, Perry CGR. Cardiomyopathy in Duchenne muscular dystrophy and the potential for mitochondrial therapeutics to improve treatment response. *Cells.* 2024;13(14):1168. doi:10.3390/cells13141168

24. Schorling DC, Müller CK, Pechmann A, et al. Coagulation disorders in Duchenne muscular dystrophy? Results of a registry-based online survey. *Acta Myol.* 2020;39(1):2-12. doi:10.36185/2532-1900-001

25. Barber BJ, Andrews JG, Lu Z, et al. Oral corticosteroids and onset of cardiomyopathy in Duchenne muscular dystrophy. *J Pediatr.* 2013;163(4):1080-1084.e1. doi:10.1016/j.jpeds.2013.05.060

26. Dec GW. Steroid therapy effectively delays Duchenne's cardiomyopathy. *J Am Coll Cardiol.* 2013;61(9):955-956. doi:10.1016/j.jacc.2012.12.011

27. Cui Y, Shao S, Zhang L, et al. The effects of glucocorticoids on cardiac function of patients with Duchenne muscular dystrophy: benefit or not? *Eur J Pediatr.* 2025;184(5):313-320. doi:10.1007/s00431-025-06141-5

28. Meyers TA, Townsend D. Cardiac pathophysiology and the future of cardiac therapies in Duchenne muscular dystrophy. *Int J Mol Sci.* 2019;20(17):4098. doi:10.3390/ijms20174098

29. Starnes JR, Xu M, George-Durrett K, et al. Rate of change in cardiac magnetic resonance imaging measures is associated with death in Duchenne muscular dystrophy. *J Am Heart Assoc.* 2024;13(9):e032960. doi:10.1161/JAHA.123.032960

30. Lee H, Song J, Kang I, Huh J, Yoon JA, Shin YB. Early prophylaxis of cardiomyopathy with beta-blockers and angiotensin receptor blockers in patients with Duchenne muscular dystrophy. *Clin Exp Pediatr.* 2022;65(10):507-509. doi:10.3345/cep.2022.00836

31. Schultz TI, Raucci FJ, Salloum FN. Cardiovascular disease in Duchenne muscular dystrophy. *JACC Basic Transl Sci.* 2022;7(6):590-606. doi:10.1016/j.jacbts.2021.11.004

32. Local coverage determination: cardiac resynchronization therapy (CRT) (L39080). Centers for Medicare & Medicaid Services. Published 2021. Accessed August 15, 2025. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=39080

33. Al-Khatib SM, Stevenson WG, Ackerman MJ, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. *Circulation.* 2018;138(13):e272-e391. doi:10.1161/CIR.0000000000000549

34. Chung MK, Patton KK, Lau CP, et al. 2023 HRS/APHRS/LAHRS guideline on cardiac physiologic pacing for the avoidance and mitigation of heart failure. *Heart Rhythm.* 2023;20(9):e1039-e1134. doi:10.1016/j.hrthm.2023.03.1538

35. Rajdev A, Groh WJ. Arrhythmias in the muscular dystrophies. *Card Electrophysiol Clin.* 2015;7(2):303-308. doi:10.1016/j.ccep.2015.03.011

36. Villa CR, Czosek RJ, Ahmed H, et al. Ambulatory monitoring and arrhythmic outcomes in pediatric and adolescent patients with Duchenne muscular dystrophy. *J Am Heart Assoc.* 2015;5(1):e002620. doi:10.1161/JAHA.115.002620

37. Birnkrant DJ, Bushby K, Bann CM, et al. Diagnosis and management of Duchenne muscular dystrophy, part 2: respiratory, cardiac, bone health, and orthopaedic management. *Lancet Neurol.* 2018;17(4):347-361. doi:10.1016/S1474-4422(18)30025-5

38. Conway KM, Thomas S, Neyaz T, et al. Prophylactic use of cardiac medications and survival in Duchenne muscular dystrophy. *Muscle Nerve.* 2025;71(4):574-582. doi:10.1002/mus.28353

39. Tsuda T, Fitzgerald K, Scavena M, et al. Early-progressive dilated cardiomyopathy in a family with Becker muscular dystrophy related to a novel frameshift mutation in the dystrophin gene exon 27. *J Hum Genet.* 2015;60(3):151-155. doi:10.1038/jhg.2014.112

40. Ho R, Nguyen ML, Mather P. Cardiomyopathy in Becker muscular dystrophy: overview. *World J Cardiol.* 2016;8(6):356-361. doi:10.4330/wjc.v8.i6.356

41. Connuck DM, Sleeper LA, Colan SD, 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(6):998-1005. doi:10.1016/j.ahj.2008.01.018