BRIEF ARTICLE

Usefulness of Cardiac Magnetic Resonance Imaging in Patients with Neuromuscular Dystrophies (Duchenne/Becker Muscular Dystrophy)

Utilidad de la resonancia magnética cardíaca en pacientes con distrofias neuromusculares (distrofia neuromuscular de Duchenne/Becker)

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ABSTRACT

Background: Cardiac magnetic resonance imaging (CMR) is commonly used in patients with Duchene (DMD) and Becker (DMB) Neuromuscular Dystrophies. Late gadolinium enhancement (LGE) identifies areas of middle, subepicardial, or subendocardial wall fibrosis, and volumetric left ventricular ejection fraction (LVEF) is considered the gold standard in the diagnosis and prognosis of these dystrophies. Myocardial fibrosis occurs in patients with neuromuscular dystrophies.
Objectives: The purposes of our study were to determine the presence of cardiac fibrosis using CMR, to determine neuromuscular and cardiac involvement, and to evaluate the cardiovascular outcomes of these patients.
Material y métodos: A descriptive cross-sectional study of 16 consecutive patients was conducted from March 2021 to July 2022 in the Cardiac Imaging Service of Diagnóstico Médico and CEMET- Tucumán.
Results: A total of 16 patients were evaluated, 100% of them with confirmed diagnosis of DMD/DMB by laboratory, enzymes and genetic tests. Mean age was 19 years. All patients had severe stage of the Vignos Scale and were under neurological treatment. All patients were also treated with beta-blockers or angiotensin-converting enzyme inhibitors.
CMR revealed severe LVEF impairment <35% in 4 patients, segmental or global left ventricular (LV) wall motion disorders in 8 patients, and variable distribution pattern (diffuse, mesocardial, subendocardial and subepicardial patterns) of LGE in 12 patients. Non-compacted myocardium was observed in 6, and mild pericardial effusions in 2 patients.
Conclusion: CMR should be included as a screening method in patients with neuromuscular dystrophies. Its contribution to clinical, echocardiographic and therapeutic staging is of utmost importance.

Key words: Muscular Dystrophy, Duchenne - Neuromuscular Diseases - Muscular Dystrophies - Imaging Magnetic Resonance Imaging - Pronóstico

RESUMEN

Introducción: La Resonancia Magnética Cardíaca (RMC) es cada vez más frecuentemente utilizada en pacientes con Distrofia Neuromuscular de Duchenne y Becker (DMD y DMB). Por la capacidad de demostrar realce tardío con gadolinio (RTG), que identifica zonas de fibrosis de la pared media y subepicárdica, subendocárdica o global, y el cálculo de la fracción de eyección ventricular izquierda (FEVI), se considera el patrón oro en el diagnóstico y pronóstico de la afección cardíaca de estas distrofias.
Objetivos: Fueron nuestros objetivos determinar por medio de RMC la presencia de fibrosis cardiaca en pacientes con distrofia neuromuscular. Determinar el compromiso neuromuscular y cardiaco. Definir la evolución cardiovascular de estos pacientes
Material y métodos: Se realizó un estudio descriptivo de corte transversal de 16 pacientes consecutivos desde marzo de 2021 a julio de 2022 en el Área de imagen cardíaca de 2 centros de Tucumán.
Resultados: Se evaluaron 16 pacientes, todos con diagnóstico confirmado de DMD/DMB por laboratorio, enzimas, y test genéticos. La edad promedio fue 19 años. Todos tenían estadio grave de la Escala de Vignos y tratamiento neurológico. Todos tenían tratamiento con betabloqueantes o inhibidores de la enzima de conversión de la angiotensina. La RMC evidenció que 4 pacientes tenían deterioro grave de la FEVI (<35%); 8 pacientes tenían trastornos segmentarios o globales de la motilidad parietal del VI y en 12 se observó RTG, de distribución variable: difusa, mesocárdica, subendocárdica y subepicárdica. En 6 pacientes se observó miocardio no compacto y en 2 derrame pericárdico leve.
Conclusión: La RMC debe ser incluida como método de cribaje para pacientes con distrofias neuromusculares. Su aporte para la estadificación clínica y terapéutica es de suma importancia.

Palabras clave: Distrofia Muscular de Duchenne -Enfermedades Neuromusculares - Distrofias Musculares - Imagen por Resonancia Magnética - Prognosis

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INTRODUCTION

Many of the neuromuscular dystrophies (NMD) affect the heart, in some cases with clinical relevance. Both Duchenne (DMD) and Becker (BMD) dystrophies are forms of muscular dystrophinopathies with cardiac implications. (1) From a pathologic viewpoint, NMD can lead to alternating areas of myocyte hypertrophy, atrophy/necrosis and fibrosis with replacement of myocardium by connective tissue and fat, as well as generalized replacement of the entire ventricular myocardium. Cardiac involvement is present in approximately 90% DMD and BMD patients but is the cause of death in about 20% of the DMD and 50% of the BMD patients. (2, 3)

Until recently, patients with DMD often died at 15 to 20 years of age from respiratory complications, congestive heart failure, or arrhythmias. However, many patients with DMD now live into their late 20s and older. Death from cardiac or respiratory failure typically occurs in the fifth decade in BMD. This increased longevity has made cardiac function and cardiovascular health an increasingly important part of evaluating and treating NMD. (4, 5)

As part of the assessment of NMD patients, we performed cardiac magnetic resonance (CMR) imaging to complete cardiac evaluation. Our purposes in this study were to determine the presence of myocardial fibrosis, identify cardiac involvement, help define treatment, and assess cardiovascular outcomes.

METHODS

We conducted a descriptive cross-sectional study in the Department of Cardiac Imaging from the Cardiac Imaging Service of Diagnostico Medico and CEMET- Tucuman, between March 2021 and July 2022. Patients diagnosed with neuromuscular dystrophies (DMD, DMB and DMD/DMB) were included. There were no exclusion criteria based on age, sex, ethnicity or sociocultural level, but any NMD other than those mentioned above, as well as patients with peripheral neuropathies, were excluded. Neurological variables by Vignos Scale (6) (Table 1), specific neurological treatment (corticosteroids or deflazacort), cardiovascular signs and symptoms, and treatment with beta-blockers or renin angiotensin system inhibitors were considered. CMR evaluated left ventricular ejection fraction (LVEF), distribution of late gadolinium enhancement (LGE), segmental motility, the presence of non-compacted myocardium and pericardial effusion.

RESULTS

A total of 16 patients were performed contrast-enhanced CMR (11 with DMD, 2 with BMD and 3 with DMD/BMD). All the patients had confirmed diagnosis by lab tests, CPK > 100 IU/L and genetic testing.

Mean age was 19 years. All were male patients with severe stage on the Vignos Scale and under neurological treatment; 100% were treated with beta-blockers or angiotensin-converting enzyme inhibitors. Seven patients were asymptomatic, and the rest presented with a variety of symptoms. Table 2 shows CMR results. Mean LVEF was 50%. LGE was found in 13 patients, and segmental motility abnormalities in 8. LGE distribution was diffuse ventricular (4 patients), mesocardial septal (1 patient), inferior and lateral subepicardial (7 patients) and subendocardial (1 patient). Non-compacted myocardium was detected in 6 patients, and mild pericardial effusion in 2.

DISCUSSION

Dystrophies are primary muscle diseases with a mutation of more than 50 genes, causing a series of pathologic changes. (7-9) Duchenne (DMD) and Becker (BMD) are described among the most common muscular dystrophies.

DMD is the most lethal type, and occurs in 1 in 3500 to 6000 live births; inheritance is sex-linked, and there is no cure for this disease. (10)

Given that the common symptom of exercise intol-

Table 1. Vignos Scale (6)

Parameters	Value
1-Walks and climbs stairs without assistance	1
2-Walks and climbs stairs with aid of railing	2
3-Walks and climbs stairs slowly with aid of railing	3
4-Walks unassisted and rises from chair but cannot climb stairs	4
5-Walks unassisted but cannot rise from chair or climb stairs	5
6-Walks only with assistance or walks independently with long leg braces	6
7-Walks in long leg braces but requires assistance for balance	7
8-Stands in long leg braces but unable to walk even with assistance	8
9-Is in a wheelchair. Can flex the elbows against gravity	9
10-Is in a wheelchair or confined to a bed. Cannot flex the elbows against gravity	10
Total	
1: Minor involvement. 10: Major involvement.	
Stage of deterioration	
minor: 1 mild: 2 to 4 moderate: 5 to 7 severe: 8 to 10	

Table 2. Findings in cardiac magnetic resonance imaging.

Results	n=16
Average LVEF 50%	
< 35%	4
> 35% -45%	1
45-55%	3
> 55%	8
Late gadolinium enhancement	13
Segmental wall motion disorders	8
Segmental disorder location	
Global hypokinesis	4
Lateral	3
Mid and basal inferior	1
Late enhancement distribution	
Ventricular diffuse	4
Mesocardial septal	1
Inferior, lateral subepicardial	7
Inferior subendocardial	1
Non-compacted myocardium	6
Pericardial effusion	2

erance is often unnoticed by DMD and BMD patients, vague symptoms such as sleep disorders, loss of appetite, nausea, abdominal pain or fullness, increased cough or secretions, and weight loss should be taken into account. Patients may experience more typical cardiac symptoms, including chest pain, trepidation, dizziness and syncope, which are often associated with arrhythmias rather than with heart failure. (11, 12)

Therefore, it is very important that cardiac function in patients with DMD be monitored regularly with electrocardiography (ECG), Doppler echocardiography (DE), and mainly with CMR. (7)

Cardiac magnetic resonance (CMR) imaging is the gold standard technique to assess biventricular function. CMR non-invasively provides important additional information on tissue characterization through late gadolinium enhancement (LGE) sequences, allowing to evaluate the risk of sudden death and choose the best therapeutic strategy. (13)

LGE is present in about 30% of NMD patients. However, the relationship between its presence, location and characteristics with prognosis is not well determined. Intramyocardial linear enhancement at the septal level is the most common finding, but other patterns such as subepicardial enhancement in the left ventricular free wall, focal enhancement or mixed patterns can also be found. (14)

CMR can provide clinically useful information even without contrast dyes. (15)

The usefulness of CMR in different dystrophies is key to describe the pathophysiology of these entities, discuss their clinical presentation and expected evolution. (16)

Echocardiography-based ventricular functional assessment has weak correlation with CMR parameters in children and young adults with DMD. While this correlation improves in the subset of subjects with adequate echocardiographic image quality, it remains modest and potentially suboptimal for clinical management. Accordingly, we conclude that CMR should be performed routinely and early in children with DMD, not only for LGE imaging but also for functional assessment. (17, 18)

CMR has a better diagnostic field for the identification of fibrosis than other imaging methods; it should be associated with other routine complementary diagnostic methods such as ECG, Doppler echocardiography and speckle tracking strain in order to decide on preventive measures. It is the technique of choice to assess LVEF, left and right ventricular volumes and LV mass. CMR offers excellent spatial and temporal resolution, and, unlike echocardiography, there is no bad ultrasound window. It must be remembered that these patients present a barrel chest or a chest with increased subcutaneous cellular tissue, making echo screening more difficult. Undoubtedly, tissue characterization capability through late gadolinium enhancement is the most important contribution of CMR, allowing early detection of fibrosis even in preclinical (both neurological and cardiac) stages of the disease, as evidenced in our patients. This finding —even at an early age— can totally change the medical approach.

A drawback worth mentioning is the medical community's lack of knowledge of the common cardiac involvement in patients with NMD. NMD is a rare disease, and initial evaluation by cardiologists is rare. Another important problem is the cost of CMR, and the limited access to this technique. In Tucumán, our province, CMR is unavailable in the public sector and partially available in the private sector. To carry out this study, funding had to be requested from foundations and the pharmaceutical Industry. Our goal is to increase the number of CMRs for NMD patients in the future. We follow up more than 70 patients of different ages and stages of the disease; there is still a lot to do and learn.

In conclusion, we consider that CMR should be included as a screening method for patients with NMD; its contribution to clinical and therapeutic staging is of utmost importance.

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