Regional Left Ventricular Myocardial Strain Alterations in Patients with Duchenne Muscular Dystrophy and Correlation with Electrocardiographic and Motor Function Alterations

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Abstract

Background: **Duchenne Muscular Dystrophy (DMD) is characterized by progressive degradation of muscle function. Myocardial dysfunction is a major cause of mortality; however, its correlation with skeletal motor function remains unclear. Objective: To assess myocardial function and to correlate it with motor function in patients with DMD.**

Methods: **This was a cross-sectional observational study of patients with DMD. Evaluations included the Motor Function Measurement (MFM) scale, electrocardiogram (ECG), and echocardiography (Echo) with speckle-tracking (STE) imaging of the left ventricle (LV). The level of significance adopted in the statistical analysis was 5%.**

Results: **Thirty-three patients with a mean age of 14.30 ± 4.09 years. The average MFM score was 52.30 ± 16.32%. Electrocardiographic abnormalities were observed in 75% of patients. Left ventricular ejection fraction (LVEF) was preserved (57.80 ± 9.62%). Global longitudinal strain (GLS) was reduced in 70% of the patients (-15.06 ± 2.46%; normal ≤ -18%), global circumferential strain (GCS) was decreased in 76% (-12.99 ± 2.89; normal ≤ -18%), and global radial strain (GRS) was reduced in 80% (20.52 ± 15.72; normal ≥ 40%). Hypokinesia and a significant reduction in regional myocardial strain (REGLSi) were also observed in the inferior and inferolateral segments of the LV. No significant correlation was found between MFM and ECHO variables.**

Conclusion: **Patients with DMD exhibit early compromise in STE parameters (GLS, GRS and GCS) and in REGLSi, particularly in the inferior and inferolateral LV regions, even with preserved LVEF (Central Figure). No significant correlation was observed between motor and cardiac function parameters.**

Keywords: **Duchenne Muscular Dystrophy; Cardiomyopathies; Electrocardiography.**

Introduction

Duchenne Muscular Dystrophy (DMD) is the most common and severe form of muscular dystrophy in children, with a global incidence ranging from 10.71 to 27.78 cases per 100,000 live births.[1-3] DMD is caused by mutations in the dystrophin gene, located on chromosome Xp21, resulting in progressive muscle degeneration, predominantly affecting boys, who typically become wheelchair-dependent between 10 and 12 years of age.[4-6]

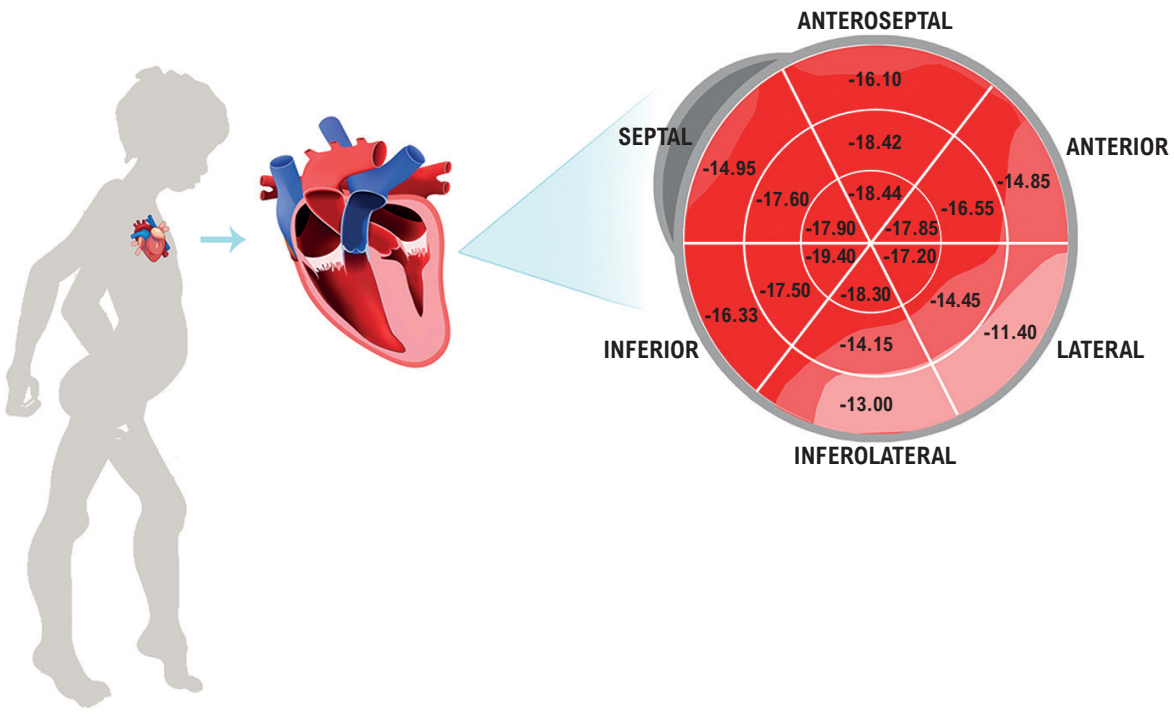
Previously, respiratory complications were the leading cause of death in this population. However, advances in ventilatory support have shifted cardiomyopathy to the primary cause of mortality, typically occurring between the ages of 20 and 30.[5,7] Early diagnosis of cardiac dysfunction is challenging, as clinical signs appear late in time, and classic symptoms of heart failure (HF) are often not observed due to the patients' limited physical activity.[8,9] Nonetheless, early detection is crucial for initiating cardioprotective pharmacological therapies, such as angiotensin-converting enzyme inhibitors (ACEIs), before cardiac dysfunction worsens, potentially delaying disease progression and improving prognosis.[10,11]

The progression of myocardial dysfunction can be monitored through cardiovascular imaging methods. Although electrocardiogram (ECG) abnormalities can be detected, they usually appear in later stages of cardiomyopathy and still lack well-demonstrated scientific correlations with other cardiovascular imaging techniques.[12] On the other hand, ECHO offers advantages over other methods, such as cardiac magnetic resonance imaging (CMR), for monitoring DMD patients due to its greater accessibility, lower cost, speed, safety, and ability to detect early cardiac function changes.[12,13] LV Regional function analysis is crucial in clinical scenarios, such as ischemic heart disease, and it is assessed using the LV myocardial segmentation and Wall Motion Score Index (WMSi),[12,14] which is more effective than only global left ventricular ejection fraction (LVEF) in predicting post-infarction

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Central Illustration: Regional Left Ventricular Myocardial Strain Alterations in Patients with Duchenne Muscular Dystrophy and Correlation with Electrocardiographic and Motor Function Alterations



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mortality. WMSi also identifies more extensive myocardial damage and is valuable in non-ischemic cardiomyopathies, such as Chagas´ disease.[15-17] However, image quality may be compromised by thoracic deformities, particularly in DMD patients.[17] Advanced ECHO techniques, such as myocardial deformation analysis using speckle-tracking, have been applied in this context and have the potential to provide early diagnosis of myocardial dysfunction, compared to monitoring solely by LVEF.

The progression of motor impairment can be monitored using the Motor Function Measure (MFM) scale, which has already been validated for this specific population.[18,19] Since the disease progressively affects both skeletal and myocardial muscles, it is plausible to assume a temporal correlation between both impairments. However, the relationship between cardiac and motor function in DMD patients is not yet fully understood, especially regarding the use of ECHO and ECG as complementary assessment methods. Understanding the temporal relationship between motor and myocardial impairments may help medical teams determine the optimal timing for cardiac function screening.

Thus, this study aimed to analyze cardiac abnormalities detected by ECG and ECHO using conventional and advanced techniques and correlate them with the MFM scale in DMD patients to enhance early diagnosis of myocardial dysfunction and ultimately provide a tool for monitoring cardiac impairment in this population.

Methods

This is an observational cross-sectional study with a convenience sample of patients diagnosed with DMD. The local Ethics Committee approved the study (protocol number HCRP 4.829.712), and the Informed Consent Forms (ICF) were signed by the guardians, as the patients were under 18 years old, who also signed the Assent Form (AF).

The inclusion criteria were having a prior clinical diagnosis of DMD confirmed through genetic testing and/or skeletal muscle biopsy and being older than seven years [18]. Patients with other muscular dystrophies, those with contraindications for ECHO examination, or those whose ECHO images were inadequate were excluded. Patients were invited to participate in the research, and the MFM was applied following the clinical indications already practiced in the outpatient setting. Those who agreed to participate in the study were voluntarily invited to undergo ECG and ECHO exams. Clinical information was collected from the institution's electronic medical records. One of the patients was not using glucocorticoids due to a family decision, as documented in the medical record, and

was therefore not included in the group receiving regular medication.

Motor function assessment

The MFM evaluates motor function according to prior validation.[20] in three dimensions: standing posture and transfers (13 items), proximal motor function (21 items), and distal motor function (7 items). Ambulatory patients performed all items, while wheelchair users received zero scores for standing-related items. The test was administered by a physiotherapist trained in working with this population. Up to two attempts were allowed per item, and the lowest score was recorded in case of doubt. Materials used in the MFM application included a mat, chair, CD, coins, tennis ball, pencil, A4 paper, stopwatch, and a six-meter measuring tape.

Electrocardiogram

A 12-lead surface ECG was performed using a Philips PageWriter TC10 device, and tracings were analyzed by an experienced cardiologist, focusing on the detection of electrically inactive zones, pathological Q waves, and R-wave amplitude in precordial leads such as V1.

Echocardiography

Transthoracic ECHO images were acquired using Vivid E9 or E95 echocardiography equipment (GE Healthcare, Horten, Norway) with an S5 MHz transducer. Image acquisition followed previously published guidelines[21] In summary, parasternal and apical images of the left ventricle (LV) were acquired at their longest possible axis to avoid LV foreshortening. Images were recorded with ECG tracings over at least three consecutive cardiac cycles at rest. All images were acquired at a rate of 55–90 frames per second and analyzed offline using EchoPac software (GE Vingmed Ultrasound AS), version 112. The following conventional ECHO parameters of LV dimensions and function were collected: left atrial (LA) dimension and volume, LV mass, LV end-diastolic and end-systolic linear dimensions—LV end-diastolic diameter (LVEDD) and LV end-systolic diameter (LVESD)—LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), and LV ejection fraction (LVEF) derived from the modified Simpson's method. Additionally, early (E) and late (A) mitral inflow velocities, deceleration time (DT), and septal and lateral mitral annular diastolic velocities via tissue Doppler imaging (TDI) (lateral e' and septal e') were measured.

Myocardial strain analysis (STE)

A single experienced physician performed two-dimensional strain analyses using three LV apical images. Whenever possible, the second of the three acquired cardiac cycles was selected for analysis. All strain measurements were collected as mid-myocardial values, and end-systolic volume values were measured while avoiding post-systolic strain measurements. The reference time was manually set at the onset of the QRS complex. End systole was defined as the moment of aortic valve closure, determined by Doppler signals in the LV outflow tract. The LV endocardial borders were manually traced at the end of systole, and the region of interest was adjusted to exclude the pericardium. Myocardial tracking throughout the cardiac cycle was visually supervised by the observer, who was always the same experienced echocardiographer. Segments with persistently inadequate tracings were excluded from the analysis. The LV was divided into 18 segments according to the latest standardization for regional LV strain measurement, allowing for the exclusion of up to two segments. Global longitudinal strain (GLS) measurements were obtained from apical longitudinal images using dedicated offline analysis software, as were global circumferential strain (GCS) and radial strain (GRS) measurements, the latter obtained from myocardial speckle tracking in parasternal short-axis views at the level of the papillary muscles.

Regional Myocardial Deformation Index

A regional myocardial deformation index (REGLSi) was created to quantify regional LV strain (REGLS) alterations proportionally among the 18 LV segments in the studied patients. Based on the initial GLS assessment in each LV segment generated by the software, LV segments with REGLS values lower than the mean of all other segments were identified. Segments 4, 5, 10, and 11 of the LV, corresponding to the inferior and inferolateral regions, showed values below the population mean. Based on this, an index of regional myocardial strain impairment (REGLSi) was developed as the mean REGLS values of the four identified segments [4, 5, 10, 11] for each patient divided by the mean of the remaining 14 LV segments (1, 2, 3, 6, 7, 8, 9, 12, 13, 14, 15, 16, 17, and 18), creating a continuous variable that expresses regional LV myocardial deformation alterations in this population.

Statistical analysis

Continuous variables were expressed as mean and standard deviation, or median and interquartile intervals according to the normality of the data, while categorical variables were presented as frequencies and percentages. The Shapiro–Wilk test was used to assess the normality of continuous variables. Comparisons between groups were performed using the Mann–Whitney test for continuous variables without normal distribution and with Students T test (non-paired). Correlation analysis between motor function, as measured by MFM, and myocardial function variables was performed using the Spearman correlation coefficient, as the data followed a normal distribution. A significance level set at $p < 0.05$ was adopted. Statistical analyses were performed using GraphPad Instat 8.0.2 software.

Results

Demographic characteristics

The study included 33 male patients with a mean age of 14 ± 4.10 years. Of these, 31 were assessed using the MFM, 32 underwent ECG evaluation, and 30 were evaluated by ECHO. The mean age at diagnosis was 6 ± 2.89 years. Among the patients, 32 (97%) were using glucocorticoids, predominantly prednisone (58%) and deflazacort (39%). Nine patients (27%) had received a clinical indication for cardioprotective therapy, mostly using ACE inhibitors, as presented in Table 1.

Motor function assessment

MFM was performed in 94% of the patients, with an average score of 52%, indicating a reduction in motor function. The greatest impairment was observed in dimension D1 (Table 2).

Electrocardiogram results

Thirty-two patients underwent ECG (97%); 24 (75%) presented a high-voltage R wave pattern in V1, and 11 (34%) had a pathological Q wave in V5-V6 (Figure 2). Notably, all patients with a pathological Q wave also exhibited a high-voltage R wave in V1 (Table 3).

Left ventricular systolic function assessment

Conventional ECHO parameters of cardiac geometry and LV function are presented in Table 4. Thirty patients underwent ECHO, and left ventricular systolic function, measured by LVEF, was preserved on average (57.80 ± 9.62%), with only 12% of patients presenting values below 50% (normality threshold) (Table 4).

Regional left ventricular systolic function

Among patients analyzed by WMSi, 15% exhibited hypokinesia in LV segments, particularly in the basal and mid-inferior segments. REGLS values were lower in the basal inferior (segment 4), mid-inferior (segment 10), basal inferolateral (segment 5), and mid-inferolateral (segment 11) segments compared to other LV segments, with a statistically significant difference ($p = 0.0013$) (Table 4).

Regional myocardial strain of the LV

Lower regional longitudinal strain (REGLS) values were observed in specific left ventricular segments compared to others, with an average of -12.90 ± 3.89% in affected segments, in contrast to -17.30 ± 3.38% in other segments ($p = 0.0013$). The created regional myocardial strain impairment index (REGLSi) (Figure 2) showed that groups with values above (G1, > 0.77) and below (G2, < 0.77) the median did not present significant differences in age, global myocardial function, or motor function (Table 5). G1 reflects less regional function impairment, while G2 is associated with greater regional LV function impairment.

Correlation between motor and cardiac function

No significant correlation was found between MFM and LVEF, GLS, GCS, GRS, or REGLSi. The correlation between MFM and cardiac function parameters was generally weak and not statistically significant.

Discussion

This study evaluated the motor functional capacity (MFM) and global and regional systolic myocardial function of the left ventricle (LV) in patients with DMD at a tertiary care center in the Brazilian public health system (SUS). Young patients with DMD already exhibit significant impairment of motor function. Most of these patients still presented preserved global LV systolic function when assessed by the left ventricular ejection fraction (LVEF) through ECHO. However, a significant percentage of them showed ECG changes that could suggest regional myocardial impairment in the dorsal regions. Indeed, when the myocardial function of the LV was studied by global and regional myocardial strain, it was observed that there is already incipient global systolic dysfunction and significant impairment of regional myocardial function in the inferior

Table 1 – Clinical characteristics of patients with duchenne muscular dystrophy

Variable	Mean ± SD or n (%)
n	33 (100%)
Age (years)	14.30 ± 4.09
Age at Diagnosis (years)	6.10 ± 2.86
Wheelchair Users (%)	90.90%
Systolic Blood Pressure (mmHg)	112.3 ± 17.35
Diastolic Blood Pressure (mmHg)	70.60 ± 11.65
Heart Rate (bpm)	88 ± 18
Medication Treatment	
n	32 (96,96%)
Prednisone (%)	19 (58%)
Deflazacort (%)	13 (39%)
Cardioprotective Therapy	
n	33
Age at BB or ACEI initiation (years)	12.00 ± 3.70
Beta-blocker (%)	5 (15%)
Angiotensin-Converting Enzyme Inhibitor (%)	9 (27%)
Digoxin (%)	1 (3%)

BB: beta-blocker; ACEI: angiotensin-converting enzyme inhibitor.

Table 2 – Motor function of patients with duchenne muscular dystrophye

Motor function measure scale	Mean ± SD or n (%)
n	31 (94%)
MFM T (%)	52.30 ± 16.32
D1 (%)	23.55 ± 25.65
D2 (%)	66.94 ± 21.02
D3 (%)	80.34 ± 18.91

MFM: Motor function measure score; D1: Dimension 1; D2: Dimension 2; D3: Dimension 3.

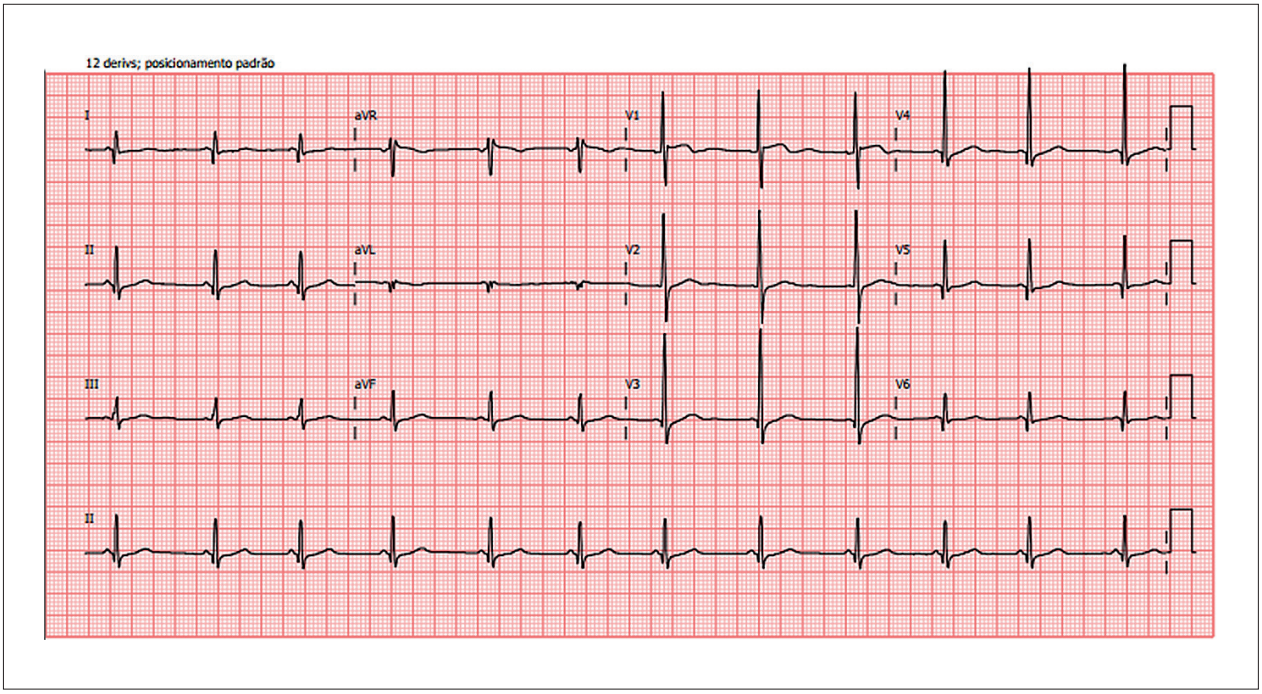


Figure 1 – *Example of an ECG from one of the patients. (ECG) Electrocardiogram; (R V1) Prominent R wave in lead V1; (Q V5–V6) Pathological Q wave in leads V5–V6. A total of 32 ECGs were obtained from the study population. Data are presented as absolute numbers and percentages.*

and inferolateral segments of the LV. However, regional abnormalities could only be demonstrated in 15% (n=4) of the patients when evaluated by WMSi (2D conventional 2D echocardiography), reinforcing the strength of RegLS to detect incipient regional myocardial damage.

Our work proposes, for the first time, the use of a regional myocardial strain score index (RegLSi) for the LV, comparing the most compromised segments with the average value of the other LV segments. The detection and quantification of regional myocardial deformation changes may represent and explain ECG alterations. The suggested proposal of REGLSi to patients with DMD needs external validation in other cohorts through future studies.

The MFM scale revealed a reduction in motor function in 52% of the patients studied and followed at our center, a result consistent with previous published data in the literature.[20,22] Dimension D1 (standing and transferring) was the most impaired (score of 24%), suggesting early functional impairment of the patients at the time analyzed, even in relatively young patients with an average age of 14 years.[19] Our data corroborate the knowledge that impairment in D1 below 40%, along with an MFM score of 70%, is typically associated with significant limitations in walking, which significantly impacts the functional capacity of the patients, even making it difficult to detect classic symptoms of heart failure, such as exertional dyspnea. On the other hand, fine motor functions (D2 and D3) remained preserved in this population of relatively young patients. This may be due to variability in disease progression among the patients or to the ability to compensate for the loss of function in D1 through other motor adaptations.[22]

Table 3 – Electrocardiogram findings of patients with Duchenne Muscular Dystrophy

Variable	N (%)
ECGs obtained	32 (97%)
R wave in V1	24 (75%)
Q wave in V5–V6	11 (34%)
R in V1 and Q in V5–V6	11 (34%)

Cardiomyopathy is a serious and common complication in DMD, usually emerging later, after the age of 18, predominantly as dilated cardiomyopathy, which shows signs of progressive fibrosis, starting from the lateral wall of the LV [25]. However, in the patients studied here, aged under 18 years, LVEF, assessed by conventional ECO, was preserved in most of the cases. When using the advanced technique of myocardial deformation analysis (myocardial strain-STE) in its various axes, myocardial deformation impairment was observed in the majority of patients evaluated with this technique. Myocardial deformation changes were seen in the longitudinal (GLS), circumferential (GCS), and radial (GRS) axes. Patients with DMD can pose a challenge for obtaining adequate ECHO images,[23] especially those obtained from apical windows, which are necessary for analyzing not only LVEF but also STE. Difficulties are related to muscle function loss associated with

thoracic deformities. These factors lead to the use of more expensive, less available, and often less tolerated methods, especially in pediatric populations that may require sedation, such as cardiac magnetic resonance (CMR) for evaluating myocardial function and fibrosis. Despite the relative difficulty of obtaining proper apical images in ECHO, it was still feasible to apply myocardial strain measurements in the majority of the patients studied by ECHO in this study (66%). Moreover, the feasibility of strain measurements was similar between axes, which are dependent on apical images (GLS) and those that can be obtained from parasternal short-axis images (GCS and GRS). The data presented here reinforce the knowledge that there is incipient global systolic LV dysfunction in this group of patients, even at early stages of the disease.[24-26]

Table 4 – Echocardiographic and myocardial strain variables in patients with Duchenne Muscular Dystrophy

Variable	Mean ± SD or n (%)
DAE (mm)	26.34 ± 5.25
VAEi (mL/m²)	20.68 ± 7.67
Mass VE (g)	57.95 ± 23.46
Mass VEi (g/m²)	0.33 ± 0.08
LVEF (%)	57.80 ± 9.62
DDVE (mm)	39.89 ± 6.17
PPVE (mm)	6.48 ± 1.43
SIV (mm)	6.86 ± 1.40
E (cm/s)	81.50 ± 17.62
A (cm/s)	47.30 ± 14.80
E/A	2.49 ± 3.62
e' lat (cm/s)	14.42 ± 3.64
e' sep (cm/s)	12.41 ± 2.22
E/e' (avg)	6.25 ± 1.81
TD (ms)	156.72 ± 37.22
GLS (%) (n = 20)	-16.36 ± 2.92
GCS (%) (n = 21)	-15.03 ± 4.67
GRS (%) (n = 20)	26.54 ± 18.95
LVEF ≥ 50% and GLS ≤ –18%	11 (55%)
LVEF ≤ 50% and GLS ≤ –18%	2 (10%)
Altered WMSi	4 (15%)

DAE: left atrial diameter; VAEi: indexed left atrial volume; Mass VE: left ventricular mass; Mass VEi: indexed LV mass; LVEF: left ventricular ejection fraction assessed by the Simpson biplane method; DDVE: LV end-diastolic diameter; PPVE: posterior wall thickness; SIV: interventricular septal thickness; E: early diastolic filling velocity; A: Late diastolic filling velocity; E/A: E to A ratio; e' lat: Lateral mitral annular velocity; e' sep: septal mitral annular velocity; E/e': E to e' ratio; TD: deceleration time of E wave; GLS: Global longitudinal strain; GCS: Global circumferential strain; GRS: Global radial strain; WMSi: Wall motion score index.

Although demonstrating that there are already signs of incipient systolic myocardial dysfunction in this population, we detected a subprescription of cardioprotective drugs such as ACE inhibitors (27%) and beta-blockers (15%) in this population, probably clinically guided by the still preserved LVEF. This application of cardioprotective medications only after the reduction in LVEF will not really protect myocardial function.

The results of this study allowed a detailed analysis of regional LV function through conventional ECHO methods, including segmental mobility and WMSi, as well as advanced REGLS techniques. WMSi analyses are robust not only for diagnosis, but also for prognostic definition in other diseases, such as ischemic myocardial disease, which present regionalized features.[14] A small proportion (15%) of the patients studied in our sample exhibited changes in the WMSi of the LV when evaluated qualitatively by conventional ECO, despite already showing evident signs of cardiomyopathy, such as ECG changes (75%). The role of REGLS analysis in other clinical situations of ischemic and non-ischemic cardiomyopathies of the LV has been demonstrated.[16,26,27] However, REGLS indices are highly dependent on analysis software[13,28] and exhibit high variability and dispersion, which still complicates the definition of normal values and the immediate clinical applicability of this tool.[29] Although there is still a lack of evidence of normal values of REGLS, our study identified lower REGLS values in the inferior (segment 4) basal and mid (segment 10), and inferolateral (segment 5) basal and mid (segment 11) segments in patients with DMD, compared to the other fourteen LV segments, with statistical significance. Thus, the regional myocardial deformation index (REGLSi) was proposed in this work for a more accurate assessment of regional changes. Similar initiatives have been applied in other cardiomyopathies with segmental LV alterations, such as amyloidosis, where regional impairment spares the apical segments.[30] There are few previously published studies on the regional function of DMD patients using REGLS; one study showed alterations in the inferior septal and inferior LV segments,[31] but without comparisons to other LV segments. In this study, patients had a low percentage of cases that met the criteria for the categorical diagnosis of diastolic dysfunction, based on variables such as increased left atrial (LA) size, E/e' ratio, and elevated pulmonary systolic pressure. Moreover, unlike previous studies that suggested early diastolic dysfunction,[32] our research did not identify alterations in diastolic function among the patients.

DMD patients may exhibit various ECG changes, such as broad R waves in V1, pathological Q waves in V5-V6, left bundle branch block (LBBB), and autonomic dysfunctions. Correlations between these changes and replacement by fibrotic tissue in the LV, particularly in the posterobasal regions, have been identified in early phases of the disease, even through anatomical and pathological studies.[33]

Most of the patients studied in our sample, while maintaining preserved global systolic function, presented ECG changes, such as broad R waves in V1 (75%) and

pathological Q waves in V5-V6 (34%), in agreement with previous studies.[12,24] Although this study was not designed as a prospective one, it seems that ECG changes can occur early when compared to ventricular dilation and systolic dysfunction. Other studies suggested that the presence of dystrophins in Purkinje fibers may be an explanation for the early electrical changes in this population, even when compared to other causes of cardiomyopathies in children[12], and this may occur before significant myocardial fibrosis appears[34,35] The presence of high R waves in V1 may also be misinterpreted by cardiologists as a sign of right ventricular (RV) overload, as seen in other clinical situations. However, previous studies did not find correlations between these changes and the RV.[36] All of our patients studied presented

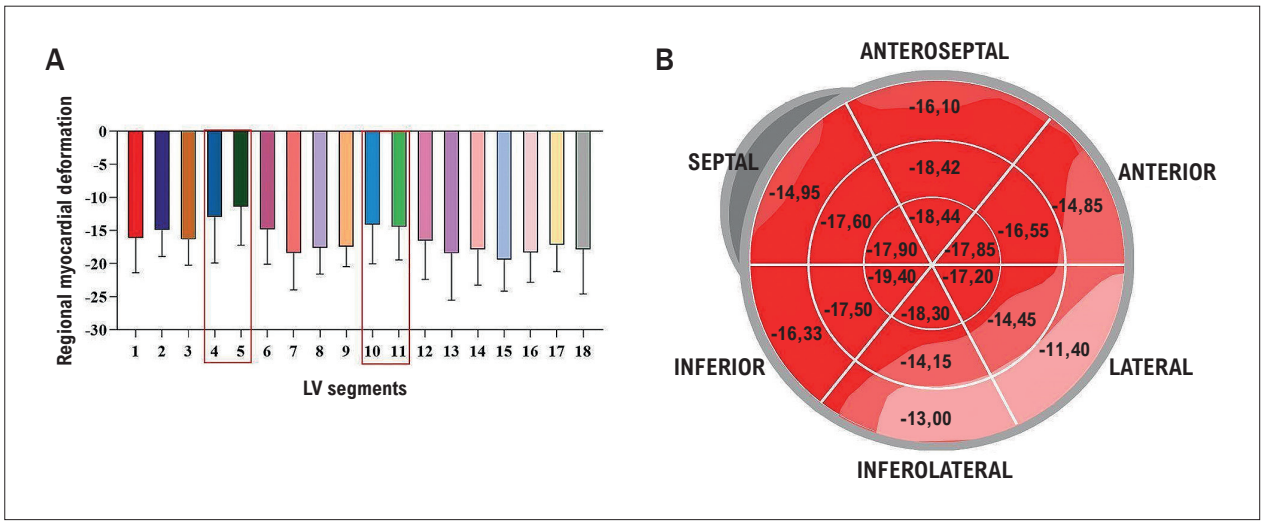


Figure 2 – *Evaluation of the mean values of regional myocardial strain of the represented patients. (A) The 18 segments are represented by numbers: The segments are: (1) Basal anterior; (2) Basal anteroseptal; (3) Basal inferoseptal; (4) Basal inferior; (5) Basal inferolateral; (6) Basal anterolateral; (7) Mid anterior; (8) Mid anteroseptal; (9) Mid inferior septal; (10) Mid inferior; (11) Mid inferolateral; (12) Mid anterolateral; (13) Apical anterior; (14) Apical anteroseptal; (15) Apical inferoseptal; (16) Apical inferior; (17) Apical inferolateral; (18) Apical anterolateral (4, 5, 10, and 11). (B) "Bull's eye" plot with average values of regional longitudinal myocardial strain (REGLS) of the left ventricle (18-segment model).*

Table 5 – Comparison of the variables of motor and cardiac function between groups: G1 (patients with REGLSi values above the population median) and G2 (REGLSi values below the median)

Variable	G1	IQR G1	G2	IQR G2	p
n	10		10		
Age (years)	14.00		11.50	[11.00 – 15.00]	0.3998
MFM (%)	40.60	[32.30 – 58.90]	60.45	[50.03 – 62.50]	0.0987
LEVF (%)	57.50	[51.75 – 62.00]	56.00	[54.00 – 62.00]	> 0.9999
GLS (%)	-16.85	[-18.53 – -15.80]	-16.20	[-18.20 – -13.60]	0.4690
GCS (%)	-15.63	[-17.45 – -13.49]	-14.17	[-22.56 – -10.94]	0.9591
GRS %)	19.68	[2.77 – 37.80]	33.83	[-22.36 – -36.08]	0.3282

(G1) Group with regional myocardial strain index (REGLSi) greater than or equal to the median (0.77); (G2) Group with regional myocardial strain index (REGLSi) below the median (0.77). (MFM) Motor Function Measure; (LVEF) Left ventricular ejection fraction assessed by the Simpson biplane method; (GLS) Global longitudinal strain; (GCS) Circumferential myocardial strain; (GRS) Radial myocardial strain. All parameters are expressed as percentages, except for age (years). Values are presented as median and IQR [interquartile range]. Comparisons between groups were performed using the Mann–Whitney U test.

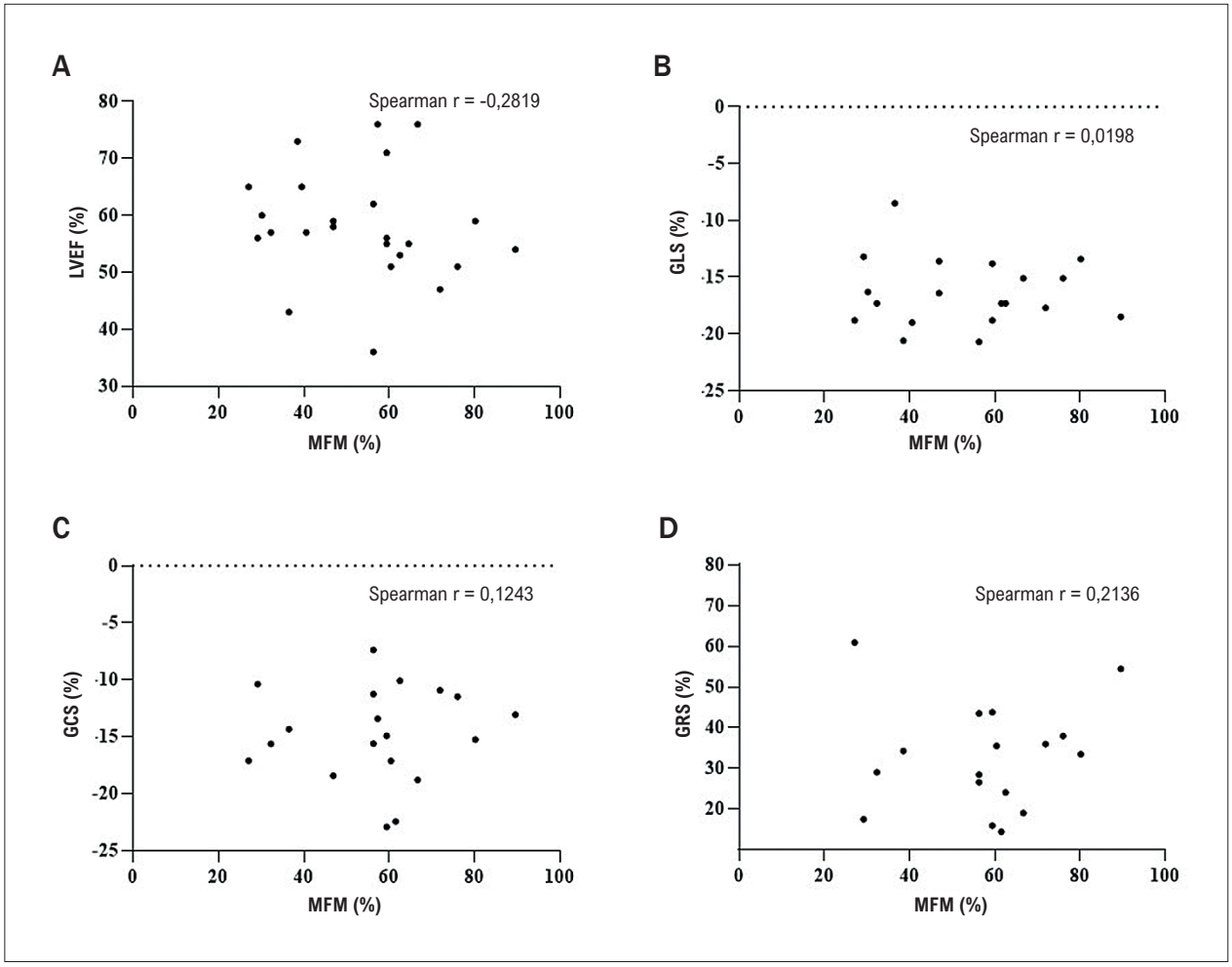


Figure 3 – *Correlation between the score of the Motor Function Measure (MFM) scale and longitudinal myocardial strain. Correlation between the Motor Function Measure (MFM) score and echocardiographic parameters of left ventricular systolic function. (A) Correlation between Left ventricular ejection fraction assessed by the Simpson biplane method (LVEF) and MFM score. (B) Correlation between global longitudinal strain (GLS) and MFM score. (C) Correlation between global circumferential strain (GCS) and MFM score. (D) Correlation between global radial strain (GRS) and MFM score. MFM, GLS, GCS, GRS, and LVEF are expressed as percentages. Pearson's correlation coefficients (r) are shown in each panel.*

normal RV dimensions by conventional echocardiography. It should be considered that RV assessment by imaging methods is often challenging in cardiology. High R waves in V1 can also be interpreted as evidence of septal hypertrophy, but, in our study, none of the patients showed increased interventricular septal thickness as assessed by ECHO. Thus, the findings of this study raise the hypothesis that broad R waves in V1 may be an electrocardiographic sign secondary to probable vector truncation in dorsal LV regions, as suggested by the regional myocardial function changes discussed above and measured by REGLSi.

Given the progression of motor and cardiac dysfunctions in DMD patients and the need for cardiac function assessment by complex imaging methods (ECHO and CMR), we postulate that identifying a correlation between these two dysfunctions, cardiac and skeletal, would be of clinical interest. To date, no other study has evaluated the correlation between these functional measurement variables. However, no significant linear correlation was observed between the motor function variables studied here, such as MFM or its dimensions D1, D2, and D3, and the LV ventricular function variables assessed by ECHO, whether conventional, such as LVEF, or advanced myocardial deformation variables, such as GLS, GCS, GRS, or REGLSi. The lack of correlation between motor and cardiac function variables may be due to the limited sample size of the sample and so may be cautiously interpreted. It could represent independent disease progression trajectories in terms of the loss of function in skeletal muscle and myocardium in this disease.

Study limitations

One limitation of this study is the limited number of patients, which may hinder the analysis of indices

with greater statistical variability. However, the sample, constructed by convenience, is similar to that of other single-center studies. Additionally, the research was conducted at a tertiary center, with many patients coming from other cities, which made access to the hospital difficult. Multicenter studies on strain by ECHO in this population should ensure similarity in image acquisition and analysis software. The limitation in image acquisition in some patients, though consistent with literature, should also be considered. A good exposition of the left atrium in images was sometimes limited, probably by the thoracic deformities, as also was the acquisition of right ventricle-focused images to better quantify RV function by conventional ECHO using TAPSE, S'or area fractional change. Finally, patients were not systematically and scientifically evaluated with CMR, although some may have undergone the examination by clinical indication. The use of CMR, once it is a well-established gold-standard method to identify myocardial fibrosis in DMD cardiomyopathy, could be tested in this study as a reference for REGLS, and this should be explored in future studies.

Clinical applications

Since current guidelines initiate cardioprotective drug therapy only after the left ventricular ejection fraction (LVEF) decreases, through ECHO or other methods, and considering the high cardiovascular mortality, this study reinforces the need for early detection of myocardial dysfunction using advanced ECHO techniques. Additionally, it highlights the importance of ECG findings in this population. Although this study did not have a prospective design, it opens the idea to explore the Echo parameters of global and regional myocardial deformation in future studies to test the power of cardioprotective drug use before the compromise of LVEF.

Conclusions

Patients with DMD studied here already present significant impairment of motor function and preserved global LV systolic function when assessed by LVEF via ECHO. However, a significant percentage of them already show ECG alterations that could suggest regional myocardial impairment in dorsal regions. These patients also exhibit incipient global systolic dysfunction with GLS, GCS, and GRS impairment and significant regional myocardial function compromise (REGLSi). The study could not demonstrate a correlation between motor and myocardial function in DMD patients.

Author Contributions

Conception and design of the research: Mattielo-Sverzut AC, Sobreira CFR, Schmidt A, Romano MMD; Acquisition of data: Costa FA, Romano MMD; Analysis and interpretation of the data: Costa FA, Sapalo AT, Romano MMD; Statistical analysis and Writing of the manuscript: Costa FA; Funding acquisition: Romano MMD; Critical revision of the manuscript for intellectual content: Schmidt A, Romano MMD.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto under the protocol number HCRP4.829.712. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

Use of Artificial Intelligence

During the preparation of this work, the author(s) used Chat GPT e Grammarly for spelling and grammar editing and for the creation of the central illustration. After using this tool/service, the author(s) reviewed and edited the content as needed and take full responsibility for the content of the published article.

Availability of Research Data

The underlying content of the research text is contained within the manuscript.

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