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Leveraging Cardiac Magnetic Resonance Imaging to Assess Skeletal Muscle Progression in Duchenne Muscular Dystrophy

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Abstract

Duchenne Muscular Dystrophy (DMD) is characterized by muscle deterioration and progressive weakness. As a result, patients with DMD have significant cardiopulmonary morbidity and mortality that worsens with age and loss of ambulation. Since most validated muscle assessments require ambulation, new functional measures of DMD progression are needed. Despite several evaluation methods available for monitoring disease progression, the relationship between these measures is unknown. We sought to assess the correlation between imaging metrics obtained from cardiac magnetic resonance imaging (CMR) and functional assessments including quantitative muscle testing (QMT), spirometry, and accelerometry. Forty-nine patients with DMD were enrolled and underwent CMR, accelerometry and QMT at baseline, 1-year and 2-year clinic visits with temporally associated pulmonary function testing obtained from the medical record.

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Declaration of Competing Interest

None

Imaging of the upper extremity musculature (triceps and biceps) demonstrated the most robust correlations with accelerometry ($p<0.03$), QMT ($p<0.02$) and spirometry ($p<0.01$). T_1-mapping of serratus anterior muscle showed a similar, but slightly weaker relationship with accelerometry and QMT. T_2-mapping of serratus anterior demonstrated weak indirect correlation with aspects of accelerometry. These images are either routinely obtained in standard CMR or can be added to a protocol and may allow for a more comprehensive assessment of a patient's disease progression.

Keywords

Duchenne Muscular Dystrophy; MRI; spirometry; accelerometry; quantitative muscle testing

1. Introduction

Duchenne Muscular Dystrophy (DMD) is the most common neuromuscular disorder in childhood, affecting approximately one in every 4,000 male births.[1] Affected individuals have reduced or absent dystrophin protein, leading to muscle breakdown and progressive weakness. This leads to loss of ambulation in early teenage years followed by significant cardiopulmonary morbidity and mortality.[2]

Current guidelines for motor function assessment include the North Star Ambulatory Assessment, timed functional tests (10-meter walk/run, supine/sit to stand, 4-stair climb) and 6-minute walk test (6MWT).[3] While these evaluations are often used as primary endpoints in clinical trials,[4] they require that patients are ambulatory. Most DMD cardiomyopathy studies selectively enroll older patients who are more likely to benefit from cardiovascular therapies, however, the majority of these patients are non-ambulatory, making these established endpoints impractical. Alternative skeletal muscle outcome measures in non-ambulatory patients with DMD are not well established.

Quantitative muscle testing (QMT) is a reliable method to determine strength in ambulatory and non-ambulatory patients with DMD.[5] QMT correlates with 6MWT in ambulatory patients.[6] Still, it requires maximal effort and only measures this effort at one moment in time. Accelerometry has been proposed as a reliable method to measure total physical activity in clinical trials.[7] Studies in DMD have shown a strong correlation with 6MWT and QMT and have demonstrated the utility of longitudinal assessment.[5, 8–10]

Pulmonary function testing, specifically forced vital capacity (FVC), has been historically used to monitor disease progression.[11] However, patients with DMD may not exhibit overt signs and symptoms of respiratory decline on standard clinical assessments, including pulmonary function testing.[12] A significant drawback of using spirometry as a measure for pulmonary status in DMD is that the maneuvers are effort-dependent and subject to variability with common DMD co-morbidities such as scoliosis.[13] As a result, newer non-invasive modalities, such as ultrasound or magnetic resonance imaging (MRI), are being explored as viable non-volitional adjuncts to standard spirometry for early detection of pulmonary disease.[14]

Use of MRI has increased in recent years as a non-invasive assessment of muscle and tissue composition. Recently, Barnard and colleagues showed a strong relationship between clinical function and MR biomarkers, including both upper and lower extremities.[15] This suggests that MR biomarkers may be helpful to predict ambulation and muscle function and as clinical trial endpoints. Similarly, MRI of rib cage musculature in DMD has showed progressive replacement of muscle with fibro-fatty tissue compared to healthy controls, although how this affects overall respiratory control is unknown.[16] While skeletal MRI imaging is not a common tool used in clinical practice, cardiac MRI (CMR) has become the non-invasive imaging modality of choice for clinical care and research.[17] MRI of the upper arm has been described as a quick and easy addition to a clinical or research CMR.[18] The objective of this study was to examine whether clinical CMR could be used to evaluate skeletal muscle progression as assessed by muscle strength (QMT), lung function (spirometry) and physical activity (accelerometry). The use of CMR could improve clinical assessment of skeletal muscle progression and allow for more comprehensive assessment in clinical trials at a fraction of the cost and time of dedicated imaging. We hypothesized that, in patients with DMD, there would be a correlation between CMR imaging of skeletal musculature and QMT, accelerometry and spirometry.

2. Methods

2.1 Participants

This single-center, prospective study included 49 patients with DMD recruited from the multidisciplinary Neuromuscular Cardiology Clinic and the Muscular Dystrophy Association Clinic at Vanderbilt Children's Hospital. Inclusion criteria consisted of clinical phenotype of DMD and diagnostic confirmation via muscle biopsy or genetic testing of the dystrophin gene. The study, consent forms and protocol were approved by The Vanderbilt Institutional Review Board. Written informed consent was obtained from participants over 18 years of age. For participants under 18 years of age, written consent was obtained from parents and written assent from participants.

Participants were scheduled for baseline visit, 1-year follow up visit, and 2-year follow up visit. Visits included full medical history, including past medical history, current and previous medications, and ambulatory status, all obtained either from the electronic medical record or directly from patients. Study visits also included CMR, QMT, and accelerometry.

2.2 Cardiovascular magnetic resonance

Cardiac MRI was performed for DMD subjects using a 1.5 Tesla Siemens Avanto or Avanto FIT (Siemens Healthcare Sector, Erlangen, Germany). Breath-held modified Look-Locker inversion recovery (MOLLI) sequences were performed before contrast administration at the base, mid-left ventricle (LV), and apex in the short axis plane.[19, 20] An additional MOLLI was performed through the dominant arm before contrast administration (if right-handed, through right arm). MOLLI sequences were motioncorrected, ECG-triggered images obtained in diastole with typical imaging parameters: non-selective inversion with a 35-degree flip angle, single shot SSFP imaging, initial inversion time of 120ms with 80ms increments, field of view 340 × 272 mm^2, matrix size 256 × 144, slice thickness 8mm, voxel

size 1.3 × 1.9 × 8.0 mm^3, TR/TE 2.6ms/1.1ms, parallel imaging factor of 2. The matrix size was decreased to 192 × 128 for heart rates >90 (approximate voxel size 1.8 × 2.1 × 8 mm^3). The MOLLI was acquired as a 5(3s)3, to reduce bias from higher heart rates.[21] Motion correction as described by Xue and colleagues was performed and a T_1 map was generated on the scanner.[22] Any image felt to be inadequate due to poor breath holds or poor motion correction was repeated at the time of the scan. T_2 mapping was performed using a breath-held, electrocardiogram (ECG)-triggered, bSSFP sequence with motion correction at the base, mid-LV, and apex in the short axis plane. T_2 mapping was not performed through the arm. Typical imaging parameters were as follows: Adiabatic T_2 preparation with 35 degree flip angle, field of view 340 × 272 mm^2, matrix size 192 × 144, slice thickness 8mm, voxel size 1.8 × 1.9 × 8.0 mm^3, TR/TE 2.5ms/1.1ms, parallel imaging factor of 2.

2.3 Image processing

Images were processed and reviewed using Medis® Suite MR software (Medis Medical Imaging Systems Inc., Raleigh, North Carolina, USA). One reader (JK) manually outlined regions of interest (ROIs) in the anterior compartment (biceps brachii, brachialis, coracobrachialis) and posterior compartment (triceps brachii) within T_1 maps of the arm in available CMRs (Figure 1A). For T_1 and T_2 maps obtained in the short axis stack, three ROIs within the serratus anterior were outlined and measured (Figure 1B–C) with the average used for analysis. Position was determined via direct visualization and assistance using localization from coronal and axial static balanced steady-state free precession images and single-shot fast spin echo images. Review of both questionable imaging as well as randomly selected representative images from the cohort were reviewed and confirmed by a second reviewer (JS).

2.4 Accelerometry

DMD patients wore an Actigraph GT3X accelerometer (Actigraph, Pensacola FL, USA) on their dominant wrist and ankle for 7 days and 24 hours per day. Actigraph GT3X accelerometers recorded acceleration in three orthogonal axes (x, y, z) at 30 Hz (i.e., 30 recordings per second per axis). Accelerometer recordings were uploaded to ActiLife software (Actigraph, Pensacola FL, USA, version 6.13.3), integrated into 15-second epochs, and converted into an omnidirectional acceleration estimate, or vector magnitude (VM), calculated as the square root of the sum of the triaxial signals squared, or √(x2 + y2 +z2). Accelerometer wear and non-wear periods were identified with Choi's algorithm.[23] A participant's accelerometer recordings were considered valid if they included ≥3 days with ≥2 weekdays and ≥1 weekend day, each with ≥10 hours of wear from 6:00 am to 9:00 pm. Participants were classified as awake for their accelerometer recordings between 6:00 am and 9:00 pm.

The adherence and physical activity measures calculated for the wrist and ankle accelerometers of patients with DMD included minutes per day of wearing an accelerometer (min/day wear), minutes per day of wearing and awake (min/day awake), VM's generated while wearing (VM total), VM's generated per minute while wearing (VM/min wear), and VM's generated per minute while wearing and awake (VM/min awake).

2.5 Quantitative Muscle Testing

The QMT assessment was performed at each visit using a handheld myometer as previously described.[24] Arm QMT score (pounds) was the sum of flexion and extension values for both elbows. Leg QMT was the sum of flexion and extension values for both knees. Total QMT score was the sum of values for elbows and knees. QMT scores were indexed to age up to age 20 as previously described.[5]

2.6 Pulmonary Function Testing (PFTs)

A review of the EMR was performed retrospectively and any PFTs obtained clinically within 6 months of the visit were added to the database. Routine spirometry for DMD measures, such as forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), and maximum inspiratory/expiratory pressures (MIP, MEP), were recorded for the corresponding study visit.

2.7 Statistical analysis

Study data were stored and managed in REDCap (Research Electronic Data Capture, Vanderbilt University). Accelerometry and QMT measurements were paired with the CMR from each clinic visit. The first pairing of PFTs and CMR imaging was used for analysis. Spearman rank correlation tests were used to assess relationship between continuous variables. Wilcoxon signed-rank was used to detect the progression of CMR relaxation time across all 3 study visits. Subset analysis was performed to assess the effect of ambulatory status, current steroid use, and steroid ever-use on correlations. Statistical analysis was performed using STATA, version 16 (StatCorp LLC, College Station, TX, USA) software. All tests were 2-sided and a p-value <0.05 was considered significant. For Spearman rank coefficient correlations, the following cut-offs were used: $r \leq 0.35$, weak, $r = 0.36$ to 0.69, moderate; $r = 0.7$ to 1.0, strong. Intraclass correlation coefficients (ICC) were calculated to assess inter-observer variability.

3. Results

Forty-nine patents with DMD were enrolled. All participants were male. Demographic information is shown in Table 1. Forty-eight (98.0%) patients completed the first CMR, 47 (95.9%) completed the second CMR and 37 (75.5%) completed the third CMR. The upper arm and serratus anterior muscles were visualized and measured in 95/132 (72%) and 123/132 (93%) of CMRs. Imaging from fourteen control subjects without DMD were compared with the first CMR imaging of the DMD subjects (Table 2). Longitudinal progression across the three clinic visits was also monitored (Table 3). The average T_1 relaxation time for upper arm compartments decreased over the three years with a drop from 697.7ms ± 309.7 to 582.2ms ± 302.3 ($p = 0.007$) for the triceps muscle and 695.4ms ± 351.4 to 564.8ms ± 309.4 for the biceps muscles ($p = 0.03$). The average T_1 for serratus anterior also decreased from 508.4ms ± 398.2 to 376.8ms ± 237.6, but this did not reach statistical significance ($p = 0.41$). The T_2 for serratus anterior did not change (115.9ms ± 81.9 to 116.3ms ± 79.5). Inter-observer variability showed moderate to good reliability with consistent intra-class correlation coefficients (ICC) across all four measurements

(triceps ICC=0.79, p<0.001, biceps ICC=0.72, p=0.003, SA T_1 ICC =0.64, p=0.003, SA T_2 ICC=0.82, p<0.001).

The correlation of accelerometry VMs and CMR imaging is outlined in Table 4. All accelerometry measures were moderately correlated with upper arm imaging. Triceps muscle groups showed strongest correlation with the ankle VM/min (rho=0.55, p=0.003) and wrist VM/min (rho=0.52, p=0.002). A similar correlation trend was seen with biceps measurements and ankle VM/min (rho=0.54, p=0.003) and wrist VM/min (rho=0.52, p=0.002) (Figure 2.A–B). Correlations of muscle activity with serratus anterior mapping were not as strong as compared to upper arm musculature. Only wrist VM/min showed a moderate correlation with serratus anterior T_1 relaxation times (rho=0.43, p=0.005); all other measurements only exhibited a weak association. T_2 mapping showed slightly stronger correlations with accelerometry than T_1 mapping, although these showed inverse relationships. Ankle VM/min had the strongest correlation with T_2 relaxation times (rho=−0.49, p=0.003).

While triceps imaging showed a more robust correlation with QMT indexed to age, biceps and T_1 serratus anterior imaging demonstrated a similar, albeit less strong, relationship (Table 5). Total arm QMT showed the strongest correlation with triceps imaging (rho=0.51, p=0.002). Overall, total QMT showed a moderate correlation with triceps, biceps and T_1 serratus anterior (Figure 2E). T_2-mapping failed to demonstrate a statistically significant correlation with any QMT measurements.

Pulmonary function testing was available in approximately two-thirds of the enrolled patients. FVC and FEV_1 were obtained more than twice as often as ancillary measurements such as MIP and MEP. FVC%p and FEV_1%p both demonstrated moderate correlation with triceps and biceps (Table 6) (Figure 2C–D). There was no relationship between serratus anterior maps (T_1 or T_2) and lung function testing. No consistent relationship was noted between maximal pressures and any CMR imaging.

An overall decrease in accelerometry VM counts were recorded in both wrist and ankle measurements throughout of the study. Similarly, QMT showed a steady decline over three years. No consistent trend was noted in lung function testing over the same time period.

Subset analysis of previous or current steroid use suggest little difference in correlation of imaging and any of the muscle assessments (supplemental table A1–3). While triceps imaging exhibited the most robust correlations with accelerometry, QMT and spirometry, there was little disparity between the previous and current use cohorts. Additional subset analysis demonstrated notable differences in respect to ambulatory status (supplemental B1–3). Overall, imaging in ambulatory patients showed an indirect correlation (as demonstrated by negative rho values) with muscle assessments, while imaging in non-ambulatory patients had consistent direct correlations. This relationship was most persistent with imaging of both triceps and biceps and observed across accelerometry, QMT and spirometry. However, these correlations were not statistically significant.

4. Discussion

The major finding of this study is the correlation of the CMR characterization of skeletal muscles with muscle strength and physical activity in patients with DMD. These finding are important because skeletal muscle outcome measures are limited in non-ambulatory patients with DMD. A combined assessment of skeletal muscles in the chest wall from the standard parametric mapping and a rapid additional assessment of the arm during CMR may provide an adequate prospective assessment of DMD progression and lung function decline in cardiac studies. These images can also be assessed retrospectively from existing clinical or research CMRs. While previous studies, such as Kimura et al. (2014), have shown correlation between accelerometry and skeletal muscle strength,[25] to our knowledge, this study is the first to assess accelerometry and strength testing with correlation to imaging of the upper arm and respiratory musculature.

The correlation between biceps and triceps CMR and accelerometry was similar for wrist and ankle accelerometry. Similarly, while not as robust as with the upper extremity, there was persistent correlation between wrist and ankle VM counts for both T_1 and T_2 serratus anterior muscle imaging. This suggests that changes in physical activity are correlated with skeletal muscle imaging of seemingly unrelated muscle groups and highlights the systemic nature of DMD and the parallel progression of skeletal muscle disease.

Over the course of the study, all VM counts decreased, suggesting a decrease in total movement of upper and lower extremities. Ankle VM counts were also lower than wrist VM counts, which is consistent with the natural course of DMD affecting leg musculature before the arm. Since accelerometry is a recording of physical activity over time, it is able to provide an effort-independent measure of total movement. The strongest correlation exists between upper extremity musculature imaging and VM counts/minute wear of the ankle and wrist accelerometers. While the muscles of the biceps and triceps are not directly involved in movement of the ankle or wrist, there remains a moderate relationship.

Quantitative muscle testing is a reliable measure of isometric strength of selected muscles in patients with DMD.[26] The consistently stronger correlation of indexed arm QMT to upper extremity imaging suggests that muscle function may be directly related to skeletal muscle composition changes. This finding agrees with previous studies showing that functional measurements correlate with muscle MRI values quantifying fatty muscle degeneration,[27] however, there are no studies of which we are aware that utilize CMR for either upper arm or chest wall musculature.

T_2 serratus anterior muscle imaging showed a consistent negative correlation with accelerometry and QMT measurements except for QMT indexed to age. This finding is congruent with the expected natural history of DMD as the muscle is progressively replaced by fibro-fatty tissue.[28] The increased muscle damage results in an expected prolongation of the T_2 relaxation time,[29] while the strength and motion of the extremities gradually decline.[30]

Another major finding of this study is the correlation between upper extremity imaging and measurements of spirometry, specifically FVC percent predicted and FEV_1 percent

predicted. We hypothesize that the lack of correlation of spirometry with serratus anterior imaging is due to the muscle group's lack of involvement with normal respiration. The serratus anterior is considered an "accessory muscle" which is recruited during times of increased respiratory need respiratory dysfunction. Since lung function testing is effort-dependent and often complicated by various factors in patients with neuromuscular disease, including fatigue or poor technique, the ability to monitor or predict lung function decline with effort-independent modalities would be invaluable. Our study failed to show an expected decline in spirometry measures over the three years. A plausible explanation could be that our cohort included ambulatory and non-ambulatory patients, who would be expected to have different decline rates of pulmonary function.[31]

While the serratus anterior muscle is not directly involved in respiration, it can become involved in respiration when the primary musculature (diaphragm, intercostals) cannot provide adequate strength. The serratus anterior T_1 showed a persistent decreasing trend with an approach towards the T_1 relaxation time of adipose tissue, which is ~250ms. This is consistent with findings by Barnard and colleagues, who used chemical shift-encoded MRI to create fat-water fusion images and found extensive fatty-infiltration of the serratus anterior muscle.[16] While a similar trend was not found in the T_2 measurements, this may be secondary to image quality, with the intersection of edema, bone, and muscle interfaces making detection of the serratus anterior on T_2 maps difficult.

Our subset analysis found that ambulation modifies the correlation between imaging and muscle assessments as seen by the dual directionality of correlation coefficients. Early disease progression in DMD is characterized by degenerating and regenerating myoblasts. The resulting muscle inflammation and edema may cause an increase in the T_1 relaxation seen in the early stages of disease.[32] This rise in T_1 relaxation time, in conjunction with decreasing activity level, may account for the indirect correlations observed in ambulatory patients. Similarly, in later stages of DMD that follow the loss of ambulation, rapid declines in T_1 are observed as muscle is replaced with adipose tissue.[33] The declining T_1 time may parallel loss of muscle function in the non-ambulatory cohort. However, given the relatively small number of patients in each subset, these correlations were not statistically significant and these findings must be validated in a larger cohort.

Additionally, while subset analysis of steroid use demonstrated statistically significant differences in correlation coefficients, there was slight disparity between the groups suggesting that steroid use (or lack thereof) had little meaningful effect on the relationship between imaging and muscle strength assessments. Since previous studies have shown that steroid treatment in DMD can affect MR imaging[34], strength[35], and spirometry[36], we suspect that similar effects within all assessments may account for the consistent correlations regardless of steroid use.

4.1 Limitations

There were several important limitations to this study. First, the study was performed at a single center. However, the Vanderbilt Neuromuscular Cardiology Clinic and the Muscular Dystrophy Association Clinic at Vanderbilt Children's Hospital have a wide catchment area that extends into three states. The study had a relatively small sample size

with of 49 enrolled patients. However, this is the largest study of which we are aware evaluating correlations of CMR of skeletal muscles with muscle strength, spirometry, and accelerometry testing.

Second, our CMR protocol was not specifically designed to capture upper extremity or chest wall musculature. While the inclusion of upper extremity imaging required approximately 1 minute of additional imaging time, all serratus anterior measurements were obtained from images acquired as part of the CMR protocol, so no additional imaging time was required. Additionally, upper extremity and chest wall muscular imaging can be affected by the longer distance from iso-center, since images and patient position were not optimized for these image locations. This may have skewed final images and altered the measured T_1 and T_2 relaxation time, however, we were able to demonstrate moderate to good reliability inter-observer variability with all measurements. For studies where skeletal muscle changes are the primary outcome, dedicated skeletal muscle imaging would be strongly recommended. Third, we did not assess skeletal musculature directly related to respiration, such as the diaphragm or intercostal muscles. The CMR protocol did not include visualization of the diaphragm and the variation and inconsistency in measurement of intercostal muscles precluded us from including the data in this study.

Fourth, lung function testing was not performed at a standard time interval from the clinic visits but rather was collected retrospectively and some data were obtained at partner institution clinics. Given that spirometry is effort-dependent, there is risk in performing lung function testing in conjunction with several other diagnostics such as MRIs or strength testing. Additionally, including both ambulatory and non-ambulatory patients could significantly alter the trajectory of lung function decline as ambulatory status directly affects pulmonary function testing endpoints.[11] Finally, the failure of our study to find a correlation with maximal inspiratory/expiratory pressures is likely secondary to the low number of patients in whom this was measured, which is partially because the guidelines for routine monitoring of this modality were not published until after conclusion of enrollment for this study.

5. Conclusions

In patients with DMD, CMR of upper extremity muscle groups and serratus anterior muscle have a good correlation with physical activity as measured with accelerometry, strength as measured by QMT, and lung function as measured by spirometry. These measures do not require ambulation and can be easily integrated into a standard CMR examination. The combination of these tools may create a more comprehensive assessment of a patient's disease progression.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

CMR	Cardiac Magnetic Resonance
DMD	Duchenne Muscular Dystrophy
FEV_1	forced expiratory volume in 1 second
FEV_1%p	forced expiratory volume in 1 second percent predicted
FVC	forced vital capacity
FVC%p	forced vital capacity percent predicted
LV	left ventricle
MIP	maximal inspiratory pressure
MEP	maximal expiratory pressure
MOLLI	modified Look-Locker inversion recovery
MRI	magnetic resonance imaging
PFT	pulmonary function test
QMT	quantitative muscle testing
ROI	region of interest
SA	serratus anterior
SSFP	steady-state free precession
VM	vector magnitude

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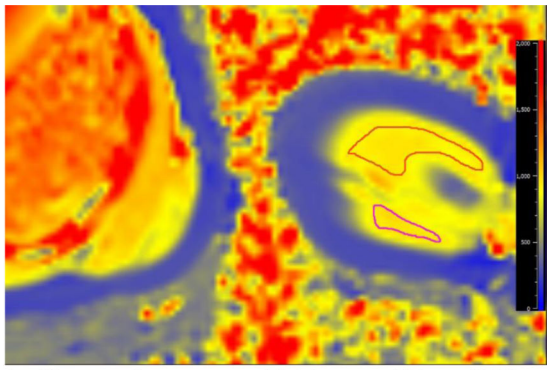
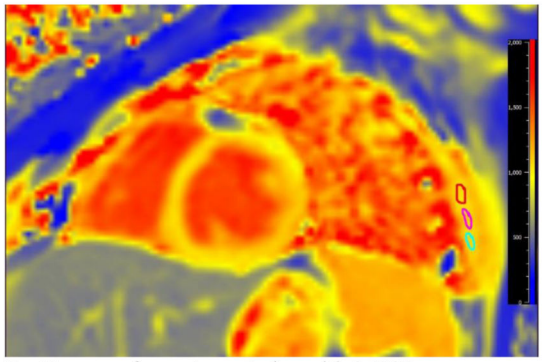
Highlights

- Most muscle assessments for Duchenne Muscular Dystrophy require ambulation
- Existing cardiac MRI protocols involve incidental imaging of skeletal musculature
- Measures of muscle function independent of ambulation are needed
- Correlation exists between cardiac MRI and tests of muscle function



A. T_1 map of upper arm with triceps and biceps ROI



B. T_1 map of serratus anterior with 3 ROIs

C. T_2 map of serratus anterior with 3 ROIs

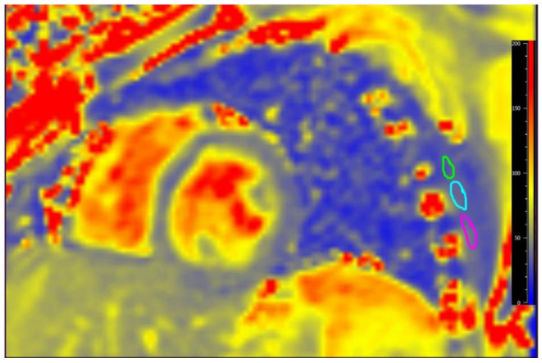


Figure 1.

CMR map of upper arm and serratus anterior. Figure 1A is an imaging slice obtained perpendicular to the patient's dominant arm humerus pre- and post-contrast administration. Figures 1B and 1C are both representative short axis slices (1B is native T1 map, 1C is T2 map) through the mid-LV at the level of the papillary muscles.

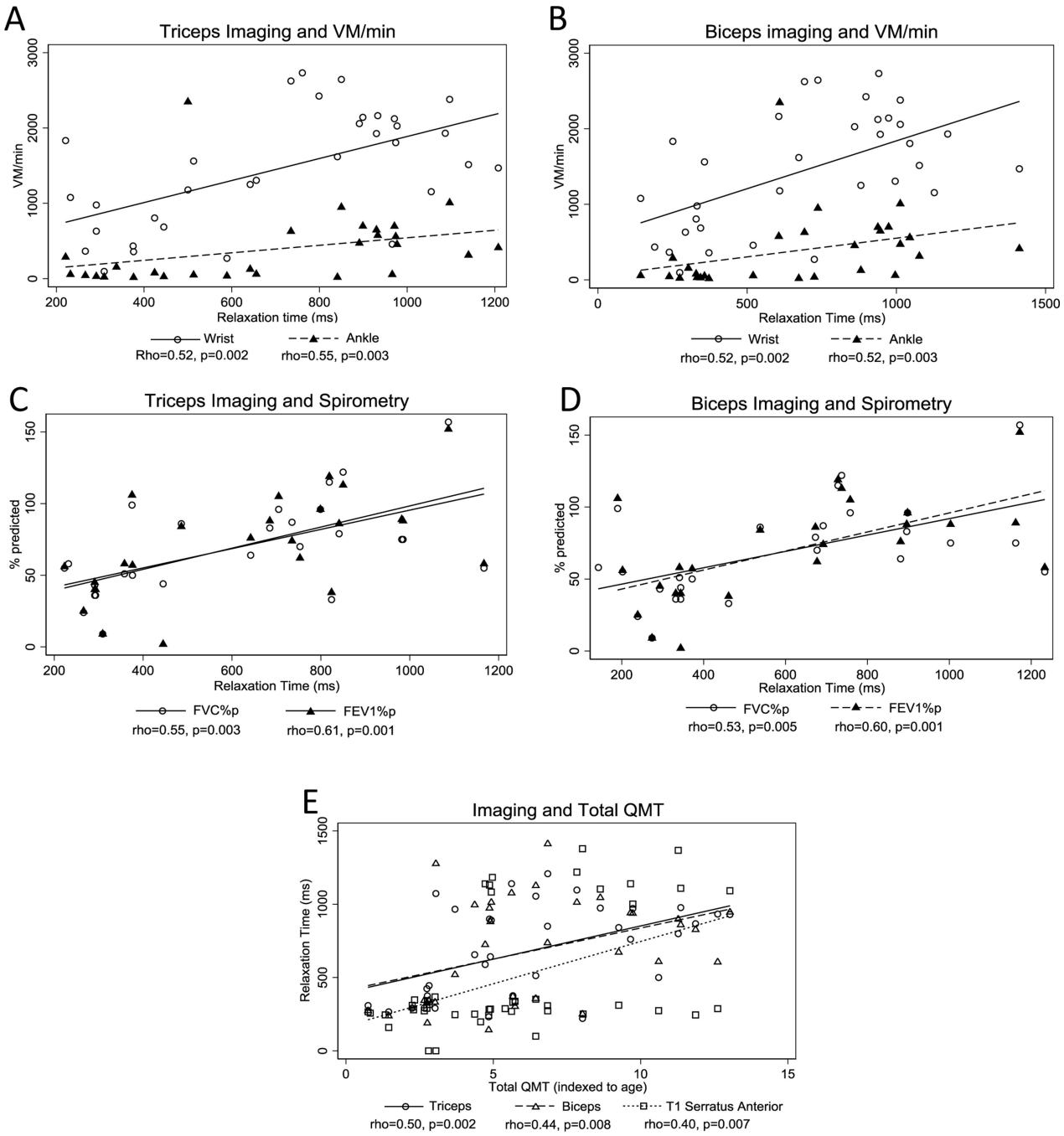


Figure 2.
Correlation of Imaging and accelerometry, QMT and spirometry

Table 1

Demographic and anthropometric characteristics

	Mean ± SD (range)
Age (yrs)	13.3 ± 4.2 (8.0 – 24.3)
Height (cm)	145.5 ± 18.5 (112–180)
Weight (kg)	50.7 ± 19.7 (18.9 – 103.2)
Race	
Non Hispanic White	38 (84.4%)
Hispanic/Latino	7 (15.6%)
Black	4 (8.2%)
Asian	2 (4.1%)
Ambulatory	17 (34.7%)
Prior steroid use	16 (32.7%)
Currently on steroids	33 (67.4%)
On nightly positive pressure ventilation	8 (16.7%)
Use of insufflator/exsufflator (cough assist)	11 (23.4%)
Tracheostomy	1 (2.1%)

Table 2.

Control and Subject CMR #1 Relaxation Times

	Controls		DMD Patients		
	n	**Mean ± SD (IQR)**	**n**	**Mean ± SD (IQR)**	**P-value**
Triceps	14	869.8 ± 30.5 (852 – 884)	37	697.7 ± 309.7 (221 – 1208)	0.002
Biceps	14	862.3 ± 18.6 (852 – 873)	37	695.4 ± 351.4 (143 – 1412)	0.007
Serratus Anterior T_1	14	913.8 ± 37.6 (886 – 944)	46	508.4 ± 398.2 (94 – 1485)	<0.001
Serratus Anterior T_2	14	34.9 ± 2.1 (34 – 36)	46	115.9 ± 81.9 (17 – 407)	<0.001

Table 3

CMR Relaxation Times

	CMR #1		CMR #2		CMR #3			
	n	**Mean ± SD (IQR)**	**n**	**Mean ± SD (IQR)**	**n**	**Mean ± SD (IQR)**	**P-value[1]**	**P-value[2]**
Triceps	37	697.7 ±309.7 (221 – 1208)	34	587.2 ±290.5 (223 – 1068)	24	582.2 ±302.3 (140 – 1167)	0.003	0.007
Biceps	37	695.4 ±351.4 (143 – 1412)	34	573.4 ± 318.8 (172 – 1145)	24	564.8 ±309.4 (263 – 1233)	0.051	0.032
Serratus Anterior T_1	46	508.4 ±398.2 (94 – 1485)	45	445.6 ± 335.4 (136 – 1369)	35	376.8 ±237.6 (207 – 1194)	0.032	0.407
Serratus Anterior T_2	46	115.9 ± 81.9 (17 – 407)	45	111.3 ±84.0 (23 – 407)	35	116.3 ±79.5 (23 – 410)	0.959	0.810

[1] P-value for Wilcoxon signed rank comparison of CMR 1 with CMR 2.

[2] P-value for Wilcoxon signed rank comparison of CMR 1 with CMR 3.

Table 4

Correlation between CMR#1 imaging and accelerometry vector magnitudes (VM)

	Wrist VM (counts)	Wrist awake VM	Wrist VM/min	Wrist awake VM/min	Ankle VM	Ankle awake VM	Ankle VM/min	Ankle awake VM/min
Triceps (ms)	Rho=0.42 p=0.015 (n=33)	Rho=0.40 p=0.028 (n=31)	Rho=0.52 p=0.002 (n=33)	Rho=0.50 p=0.004 (n=31)	Rho=0.53 p=0.004 (n=28)	Rho=0.47 p=0.014 (n=26)	Rho=0.55 p=0.003 (n=28)	Rho=0.39 p=0.051 (n=26)
Biceps (ms)	Rho=0.47 p=0.006 (n=33)	Rho=0.45 p=0.011 (n=31)	Rho=0.52 p=0.002 (n=33)	Rho=0.51 p=0.003 (n=31)	Rho=0.49 p=0.008 (n=28)	Rho=0.45 p=0.021 (n=26)	Rho=0.54 p=0.003 (n=28)	Rho=0.39 p=0.051 (n=26)
T_1 SA (ms)	Rho=0.35 p=0.029 (n=40)	Rho=0.24 p=0.157 (n=37)	Rho=0.43 p=0.005 (n=40)	Rho=0.35 p=0.036 (n=37)	Rho=0.35 p=0.038 (n=35)	Rho=0.25 p=0.181 (n=30)	Rho=0.35 p=0.032 (n=35)	Rho=0.33 p=0.072 (n=30)
T_2 SA (ms)	Rho=−0.23 p=0.149 (n=40)	Rho=−0.26 p=0.116 (n=37)	Rho=−0.39 p=0.013 (n=40)	Rho=−0.44 p=0.007 (n=37)	Rho=−0.45 p=0.013 (n=35)	Rho=−0.36 p=0.049 (n=30)	Rho=−0.49 p=0.003 (n=35)	Rho=−0.47 p=0.009 (n=30)

Table 5

Correlation between CMR #1 imaging and quantitative muscle testing (QMT) indexed to age

	Total QMT (pounds/yr)	Arm Indexed (pounds/yr)	Leg Indexed (pounds/yr)
Triceps (ms) n=35	Rho=0.50 p=0.002	Rho=0.51 p=0.002	Rho=0.46 p=0.005
Biceps (ms) n=35	Rho=0.44 p=0.008	Rho=0.42 p=0.011	Rho=0.42 p=0.012
T_1 Serratus Anterior (ms) n=45	Rho=0.40 p=0.007	Rho=0.40 p=0.007	Rho=0.38 p=0.010
T_2 Serratus Anterior (ms) n=44	Rho=−0.20 p=0.195	Rho=−0.22 p=0.155	Rho=−0.18 p=0.249

Table 6.

Correlation between imaging and spirometry measures

	FVC%p	FEV_1%p	MIP	MEP
Triceps (ms)	Rho=0.55 p=0.003 n=26	Rho=0.61 p=0.001 n=25	Rho=0.07 p=0.855 n=10	Rho=0.34 p=0.310 n=11
Biceps (ms)	Rho=0.53 p=0.005 n=26	Rho=0.60 p=0.001 n=25	Rho=0.16 p=0.663 n=10	Rho=0.36 p=0.273 n=11
T_1 Serratus Anterior (ms)	Rho=0.12 p=0.482 n=34	Rho=0.07 p=0.696 n=33	Rho=−0.23 p=0.459 n=13	Rho=−0.31 p=0.273 n=14
T_2 Serratus Anterior (ms)	Rho=0.11 p=0.527 n=34	Rho=0.17 p=0.331 n=33	Rho=0.19 p=0.372 n=13	Rho=0.37 p=0.191 n=14

FVC%p: forced vital capacity percent predicted, FEV_1%p: forced expiratory volume in 1 second percent predicted, MIP: maximal inspiratory pressure, MEP: maximal expiratory pressure