Electromechanical Discoordination is present in patients with Duchenne Muscular Dystrophy independent of tissue fibrosis.

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BACKGROUND

- Progressive ventricular dysfunction is a cardinal symptom in Duchenne Muscular Dystrophy (DMD).
- The aim of this study was to examine the left ventricular (LV) function of patients with DMD using MRI-derived ventricular electro-mechanical discoordination indices including: 1) **systolic stretch fraction (SSF)** and 2) **diastolic relaxation fraction (DRF).**

METHODS

- Adolescents with DMD (n=31) and healthy controls (n=20) of similar age underwent MRI for standard volumetric and functional analysis. Segment-specific circumferential strain and strain rate indices were evaluated along with standard mechanical dyssynchrony.
- Patients also underwent MRI with Gadolinium enhancement to evaluate for the presence of fibrosis.
- In order to evaluate for SSF and DRF, the relative ratio of contraction to relaxation of the individual segments of the LV is calculated from segment-specific myocardial strain and strain rate curves.
- Under ideal conditions, all the segments of the LV myocardium are in the ejection phase and contracting. This is indicated by a negative strain rate (**Figure 1**).
- In the setting of myocardial discoordination of the LV, some segments are relaxing while other segments are experiencing contraction, described by a positive strain rate. This discoordination causes a decrease in the efficiency of the myocardium.

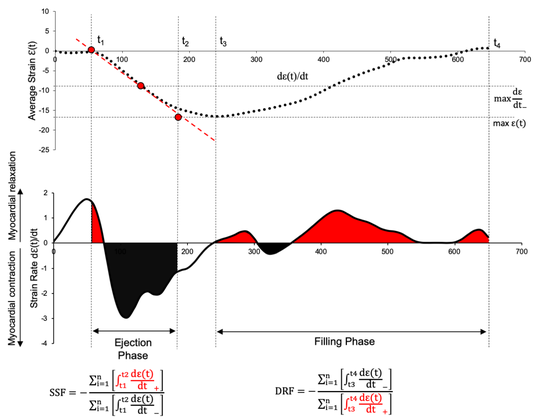

Figure 1. Algorithm for the LV discoordination indices: systolic stretch fraction (SSF) and diastolic relaxation fraction (DRF). From the segment specific strain ε(t) and strain rate (dε(t)/dt, the mean strain was calculated to define the temporal boundary of the ejection vs. filling phases. For the calculation of the SSF and DRF, the strain rate curves were separated into positive and negative components to calculate the ratio of myocardial relaxation and contraction during the ejection and filling phases.

Table 1. MRI Hemodynamics (DMD v. Control)

	Control (n=20)	DMD (n=31)	*P*-Value
Age (yrs)	14.79 ± 3.10	13.55 ± 3.67	0.207
BSA (m^2)	1.42 ± 0.31	1.36 ± 0.37	0.57
Sex (Female)	55%	0%	
SSF	0.007 (0.005 - 0.013)	0.03 (0.02 - 0.04)	0.002
DRF	0.3 (0.26 – 0.33)	0.37 (0.31 – 0.47)	0.001
LV EDVi (mL/m^2)	62.59 ± 11.18	82.86 ± 26.13	0.001
LV ESVi (mL/m^2)	22.68 ± 5.92	42.19 ± 25.67	<0.001
LV Svi (mL/m^2)	55.66 ± 15.32	52.9 ± 15.87	0.598
LV CI ($L/min/m^2$)	2.77 ± 0.65	3.88 ± 1.11	<0.001
LV EF (%)	63.58 ± 4.48	51.35 ± 9.21	<0.001
LV CO (L/min)	3.77 ± 0.84	5.00 ± 1.65	0.002

All values are reported as means with corresponding ± SD or median with interquartile range. SSF, systolic stretch fraction; DRF, diastolic relaxation fraction, LV EDV, left ventricular end diastolic volume; LV ESV, left ventricular end systolic volume; LV SV, left ventricular stroke volume; LV CI, left ventricular cardiac index; LV EF, left ventricular ejection fraction; LV CO, left ventricular cardiac output.

Results

Table 2. MRI Hemodynamics (Gd- v. Gd +)

	Gd - (n=14)	Gd + (n=17)	*P*-Value
Age (yrs)	12.6 ± 3.6	14.3 ± 3.6	0.183
BSA (m^2)	1.23 ± 0.31	1.47 ± 0.38	0.082
SSF	0.03 (0.01 – 0.04)	0.022 (0.016 – 0.042)	0.703
DRF	0.368 (0.329 – 0.464)	0.399 (0.303 – 0.537)	0.287
LV EDVi (mL/m^2)	79 ± 17	86.11 ± 32.23	0.473
LV ESVi (mL/m^2)	32 (29-38)	39 (36-42)	0.212
LV Svi (mL/m^2)	53 ± 15	53.2 ± 17.2	0.912
LV CI ($L/min/m^2$)	4.0 ± 1.2	3.8 ± 1.05	0.644
LV EF (%)	55 ± 6.7	47.8 ± 9.8	0.018
LV CO (L/min)	4.8 ± 1.7	5.2 ± 1.7	0.487

All values are reported as means with corresponding ± SD or median with interquartile range. SSF, systolic stretch fraction; DRF, diastolic relaxation fraction, LV EDV, left ventricular end diastolic volume; LV ESV, left ventricular end systolic volume; LV SV, left ventricular stroke volume; LV CI, left ventricular cardiac index; LV EF, left ventricular ejection fraction; LV CO, left ventricular cardiac output.

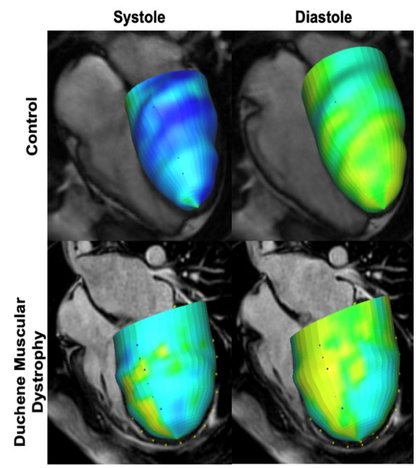

Figure 2. LV endocardial and epicardial segmentation-generated 3D-circumeferential strain model comparing patients with DMD and controls in systole and diastole.

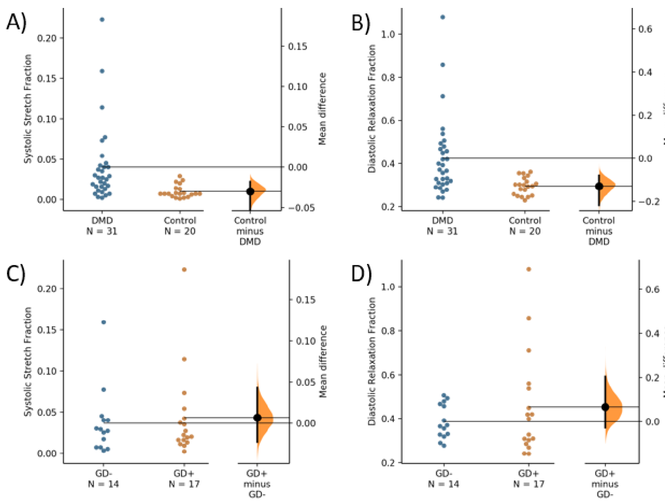

Figure 3. Graphical representation of the LV electromechanical discoordination results. A) Systolic stretch fraction (SSF) was elevated in patients with DMD, B) as was diastolic relaxation fraction (DRF). There were no group differences noted between DMD patients that were Gd- or Gd+ for C) SSF or D) DRF.

CONCLUSION

- Patients with DMD showed increased levels of LV electromechanical discoordination compared to controls
- This difference was independent of qualitative presence of fibrosis noted by Gadolinium enhancement.
- This allows speculation that changes in electromechanical discoordination may precede visible fibrotic change in DMD.
- Future studies will involve echocardiographic evaluation of SSF and DRF for MRI validation and for the assessment of clinical prognosis