Intra-myocardial and Pericardial Fat Quantification in Boys with Duchenne Muscular Dystrophy and Healthy Controls at 3T

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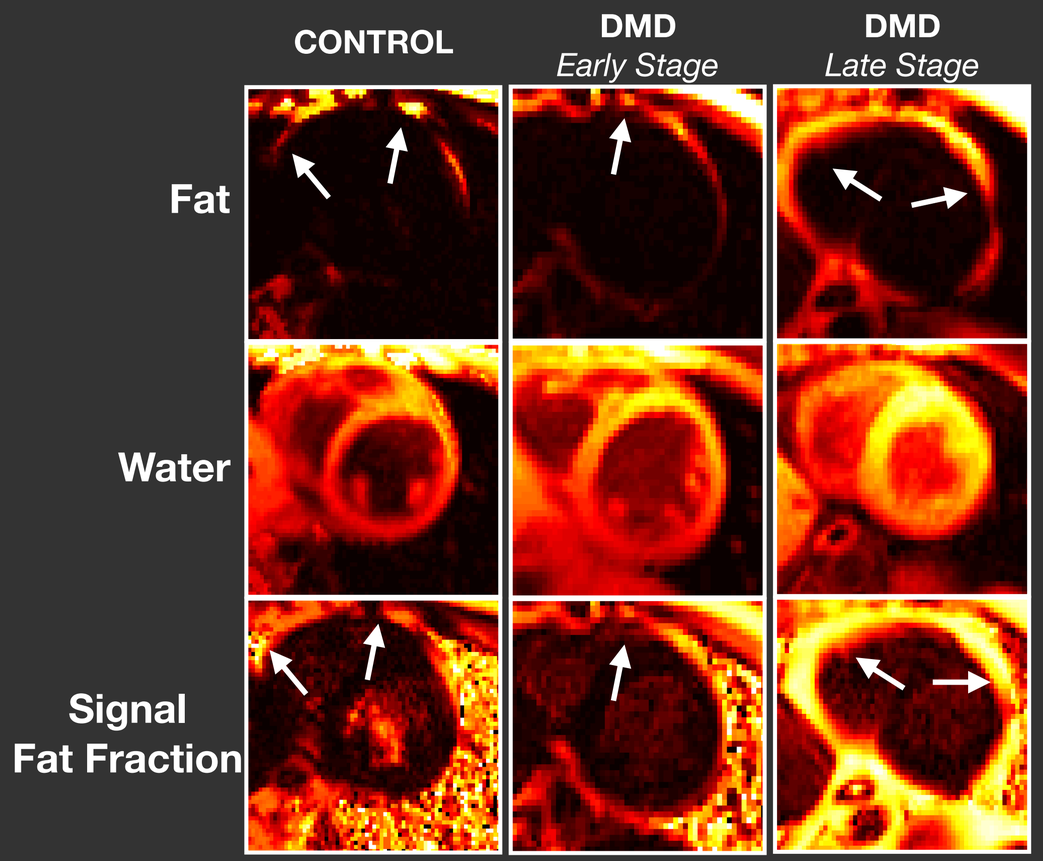
Impact: This work investigates the myocardial fibro-fatty infiltration using a chemical-shift based water-fat separation MRI technique. This pilot study detected increased pericardial fat in Duchenne Muscular Dystrophy (DMD) patients compared to healthy controls, but intra-myocardial differences were found only at the apical level between the two groups. This data suggests that intra-myocardial fat is a late outcome in DMD.



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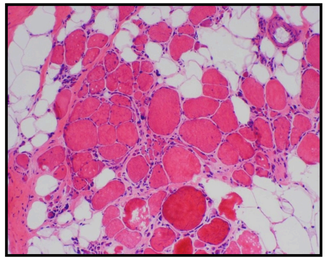
Duchenne Muscular Dystrophy

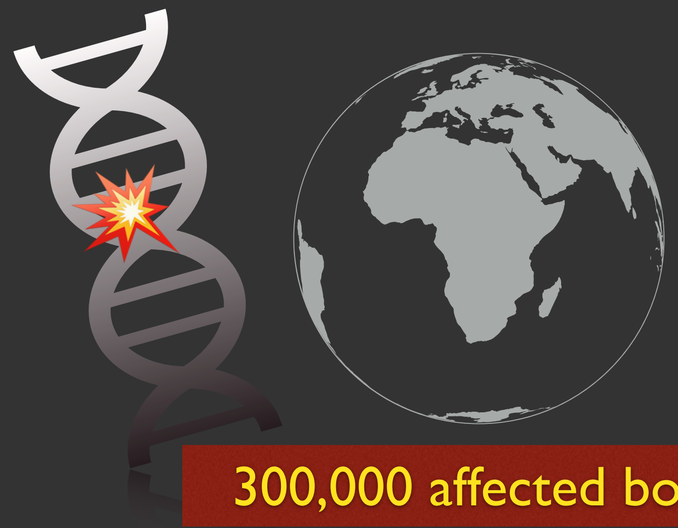
Duchenne Muscular Dystrophy:

- A fatal X-linked genetic disorder characterized by progressive muscle weakness.
- Associated with pediatric onset cardiomyopathy and fatal heart failure.
- On-going research aims to investigate cardiac MRI biomarkers, including myocardial fibro-fatty infiltration, to identify the on-set of microstructural remodeling in boys with DMD[2].
- Based on histology, some of the pathological changes in DMD are shared between skeletal and cardiac muscle[5], yet the onset of intra-myocardial fat and excessive pericardial fat remains understudied.

Histological slide of DMD Muscle



- Chemical-shift[3] based water-fat separation MRI techniques have been used to assess the level of fat infiltration in skeletal muscle of DMD subjects[4].



300,000 affected boys

Intra-myocardial and Pericardial Fat Quantification

Study Objectives:

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DMD CARDIAC MRI EXAM AT 3T HAS POTENTIAL TO YIELD BIOMARKERS SENSITIVE TO MYOCARDIAL CHANGES

IMAGING PROTOCOL:

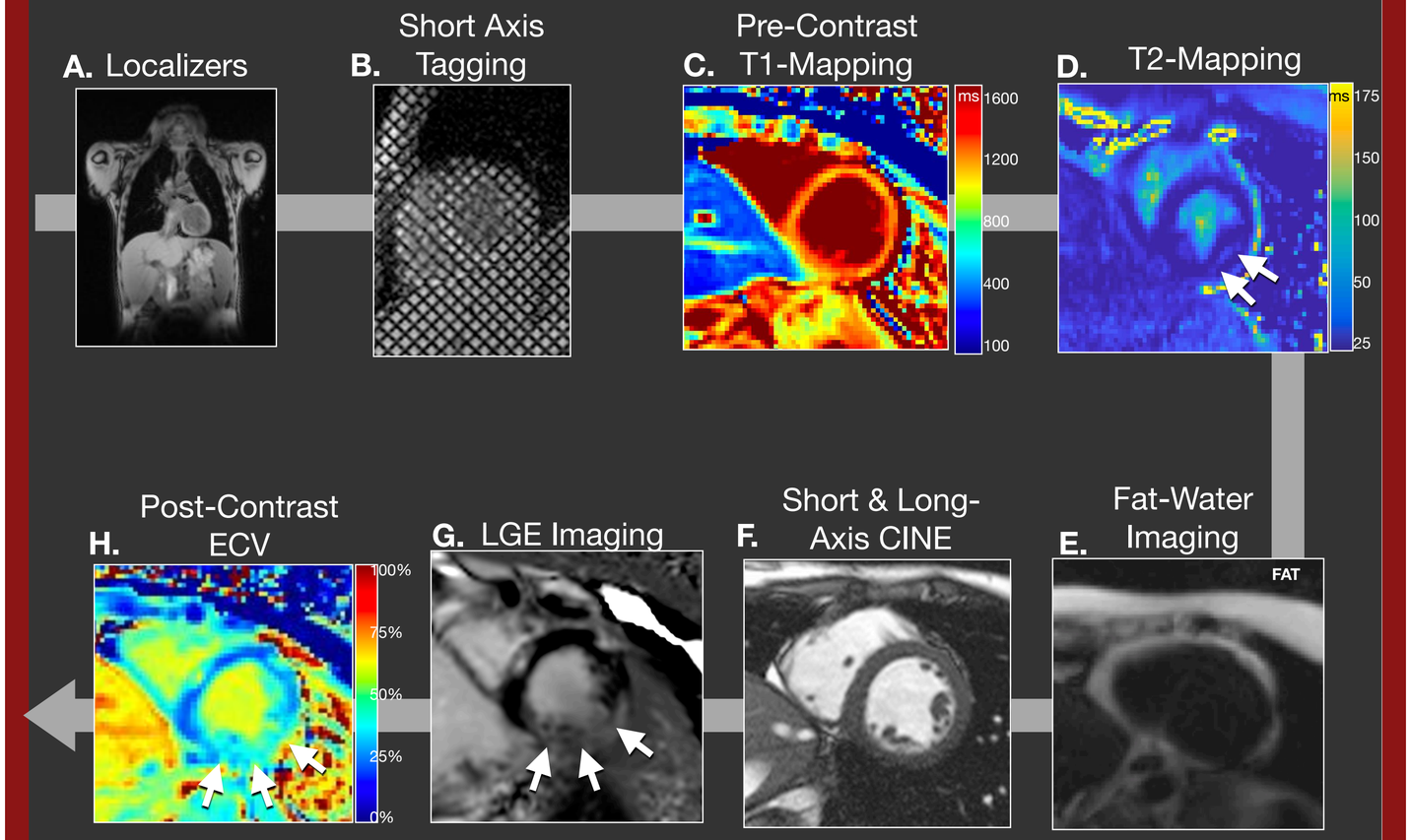
The DMD cardiac MRI exam at 3T has potential to yield biomarkers sensitive to myocardial changes. This workflow includes both structural and functional imaging and features the following:

- High resolution, static black-blood imaging **(A)**
- Short- and long axis tagged images **(B)**
- Pre- and post-contrast T1 mapping and ECV **(C and H)**
- T2 mapping **(D)** and ADC mapping (not pictured)
- Dynamic (CINE) white blood bSSFP imaging **(F)**
- Post-contrast static late gadolinium enhancement (LGE) imaging **(G).**

Fat-Water Imaging (E)

The cMRI exam consisted of a multi-echo (Dixon) GRE sequence for fat-water separation imaging[3] to assess fibro-fatty infiltration. These Images were acquired during free-breathing with ECG gating.

Imaging Parameters	
Matrix size	192 x 108 mm^2
Pixel size	2x2x8 mm^3
Flip angle	12°
TE	1.27; 4.17; 6.7; 9.23
TR	11.2 ms



INTRA-MYOCARDIAL AND PERICARDIAL FAT QUANTIFICATION

STUDY OBJECTIVES:

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Imaging:

Boys with DMD (N=22, 13 ± 3.1 years) and healthy boys (N=11, 12.6 ± 2.5 years, were prospectively enrolled in an IRB-approved and HIPPA-compliant study for a cardiac MRI (cMRI) exam at 3T (Siemens Skyra) after providing informed consent.

Study Population:

	DMD (N=22) Median (IQR)	Control (N=11) Median (IQR)
Age (yrs)	13 (4.0)	13 (4.3)
Height* (cm)	134 (26.0)	163 (16.8)
Weight (kg)	50.0 (26.3)	50.8(13.2)
BMI* (kg/m^2)	26.1 (11.3)	17.9 (1.7)
Heart rate* (bpm)	87 (24)	65 (30)
LVEF* (%)	50.1 (11.5)	57.9 (7.28)

** $p < 0.05$*
BMI - body mass index
LVEF - Left ventricular ejection fraction

Boys with DMD are <u>shorter</u> in height, have <u>increased</u> BMI and heart rate, and <u>decreased</u> LVEF compared to healthy controls.

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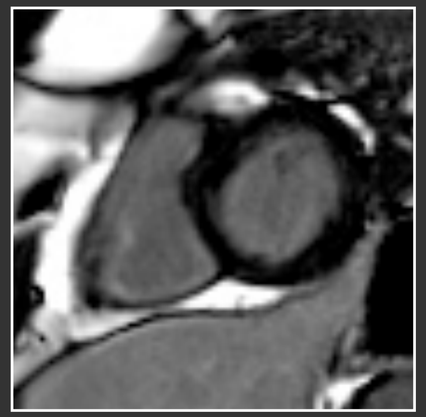
Study Population:

	LGE+ (N=6) Median (IQR)	LGE- (N=13) Median (IQR)
Age (yrs)	12 (7.0)	13 (4.5)
Height (cm)	130 (17.0)	133 (16.8)
Weight (kg)	49.9 (14.6)	50.5 (31.5)
BMI (kg/m²)	25.2 (5.1)	27.3 (12.5)
Heart rate* (bpm)	73.5 (13)	98 (24.3)
LVEF* (%)	43.3 (11.6)	54.4 (10.1)

** $p < 0.05$*
BMI - body mass index
LVEF - Left ventricular ejection fraction

DMD boys with who are LGE+ have an <u>increased</u> heart rate and a <u>decreased</u> LVEF compared to DMD boys who are LGE-.

LGE +



LGE -

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Post-processing:

- Water- and fat-separated images for basal, mid-ventricular, and apical short- axis slices were used to calculate maps of signal fat fraction.

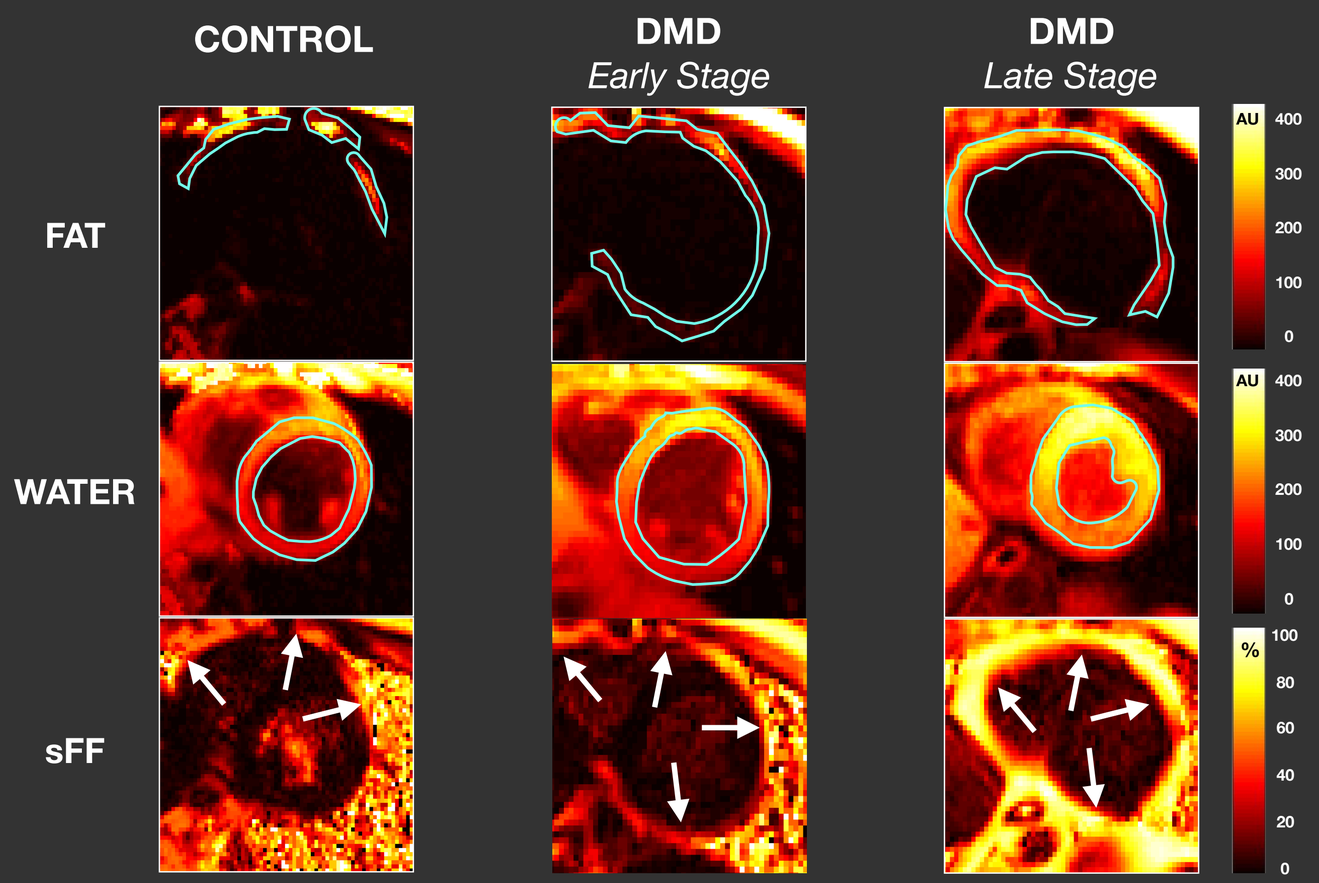
$$sFF = Fat/(Water+Fat)$$

- To account for noise bias, the sFF in regions of low fat content were generated by:

$$sFF = 1 - sWF$$

$$(sWF = Water(Water+Fat).$$

- A region of interest (ROI) encompassing the left ventricular (LV) myocardium and ROIs containing pericardial fat were segmented, extracted, and analyzed for their corresponding sFF values.
- Summary statistics were extracted from all ROIs and pericardial fat volume (cm^3) was quantified from the corresponding regions for each slice location.
- Mann-Whitney U-tests were used to compare boys with DMD and healthy controls. Spearman's correlation test was performed to assess relationships between measured parameters (sFFs and pericardial fat volume) and demographic characteristics (age, height, weight, BMI, and HR) of DMD boys and healthy controls.
- Data is reported as median and IQR. $P<0.05$ was considered significant.



Analysis performed at basal, mid-ventricular, and apical slices.

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Results:

Pericardial fat Volume (cm^3):

	DMD (N=22) Median (IQR)	CONTROL(N=11) Median (IQR)
Base*	8.99 (3.51)	5.50 (2.29)
Mid*	7.09 (2.94)	4.08 (1.30)
Apex*	5.81 (3.34)	3.65 (1.78)

Pericardial sFF (%):

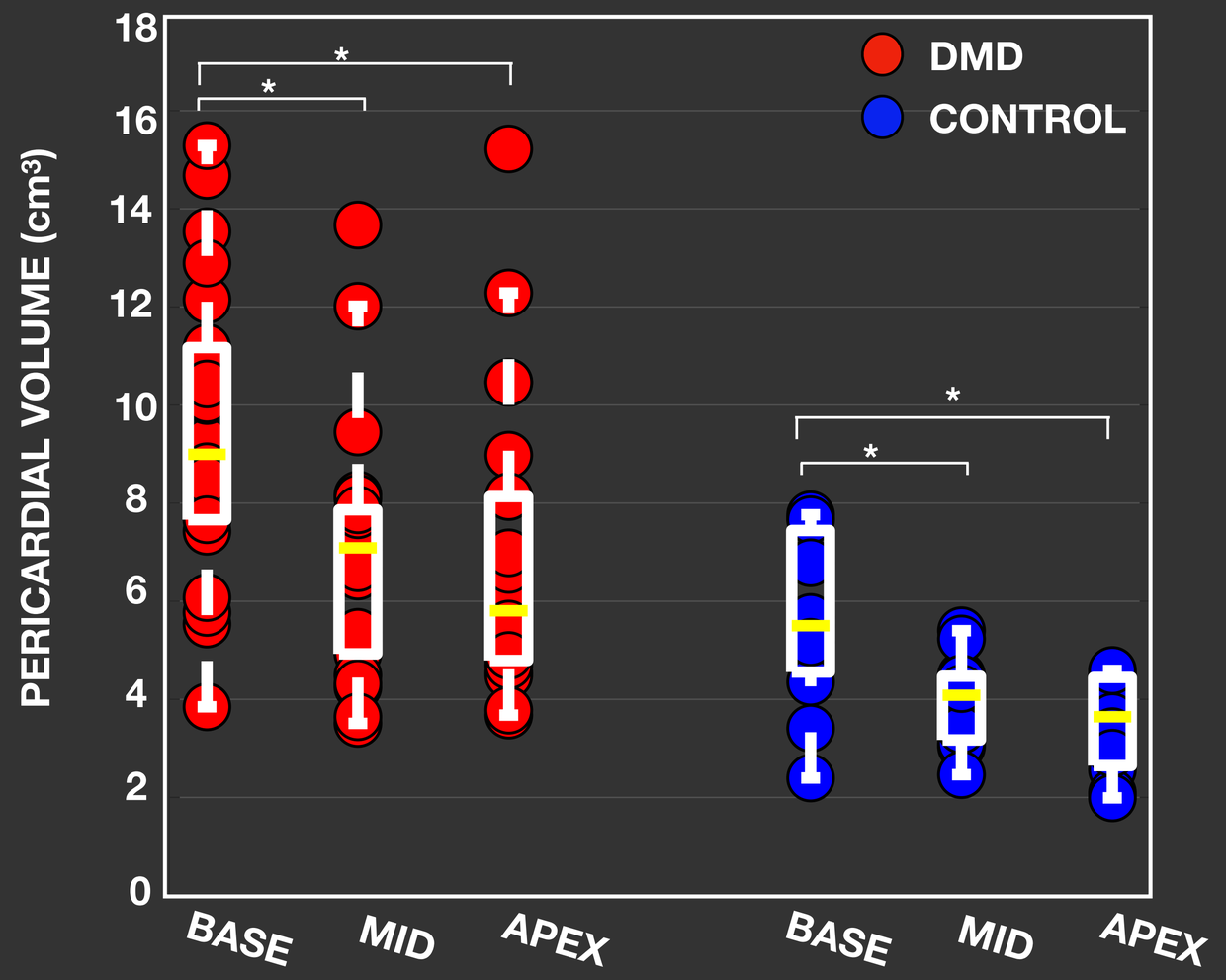
	DMD (N=22) Median (IQR)	CONTROL(N=11) Median (IQR)
Base*	65 (22)	45 (18)
Mid*	65 (17)	48 (12)
Apex*	60 (27)	49 (8.9)

Myocardial sFF (%):

	DMD (N=22) Median (IQR)	CONTROL(N=11) Median (IQR)
Base	7.1 (3.6)	5.6 (2.8)
Mid	5.2 (2.2)	5.6 (2.2)
Apex*	6.1 (4.4)	3.9 (2.6)

*$p < 0.05$

Decreasing trend observed in pericardial fat volume measured at basal, mid-ventricular, and apical slices for both groups.



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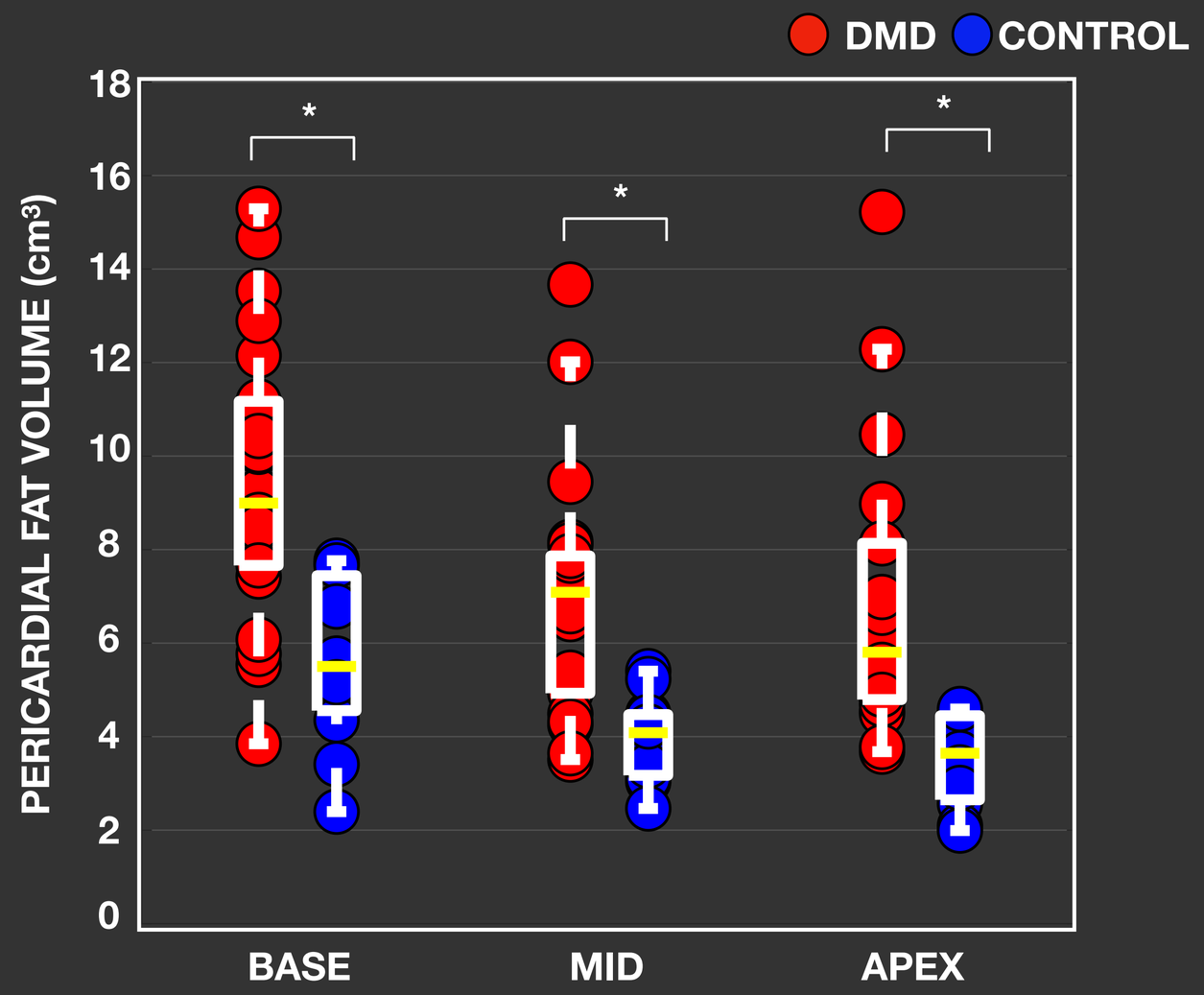
*$p < 0.05$

We observe significantly more pericardial fat in DMD compared to healthy controls across all slice locations.



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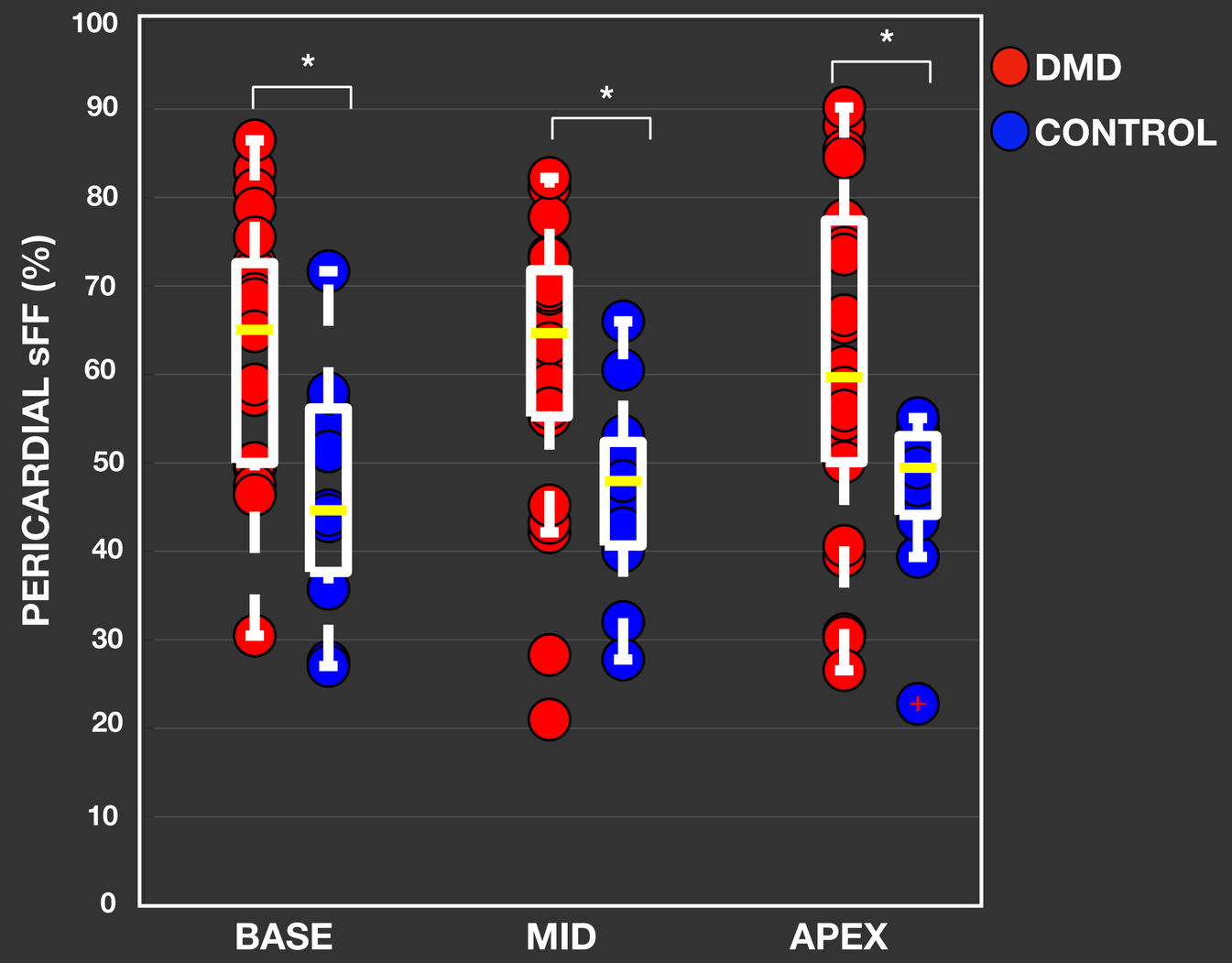
We observe <u>increased</u> pericardial signal fat fraction in DMD compared to healthy controls across all slice locations.



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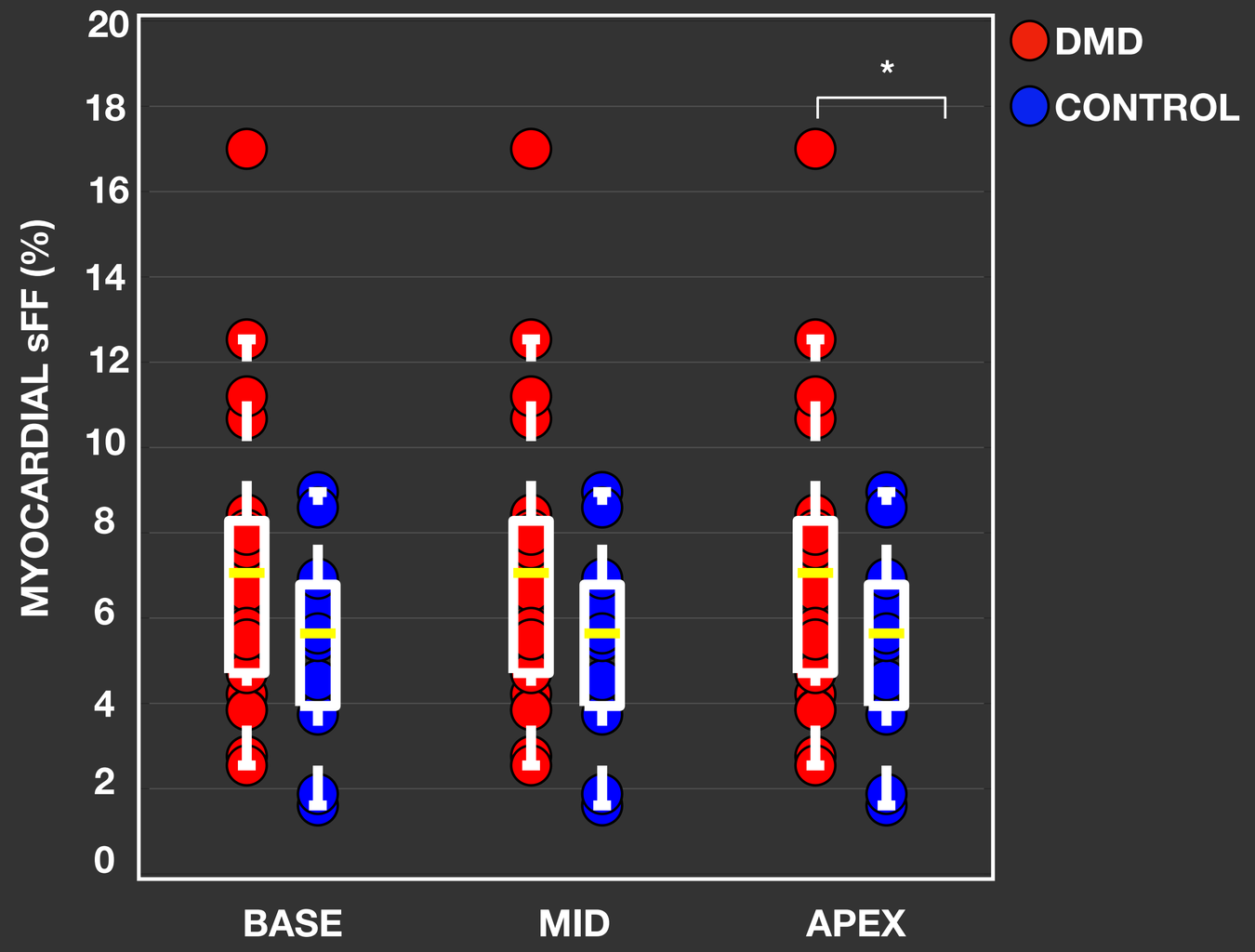
No significant difference detected for myocardial sFF between DMD patients and healthy controls at basal and mid-ventricular slice locations, but DMD patients have increased myocardial sFF near the apex of the heart.



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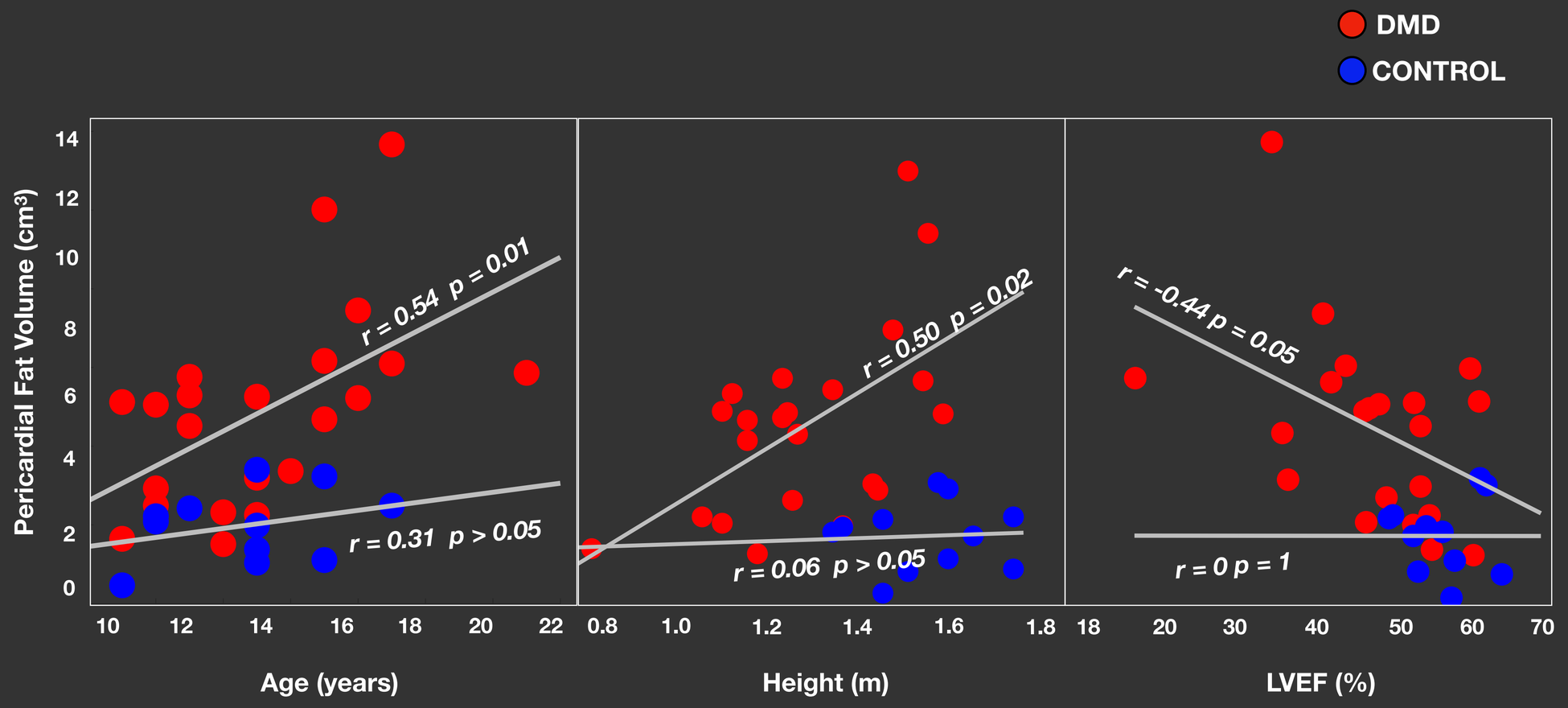
Pericardial fat volume increases with age and height in DMD, but decreases with LVEF.



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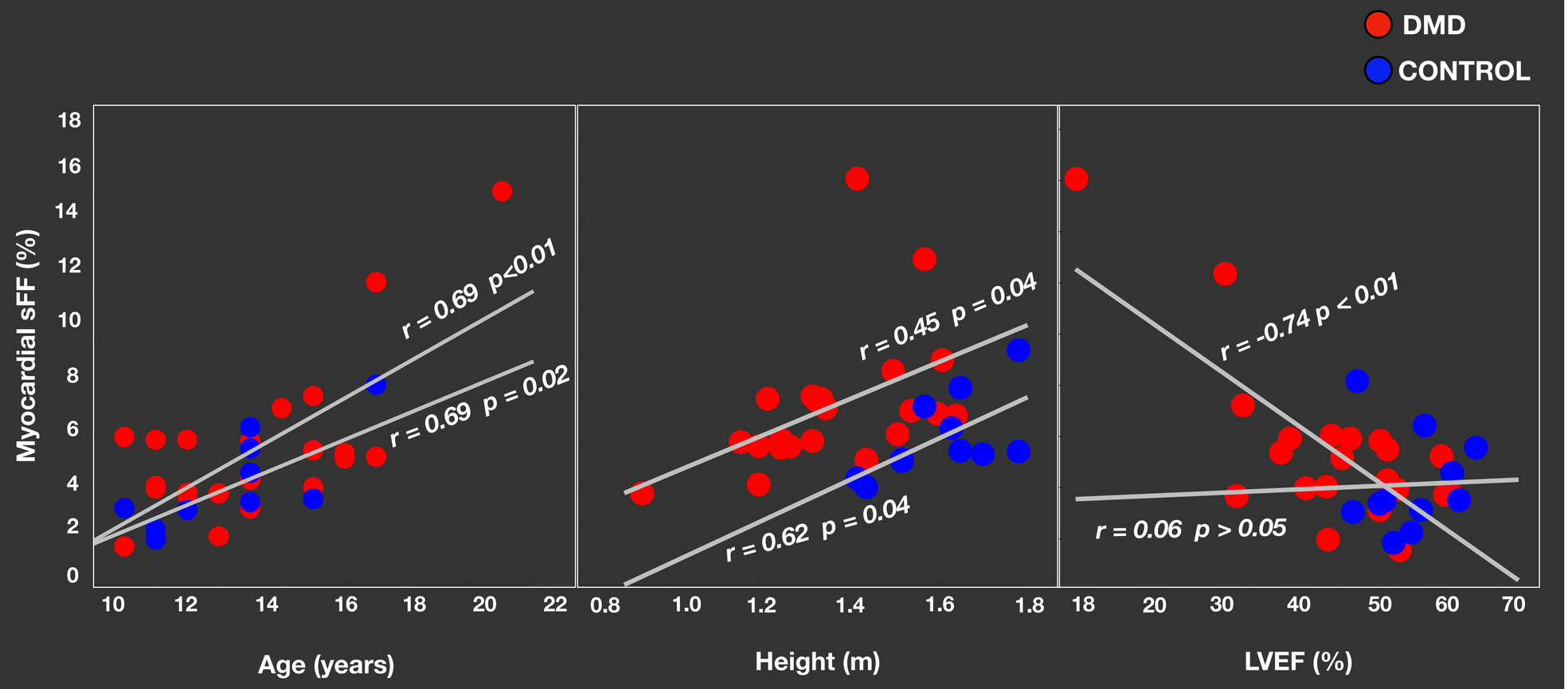
Myocardial sFF increases with age and height in DMD and healthy controls, but decreases with LVEF in DMD patients.



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Results:

Pericardial Volume (cm^3):

	LGE+ (N=6) Median (IQR)	LGE- (N=13) Median (IQR)
Base	8.38 (4.89)	8.47 (3.81)
Mid	6.78 (2.94)	7.12 (2.98)
Apex	5.91 (4.93)	5.54 (2.62)

Pericardial sFF (%):

	LGE+ (N=6) Median (IQR)	LGE- (N=13) Median (IQR)
Base	68 (25)	65 (19)
Mid	50 (25)	66 (14)
Apex	52 (25)	67 (23)

Myocardial sFF (%):

	LGE+ (N=6) Median (IQR)	LGE- (N=13) Median (IQR)
Base	6.1 (6.4)	7.5 (2.7)
Mid	4.9 (8.7)	5.2 (2.1)
Apex	5.8 (4.1)	5.9 (4.8)

*$p < 0.05$

We detected no difference in pericardial volume, pericardial sff, and myocardial sff between LGE+ and LGE- DMD subjects.

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Discussion:

- Herein we have shown the potential for water-fat separation MRI to detect fibro-fatty infiltration in the heart of boys with DMD and healthy controls.
- We report pericardial fat volume, pericardial sFF, and myocardial sFF from the basal, mid-ventricular, and apical slice locations.
- We observed increased amounts of pericardial fat and, subsequently, an increased signal fat fraction in DMD patients compared to healthy controls.
- It is unclear if the elevated pericardial fat volume and correlation with age is part of the cardiac disease process or due to increased BMI alone.
- A previous multi-ethnic study of atherosclerosis (MESA) reported that pericardial fat volume is associated with a higher risk of cardiovascular disease[6].
- We observed no detectable intra-myocardial sFF differences at the basal and mid-ventricular level, but we found increased myocardial sFF in DMD near the apex. It is unclear if that is the initial site of fibro-fatty accumulation in the DMD heart.

Compared to healthy controls, DMD patients have:

1. Increased pericardial fat volume
2. Increased pericardial sFF
3. Increased myocardial sFF only at apical level

Intra-myocardial fat is likely to be a late outcome and does not appear to precede reduced LVEF.

Conclusion:

- We found that DMD patients have increased pericardial fat, pericardial sFF, and increased myocardial sFF only near the apex.
- Additional work is needed to understand the correspondence of changes in sFF with age, BMI, and DMD severity.

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For more information regarding our work on cardiac MRI biomarkers for Duchenne Muscular Dystrophy see **Program #2027**.

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Program #?