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Muscle Pathology associated with Cardiac Function in Duchenne Muscular Dystrophy

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Introduction

Duchenne muscular dystrophy (DMD) is a severe, progressive, and muscle-wasting disease. Progressive congestive heart failure caused by dystrophin deficiency in the myocardium is the most common cause of death in this patient population. This study aimed to examine the associations between echocardiogram-based cardiac function indices and fibrosis of the abdominal and lower extremity muscles in patients with DMD to facilitate early detection of cardiac dysfunction and identify its predictors.

Materials and Methods

Twenty-one patients with DMD who gave their informed consent to participate in the study were enrolled. The association between cardiac dysfunction and fibrosis of the abdominal and lower extremity muscles was determined by analyzing the echocardiography and elastography data for the abdominal and extremity muscles (Figure 1). Non-parametric Spearman rank correlation coefficients were used to examine the pairwise relationships between cardiac function and muscle elasticity.

Results

All patients were male and non-ambulant. Their mean age was 18.45 ± 4.28 years. The strain ratios of the abdominal muscle and quadriceps muscles were significantly higher than those of the medial Gastrocnemius medialis (p<0.05) (Table 1). The strain ratio of the rectus abdominis muscle has a significant negative correlation with Left ventricular ejection fraction (p<0.05) (Table 2). Cardiac function and valvular insufficiency were not significantly correlated with muscle strain ratio. According to the result of our study, the only skeletal muscle which showed significant correlation with cardiac dysfunction was degree abdominal muscle fibrosis. Regarding the direct effect of abdominal muscle fibrosis on cardiac function, the use of the abdominal muscles for inspiration in patients with advanced DMD creates a negative pressure in the thoracic cavity that draws more blood into the right atrium. Based on our findings, the severity of abdominal muscle fibrosis can be used as an indirect indicator of LV function in patients with DMD. Abdominal muscles are involved in expiration and inspiration in advanced DMD, and a previous animal study reported that abdominal muscle fibrosis is weakly associated with LV fibrosis but significantly associated with cardiac function. However, the degrees of fibrosis of other lower extremity muscles were not significantly associated with other cardiac dysfunction parameters reflecting preclinical myocardial structural changes in our study.

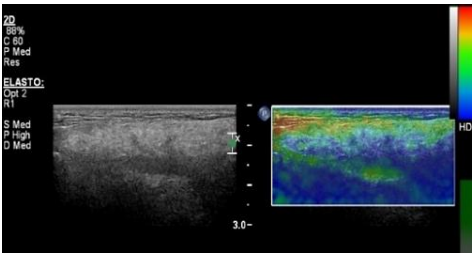

Fig 1. B-mode ultrasound and dynamic sonoelastography (DS) for measuring strain ratio and DS score

Table 1. Pairwise comparisons of the mean strain ratios (muscle/subcutaneous) using independent-samples Kruskal-Wallis test

Muscle comparison	p-value	Adjusted p-value
Rectus abdominis vs Quadriceps	0.987	1.000
Rectus abdominis vs Biceps femoris	0.003*	0.017
Rectus abdominis vs Medial GCM	0.000*	0.002*
Quadriceps vs Medial GCM	0.000*	0.002*
Biceps femoris vs Medial GCM	0.558	1.000

* Significant Spearman's rank coefficients (p<0.05)
GCM; Gastrocnemius medialis

Table 2. Correlation between cardiac function and muscle strain ratio

Strain ratio of muscles	Echocardiographic parameters					
	LVEF	E/A	E/E'	E'	LVEDd	GLS
Rectus abdominis	-0.379*	-0.249	-0.073	-0.041	0.156	0.212
Quadriceps	0.040	0.195	0.236	-0.227	-0.191	-0.094
GCM	-0.253	0.073	0.022	-0.283	0.026	0.363
Biceps femoris	-0.005	-0.180	-0.190	0.253	0.304	-0.160

* Significant Spearman's rank coefficients (p<0.05)
GCM; Gastrocnemius medialis, LVEF; Left ventricular ejection fraction, E/A; early filling flow peak velocity/atrial filling flow peak velocity, E'; early diastolic velocity, LVEDd; left ventricular end-diastolic diameter, GLS; global longitudinal strain

Conclusion

This study is the first to have found a significant association between cardiac dysfunction and the severity of respiratory muscle fibrosis in non-ambulant patients with DMD. Subsequent studies can examine the value of this parameter as an index for early diagnosis and disease progression and use it to explore new treatment targets or therapeutic effects.