Editorial

Myocardial fibrosis of the left ventricular posterior wall can be a target for early detection of cardiac involvement in patients with Duchenne muscular dystrophy

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Duchenne muscular dystrophy (DMD) is an X-linked hereditary muscular disorder that leads to degeneration and atrophy of skeletal and cardiac muscle. Skeletal muscle disease causes limb muscle weakness, with loss of ambulation at the ages of around 10 years or less. The majority of DMD patients develop dilated cardiomyopathy in their mid-teens, characterized by enlarged heart chambers and reduced cardiac wall thickness. On the other hand, intercostal and diaphragmatic respiratory muscle weakness and scoliosis leads to respiratory problems that force DMD patients to use respiratory devices. The cardiomyopathy emphasizes respiratory problems, and the DMD patient dies from cardiac and/or respiratory failure typically by 30 years of age [1].

Echocardiography is a noninvasive method of evaluating left ventricular (LV) size and systolic function to assess cardiac involvement in DMD patients, but is usually obtained after the onset of heart failure symptoms. Unfortunately, myocardial damage after the symptom onset with overt LV dysfunction may be irreversible and progressive, ending in death. Thus, earlier referral by some other methodology that identifies earlier disease is required [2]. Current treatment options are limited to glucocorticoids that produce inconsistent effects on myocardial disease. However, several studies have demonstrated that use of angiotensin-converting enzyme inhibitors, beta blockers, and aldosterone antagonists in patients with DMD reverse congestive heart failure signs and symptoms, delay progression of LV dysfunction, and improve systolic function [3]. If these treatments are initiated earlier, more beneficial effects may be potentially gained. Thus, earlier detection of subclinical myocardial disease and earlier initiation of these treatments may be necessary in DMD patients. End-stage cardiac pathology consists of alternating areas of myocyte hypertrophy, atrophy, and fibrosis [4]. On the other hand, myocardial fibrosis is initially localized to LV posterior wall (LVPW) [5,6], so that it should be a key issue to detect myocardial fibrosis in LVPW for early detection of subclinical myocardial disease in DMD patients.

In this issue of the Journal of Cardiology, Yamamoto et al. describe the usefulness of analyzing transmural myocardial strain profile (TMSP) with passive leg lifting in predicting subclinical LV dysfunction in DMD patients [7]. They used tissue Doppler-based radial strain for TMSP analysis. They have previously published another article presenting the utility of the TMSP analysis at rest in DMD patients [8]. In this previous article, they showed that a TMSP pattern with a notch can predict prevalence of wall motion abnormality at 1-year follow-up in LVPW with normally original contraction in DMD patients. The results are wonderful, and their method may be a promising tool to detect early myocardial disease in DMD patients. However, the etiology of the notch formation is unclear. They defined TMSP with a notch as the presence of an intra-myocardial descent between 2 peaks in the TMSP curve. In example pictures in their articles, it looks like the intra-myocardial descents locate in the epicardial half of LVPW. So, it can be speculated that this epicardial descent of the TMSP curve is the real essence of the abnormal sign because fibrosis begins in the outer half of the myocardium, especially in the LVPW in DMD patients [9]. It can be supposed that a descent of the TMSP curve in the outer half myocardium represents reduced radial strain of fibrotic layer in the epicardial side of LVPW. Viewed in this light, it appears reasonable that TMSP with a notch is predictive of the future presence of LVPW motion abnormality and is an early sign of subclinical myocardial disease. Previous studies have shown similar data consistent with this speculation [10,11]. In those cross-sectional studies where tissue Doppler-based strain analyses were also performed, a positive strain value in the inner layer and a negative strain value in the outer layer were simultaneously observed in LVPW of a substantial proportion of DMD patients. The previous and the current studies by Yamamoto et al. additionally provided important information about changes in wall motion of myocardium with such a biphasic TMSP pattern. The results are superb but further solution of the etiology is needed. Comparison of an echocardiographic TMSP analysis with other modalities, e.g. cardiac magnetic resonance with late gadolinium enhancement, may provide a clue to the etiology of TMSP with a notch. Also, TMSP had better be examined in various cardiomyopathies.
with different distribution of fibrosis in order to confirm the relationship between fibrosis distributions and TMSP patterns.

In their current paper published in this issue, Yamamoto et al. describe that TMSP with a notch persisting from rest to leg lifting stress is more accurately predictive of the presence of LV PW motion abnormality at 1-year follow-up, whereas presence of TMSP with a notch either at rest or during stress is predictive of the absence of LV PW motion abnormality. They speculate that increased preload by passive leg-lifting results in an increased peak strain value without changes in transmural strain distribution in normal myocardium according to Frank-Starling mechanism, but, to the contrary, the persisting TMSP with a notch at rest and during passive leg-lifting may reflect the presence of subclinical myocardial disease. It is reasonable. However, what about patients with appearance of TMSP with a notch during leg-lifting despite normal TMSP at rest, or what about patients with disappearance of TMSP with a notch during leg-lifting? It is left unanswered, but is probably a matter of degree. Temporal TMSP abnormality either at rest or during leg-lifting may be seen in patients with slighter myocardial fibrosis than in patients with persisting TMSP abnormality. It can be supposed that LV systolic dysfunction will be present much later also in patients with the temporal TMSP abnormality despite the absence of significant LV systolic dysfunction at 1-year follow-up. Future studies with much longer follow-up periods will be needed to address whether this speculation is correct or not.

There have been also other previous studies that tried to detect subclinical myocardial damage in DMD patients. Some studies used cardiac magnetic resonance but the others used echocardiography. In those cross-sectional echocardiographic studies, strain or strain rate of circumferential and/or radial directions was examined to detect subclinical myocardial damage in DMD patients [12,13]. In contrast, the present study by Yamamoto et al. was unique in terms that they analyzed TMSP with a more sophisticated tissue Doppler imaging method and they prospectively investigated time course of wall motion in myocardium with abnormal TMSP patterns. Hopefully, great efforts of these earnest researchers will lead to earlier detection of subclinical myocardial disease in DMD patients, and will help to improve prognoses in DMD patients.

References


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