

Evaluate Myocardial Function for Patient with Marfan Syndrome by Using Phase-Contrast Magnetic Resonance Imaging

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Introduction: Marfan syndrome (MFS) is an inherent mutation of the fibrillin-1 gene, which encodes the fibrillin-1 protein [1]. This protein is in charge of forming microfibrils, which is a basic material to build the elastic fibers. Previously, numerous studies investigated aortic flows of MFS and tried to figure out a specific pattern for the most life-threatening complications, aortic dissection or rupture in MFS. Milewicz et al have reported that medical and surgical treatments of aortic disease in patients with MFS and addresses the treatment of aortic disease in children and pregnant women with the condition [2]. In addition, Geiger et al also explored that the 4D flow analysis revealed significant differences between MFS and normal, and concluded that local helix flow in the patients' AAO may be associated with the increased incidence of aortic root dilatation [3]. Since myocardium is also consisted of elastic fibers [4], a scheme to evaluate myocardial function in MFS may also play an important role on surveillance of the progress of MFS. Rybczynski et al have explored the myocardial function of MFS patients by echocardiography and concluded that reduced systolic and early diastolic and early diastolic tissue Doppler velocities in adults with MFS [5]. Up to date, a scheme to evaluate myocardial function of MFS by MRI is still deficient. In this study, we used dark-blood phase-contrast (PC) MRI to compute tissue phase mapping (TPM) [6] of MFS. The three-directional wall motion velocities and time-to-peak (TTP) were computed. The indices were compared with age-matched normal controls to show the myocardial abnormality of MFS.

Methods: The study population consisted of 12 MFS patients (age: 35 ± 13 y/o; male: 11; female: 1) and 9 normal controls without history of cardiovascular diseases (age: 34 ± 12 y/o; male: 4; female: 5). The PC-MRI with 2D-FLASH sequence was performed on a 3 Tesla MR scanner (Trio, Siemens, Erlangen, Germany) using the body-arrayed coil with prospective ECG triggering, sampling 90% of cardiac cycle and navigator-guided free-breathing technique. The images at base, mid, and apex were acquired in a short-axis view with parameters of TR/TE=26/4.17 ms, flip angle=7°, pixel size= $1.18 \times 1.18 \times 6$ mm³, and Venc=15 cm/s in-plane and 25 cm/s through-plane. The scanning time of one slice is around 2 min, depending on subject's cardiac rate and respiratory rate. The regions-of-interest (ROIs) on basal, mid, and apical planes were determined manually on magnitude images and were applied to phase images for calculation of wall motion velocity. The ROIs of three planes were divided into 16 segments (Fig.1) with a home-developing program. The time courses of radial (Vr), tangential (Vphi), and longitudinal (Vz) velocities and time-to-peak (TTP) of three directions were computed. The TTP values were normalized to cardiac cycle and showed as the percentage of the systolic period (% of end systole, %ES) or diastolic period (% of end diastole, %ED). The end systolic phase for each slice was determined manually as the time point corresponding to the smallest LV cavity on midventricular images [7]. The twist velocities were defined by subtracting the apical Vphi from basal Vphi [8]. Positive twist velocities represented that the basal ventricular myocardium was relatively clockwise to the apical ventricular myocardium.

Results: As shown in Fig. 2(a), MFS showed significant higher systolic peak Vz (pVz) on base than normal controls (-6.67 ± 2.07 vs. -4.91 ± 2.17 cm/s, $p < 0.05$). In general, MFS demonstrated shorter diastolic TTP compared to normal controls (Figs. 2(b, c)), particularly significant ($p < 0.05$) on apical TTPz (36.92 ± 12.01 vs. 51.37 ± 14.21 %ED), basal TTPr (33.27 ± 13.86 vs. 44.70 ± 11.86 %ED), and apical TTPr (42.25 ± 19.15 vs. 54.09 ± 11.46 %ED). As shown in Fig. 3(a), systolic pVz were significant larger in MFS than normals on lateral-anterior segments. Figure 3(b) indicated diastolic TTPz were markedly shorter in patient than MFS on mid inferior and apical segments. In addition, Fig. 3(c) showed that diastolic TTPr were significant shorter in MFS than normals on basal septal-inferior-lateral and mid septal segments. As for twist velocity (Fig.4), MFS patients demonstrated lower peak twist velocities at both of systole and diastole than normal. In addition, the diastolic TTP were shorter in MFS than normals ($56.44 \pm 10.01\%$ vs. $62.92 \pm 6.67\%$, $p < 0.05$).

Discussion & Conclusions: In this study, wall motion velocities as well as diastolic TTP were analyzed globally and regionally to non-invasively differentiate MFS from normals. The MFS patients presented higher systolic pVz values in basal plane. Besides, MFS showed shorter diastolic TTPz and TTPr in apical and basal planes. Since MFS patients have inherently mutative fibrillin-1 protein and thus disordered elastic fibers in connective tissue, the results shown in this work may reflect deficient elasticity of myocardium in MFS. The less elastic myocardium may provide less damping effect to the force of the in-flowing (diastolic) and out-flowing (systolic) blood. Therefore, the deformation of the myocardium reached peak systolic pVz in a shorter time. In conclusion, the systolic pVz, diastolic TTPz and TTPr, and twist velocity provide satisfied information to diagnose myocardial function of MFS patients. It is helpful to use the mentioned indices to evaluate the progress of MFS and to monitor acute cardiac arrest in MFS. The long-termed follow-up investigations of MFS patients are necessary to establish the myocardial function and prognosis for MFS patients.

References: [1] Anatoli Kiotsekoglou et al. (2009), *European Journal of Echocardiography*, 10, 947-955. [2] Milewicz et al. (2005), *Circulation*, 111, 150-157 [3] J. Geiger et al (2012) *JOURNAL OF MAGNETIC RESONANCE IMAGING* 35:594-600 [4] de Souza RR (2002), *Biogerontology*, 3, 325-335 [5] Meike Rybczynski et al (2007), *Clinical Cardiology*, 30, 19-24 [6] Daniela Föll et al. (2009), *Journal of magnetic resonance imaging*, 1043-1052 [7] Steffen E. Petersen et al. (2006), *Radiology*, 238, 816-826 [8] Daniela Föll et al. (2010), *Circulation Cardiovascular Imaging*; 3, 54-64

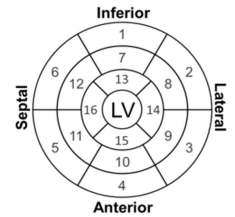


Fig.1. The regions-of-interest (ROIs) on basal, mid, and apical planes were determined manually and divided into 16 segments

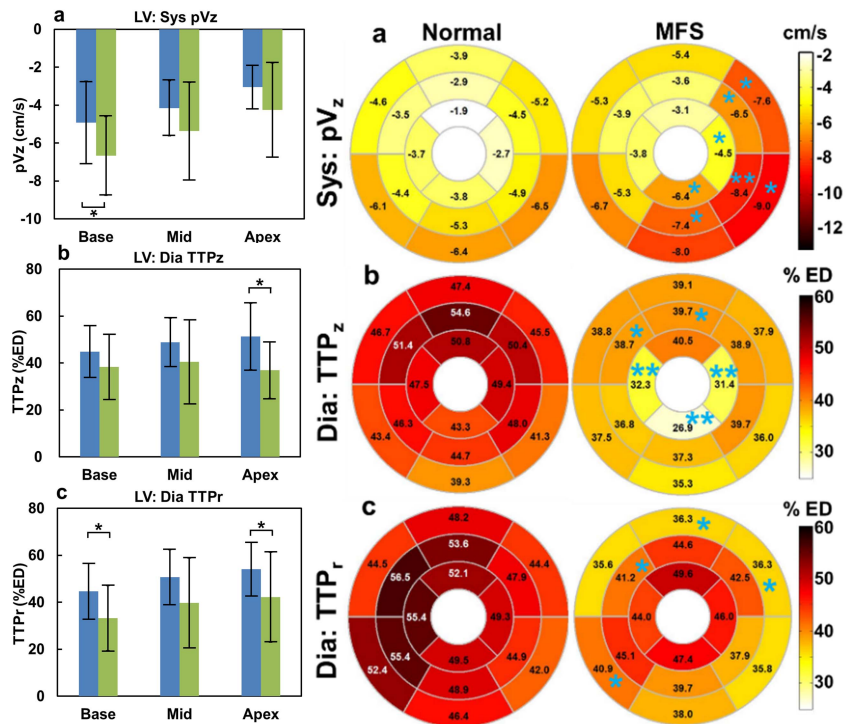


Fig. 2. The global function of pVz (a) and TTPr in volunteers (Blue) and in MFS (Green). **Fig. 3.** The regional function of systolic pVz (a), diastolic TTPz (b) and diastolic TTPr (c) in normals and MFS patients. * $p < 0.05$, ** $p < 0.01$.

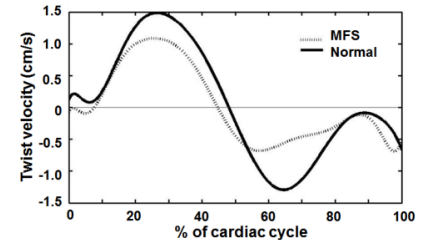


Fig. 4. The mean twist velocity time courses in MFS and normals were shown.