# Evaluate Myocardial Dyssynchrony Index in Left Ventricle for Marfan Syndrome Patients by Using Phase-Contrast Magnetic Resonance Imaging

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**Introduction:** Marfan syndrome (MFS) is a multi-systemic connective disorder and an inherent mutation affecting fibrillin-1 gene. Previous study has investigated aortic flows and tried to identify a specific pattern for the most life-threatening complications [1]. In addition, Geiger et al also explored that the 4D flow analysis revealed significant differences of flow patterns [2]. Since myocardium is also consisted of elastic fibers [3], a scheme to evaluate myocardial function in MFS may also play an important role on surveillance of the progress of MFS. Foley et al have reported that the cardiac ventricular dyssynchrony contributed to clinical syndrome of heart failure [4]. In this study, we used dark-blood tissue phase mapping (TPM) with phase-contrast MRI (PC-MRI) to quantify the left ventricular (LV) myocardial function and the myocardial dyssynchrony index. **Methods:** The study population consisted of 14 MFS patients (age: 24 ± 7 y/o; male: 10; female: 4) and 11 normal controls without history of cardiovascular diseases (age: 24 ± 5 y/o; male: 6; female: 5). Body surface area (BSA) (p=0.0045) and left ventricular end diastolic volume (LVEDV) (p=0.042) as assessed by standard MR cine SSFP sequence were significantly higher in MFS patients compared to Normals (table.1). All exams was performed on a 3 Tesla MR scanner (Trio, Siemens, Erlangen, Germany) using the body-arrayed coil with prospective ECG trigging (sampling 85-90% of cardiac cycle) and navigator-guided free-breathing technique. The images were acquired in a short-axis view with a black-blood prepared gradient echo TPM sequence (TR/TE = 26 ms /4.17 ms, flip angle = 7° , pixel size = 1.18 × 1.18 mm$^2$, slice thickness = 6 mm, Venc = 15 cm/s in-plane and 25 cm/s through-plane). The regions-of-interest (ROIs) on three planes were determined manually with a home-developed program on magnitude images and were applied to phase images for calculation of wall motion velocity. The ROIs of base, mid-ventricular, and apex were divided into 6, 6, and 4 segments, respectively (Fig. 1). The time courses of radial (Vr) and longitudinal (Vz) velocities were computed. The time-to-peak (TTP) values were normalized to the duration of systole of each subject and showed as the percentage of the end systole (%ES). The dyssynchrony index (DI) is defined as the standard deviation (SD) of the TTP among segments in each slice. Differences between two groups were assessed by two-tailed Student's t-test and $p < 0.05$ was considered statistically significant.

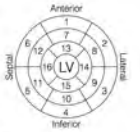


Fig 1. The ROIs of base, mid-ventricular, and apex were divided into 6, 6, and 4 segments respectively

| | Normal | MFS | Normals | MFS patients |
|---|---|---|---|---|
| Age (years) | 11 | 14 | 24.09±3.32 | 24.92±7.60 |
| Gender | 11 | 14 | 5 Female/6 Male | 4 Female/10 Male |
| BSA ($m^2$) | 10 | 11 | 1.67±0.17 | 1.94±0.25** |
| LVM (g) | 10 | 11 | 105.13±24.49 | 127.67±37.98 |
| LVMI (g/$m^2$) | 10 | 11 | 62.56±12.36 | 64.92±14.11 |
| LVESV($cm^3$) | 10 | 11 | 26.89±9.39 | 33.16±11.88 |
| LVESVI($cm^3/m^2$) | 10 | 11 | 16.06±3.40 | 16.98±5.44 |
| LVEDV($cm^3$) | 10 | 11 | 86.59±16.70 | 91.14±32.93* |
| LVEDVI($cm^3/m^2$) | 10 | 11 | 56.90±8.80 | 59.65±14.94 |
| LVEF (%) | 10 | 11 | 72.51±5.59 | 71.81±5.43 |

Table. 1 Basic characteristics of study population. Three of MFS patient has either cine SSFP image artifact or not enough cardiac phase so that LVM, LVMI, LVESV, LVEDV, LVESVI, LVESVI, LVEF cannot be computed.

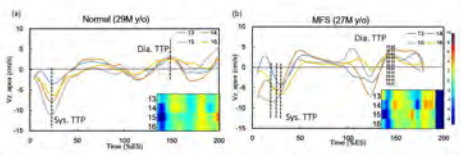


Fig 2. The time courses of apical Vz of a 29 y/o normal male and a 27 y/o male MFS patient were shown. The first local peak corresponds to systolic TTP and the diastolic TTP is at approximate 150 %ES (dashed line). The time course of apical Vz of each segment was transferred into a 2D color plot, as shown in the inserted plot.

**Results:** The representative time courses of apical Vz of a 29 y/o normal male and a 27 y/o male MFS patient were shown in Fig. 2. MFS patient showed dyssynchronized systolic TTPz and diastolic TTPz in apex. The inserted 2D color plot also demonstrated this situation. Figures 3(a, b) displayed color plots of Vr of 4 segments in apex, respectively. In general, normals exhibited more synchronized TTPr among segments than MFS patients either in systole or diastole. The same trend could be observed in apical Vz, as shown in Figs. 4(a, b). Table 2listed the quantified DI of TTPr in systole and diastole among segments of each slice. MFS patients exhibited larger DI than normal, particularly in apex for systolic TTPr (11.93 ± 4.79 %ES vs. 7.71 ± 4.36 %ES, p = 0.014) and diastolic TTPr (6.87 ± 7.03 %ES vs. 4.06 ± 1.53 %ES, p = 0.07). As for Vz (Table 3), MFS also displayed higher DI in apex: systole (5.85 ± 7.62 %ES vs. 2.61 ± 1.49 %ES, p = 0.07) and diastole (7.57 ± 3.92 %ES vs. 4.25 ± 2.29 %ES, p = 0.048). The group analysis of Vz shown in normal group exhibited a shorting motion toward apex (i.e. negative velocity) after the early diastolic peak in each slices (Figs. 5(a-c)) and was missing in MFS (Figs. 5(d-f)). **Discussion & Conclusions:** LV function is one of the most prognostic determinants of cardiac disease. Left ventricular dyssynchrony, assessed by PC-MRI and has been proved to be strongly associated with heart failure and poor prognosis [5] in MFS group. In our work, the regional Vr and Vz as well as the TTPr and TTPz of each segment of basal, mid, and apical slices were evaluated for MFS patients. In comparison with normal group, MFS group demonstrated dyssynchronized TTPr or TTPz either in systole or in diastole (Figs. 2-4). The quantified index indicated significant larger DI in systolic Vr (Table 2) and diastolic Vz (Table 3) in apex of MFS, suggesting the impaired myocardial motion and thus the apical dyssynchronization in MFS group. Foley et al have reported that the LV dyssynchrony based on radial systolic motion or diastolic velocities significantly correlated with changes in LVEF and LV mass [4]. In our study, there were no significantly difference in LVEF between two groups. It can be seen that before LVEF changed, MFS group already exhibited significant abnormal systolic TTPr and diastolic TTPz in apex, reflected by larger DI values. It might indicate that the circumstance of abnormal myocardial motion can occur prior to degenerate cardiac function (i.e. LVEF). Kiotsekoglou et al have applied tissue Doppler imaging (TDI) over the lateral tricuspid valve corner measuring peak early diastolic (E') and peak atrial diastolic annular (A') myocardial velocities. They concluded that MFS groups exhibited reduced E' and A' compared with normals (p<0.001) [6]. Our study also demonstrated that MFS patients displayed no shorting motion toward apex after the early diastolic peak, suggesting that the lack of LV elastic recoil may be associated with following weak atrial contraction [6]. In conclusion, the investigated LV myocardial function and the quantified myocardial DI can reflect the abnormal dyssynchronized conditions for MFS and provide helpful information to evaluate myocardial function before deteriorated cardiac function was shown.

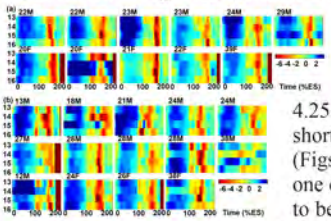


Fig 3. 2D color plots of Vr for normals (a) and MFS patients (b) in apex.

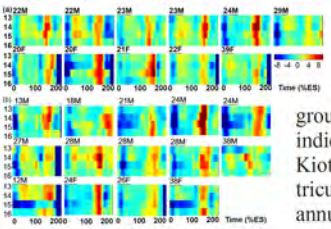


Fig 4. 2D color plots of Vz for normals (a) and MFS patients (b) in apex.

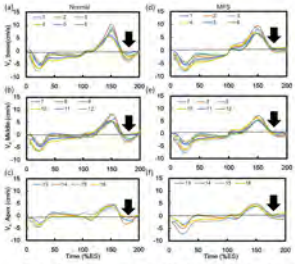


Fig. 5. The group analysis of Vz in three slices of normal group (a-c) and MFS group (d-e). Arrows indicated the characteristic of a shorting motion toward apex after the early diastolic peak in normals. This sign was missing in MFS.

Table 2. The Vr dyssynchrony index (*p<0.05)

| Dyssynchrony index (%ES) | Vr_sysTTP | | | Vr_diaTTP | | |
|---|---|---|---|---|---|---|
| segments | 1-6 (BASE) | 7-12(MIDDLE) | 13-16(APEX) | 1-6 (BASE) | 7-12(MIDDLE) | 13-16(APEX) |
| MFS | 10.08 ± 3.62 | 10.39±3.11 | 11.93±4.79 | 10.08 ± 3.62 | 7.16±3.86 | 6.87±7.03 |
| Normals | 8.31 ± 2.60 | 8.74±3.15 | 7.71±4.36 | 8.31 ± 2.60 | 5.59±2.34 | 4.06±1.53 |
| p- value | 0.07 | 0.1 | 0.014* | 0.39 | 0.11 | 0.07 |

Table 3. The Vz dyssynchrony index (*p<0.05)

| Dyssynchrony index (%ES) | Vz_sysTTP | | | Vz_diaTTP | | |
|---|---|---|---|---|---|---|
| segments | 1-6 (BASE) | 7-12(MIDDLE) | 13-16(APEX) | 1-6 (BASE) | 7-12(MIDDLE) | 13-16(APEX) |
| MFS | 3.31±2.74 | 3.66±2.85 | 5.85±7.62 | 3.91±2.25 | 4.81±3.92 | 7.57±6.57 |
| Normals | 2.61±1.38 | 4.73±7.64 | 2.61±1.49 | 3.10±1.10 | 4.27±1.86 | 4.25±2.29 |
| p- value | 0.2 | 0.33 | 0.07 | 0.11 | 0.32 | 0.048* |

**References:** [1]Kiotsekoglou A *et al,Eur J Echocardiogr* 2008, **9**(5):605-613. [2]Geiger J *et al,J Magn Reson Imaging* 2012, **35**(3):594-600. [3]de Souza RR,*Biogerontology* 2002, **3**(6):325-335. [4]Foley PW *et al,J Cardiovasc Magn Reson* 2009, **11**:50. [5]Foll D *et al,J Magn Reson Imaging* 2011, **34**(3):518-525. [6]Kiotsekoglou A *et al,Eur J Echocardiogr* 2009, **10**(8):947-955.