Evaluation of left ventricular systolic function in young adults with mitral valve prolapse

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E Malev, E Zemtsovsky, A Pshepiy, E Timofeev, S Reeva, M Prokudina. Evaluation of left ventricular systolic function in young adults with mitral valve prolapse. Exp Clin Cardiol 2012;17(4):165-168.

OBJECTIVE: To evaluate left ventricular function in young adults with mitral valve prolapse (MVP) without significant mitral regurgitation using two-dimensional strain imaging.

METHODS AND RESULTS: A total of 58 asymptomatic young subjects (mean [± SD] age 19.7±1.6 years; 72% male) with MVP were compared with 60 sex- and age-matched healthy subjects. MVP was diagnosed by billowing one or both mitral leaflets >2 mm above the mitral annulus in the long-axis parasternal view. Longitudinal, radial and circumferential strain and strain rate were determined using speckle tracking with a grey-scale frame rate of 50 fps to 85 fps. There were no significant differences in the global systolic left ventricular function of the subjects with MVP compared with the control group. In the MVP group, most of the global myocardial systolic deformation indexes were not reduced. Only the global circumferential strain showed a decrease in the prolapse subjects. Regional, longitudinal, circumferential and radial strain and strain rate were decreased only in septal segments. A decrease in the rotation of the same septal segments at the basal level was also observed.

CONCLUSION: Regional septal myocardial deformation indexes decrease in subjects with MVP. These changes may be the first sign indicating the deterioration of left ventricular systolic function as well as the existence of primary cardiomyopathy in asymptomatic young subjects with MVP.

Key Words: *Cardiomyopathy; Left ventricular systolic function; Mitral valve prolapse; Myocardial deformation*

Mitral valve prolapse (MVP) is a hereditary connective tissue disease with (sporadic or familial) autosomal dominant and X-linked inheritance (1). According to The Framingham Heart Study, MVP has an estimated prevalence of 2.4% in the general population (2-4). The overall prognosis of patients with MVP is excellent, but a small subset will develop serious complications, including arrhythmias and sudden cardiac arrest, factors that do not completely depend on the severity of mitral regurgitation (MR) (5).

In some inherited connective tissue diseases that involve the cardiovascular system (eg, Marfan syndrome), impairment of left ventricular (LV) systolic function has often been reported, which does not appear to depend on aortic dilation or secondary aortic regurgitation and MVP with associated mitral regurgitation. These cases have been described as Marfan-related cardiomyopathy (6,7). The existence of primary cardiomyopathy in connective tissue diseases is currently being debated; however, it is well known that the organization and function of the myocardium is highly dependent on the cardiac extracellular matrix, which is comprised of fibrillar proteins, such as collagen, elastin and fibronectin, as well as signalling molecules and enzymes (8).

LV contraction abnormalities in symptomatic MVP patients without severe MR – but with ventricular arrhythmias – have been discovered and described in some studies using cardiac tomography, radionuclide angiography and single photon emission computed tomography (9-11). In addition, a marked decrease of myocardial deformation indexes has been demonstrated in patients with degenerative MR (12,13). However, there are currently no data regarding LV systolic function in asymptomatic young subjects with MVP.

Transthoracic echocardiography remains the method of choice for diagnosing MVP (5) and is an effective tool for the assessment of LV systolic function based on the measurement of the LV ejection fraction. Two-dimenstional (2-D) speckle-tracking echocardiography is useful in detecting early LV dysfunction within the setting of systemic diseases with cardiac involvement (14). Therefore, the goal of the present study was to evaluate LV systolic function in young adults with MVP without significant MR using 2-D strain imaging.

METHODS

Study population

A total of 58 asymptomatic young subjects (28% female, 72% male) with MVP were consecutively enrolled. The mean (± SD) age of the subjects was 19.7±1.6 years. The control group consisted of 60 sex- and age-matched healthy subjects. All subjects provided informed consent and the protocol was approved by the local ethics committee.

Echocardiography

All echocardiographic measurements were performed by an experienced, certified echocardiographer using a Vivid 7 ultrasound system (GE Healthcare, United Kingdom), equipped with a harmonic 3.5 MHz phased-array transducer.

MVP was diagnosed by billowing one or both mitral leaflets >2 mm above the mitral annulus in the long-axis parasternal view (2,3). A maximal leaflet thickness of ≥5 mm was defined as classic MVP and otherwise was defined as nonclassic MVP. MR was assessed according to the European Association of Echocardiography recommendations for the assessment of valvular regurgitation (15).

The end-diastolic and end-systolic LV diameters were measured using B-mode echocardiography. The LV end-diastolic (EDV) and end-systolic (ESV) volumes were calculated from the apical two-chamber and four-chamber views using a modified version of Simpson's rule. The LV ejection fraction was calculated using the following formula: (EDV−ESV)/EDV×100. The left atrial volume index was measured using the biplane area-length method (from the apical two-chamber and four-chamber views) and was indexed to the surface area of the body. The transmitral flow velocity was recorded from the apical four-chamber view. The peak early diastolic velocity (E), peak atrial velocity (A), their ratio (E/A) as well as the peak E deceleration time (E-DT) were all measured. The mitral annular motion velocity was recorded at the interventricular septum and lateral wall in the apical four-chamber view using pulsed tissue Doppler echocardiography. The peak early diastolic motion velocity (e′) and the E/e′ ratio were determined.

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TABLE 1
Demographic and anthropometric characteristics of mitral valve prolapse (MVP) and control groups

Characteristic	MVP group	Control group	P
Age, years	19.7±1.6	19.9±1.5	0.62
Sex, male, n (%)	42 (72)	38 (63)	0.48
Height, m	1.89±0.11	1.79±0.09	0.0003
Weight, kg	61.6±7.9	60.5±9.5	0.64
Body surface area, m^2	1.88±0.08	1.78±0.16	0.004
Heart rate, bpm	76.8±14.3	74.2±15.7	0.51
Systolic BP, mmHg	115.1±8.5	117.8±9.4	0.25
Diastolic BP, mmHg	68.6±7.4	71.7±8.9	0.15

Data presented as mean ± SD unless otherwise indicated. BP Blood pressure; bpm Beats per minute

2-D strain imaging

Longitudinal strain and strain rate (SR) were determined using the three standard apical views, as well as radial and circumferential strain and SR from three parasternal short axis views at three levels, using speckle tracking with a grey-scale frame rate of 50 fps to 85 fps. Rotation was measured in each segment at both basal and apical levels.

At each plane, one cardiac cycle was acquired (while the subject held their breath) and stored. Image analysis was performed offline on an EchoPAC 08 workstation (GE Healthcare, United Kingdom). The LV was divided into 16 segments, with only four segments at the apical level. SR was determined as the maximal negative value during the ejection phase, and peak systolic strain as the magnitude of strain at the aortic valve closure.

Statistical analysis

Variables are presented as mean ± SD. Categorical variables are presented as percentages. Differences between groups were analyzed using the Student's *t* test for continuous variables and the χ^2 test for categorical variables. The relationship between pairs of continuous variables was expressed by Pearson correlation coefficients. Differences were considered to be statistically significant at $P<0.05$. All statistical analyses were performed using Statistica 8 software (StatSoft Inc, USA).

RESULTS

Demographic and anthropometric data

There were no significant differences between the MVP and control groups in most demographic and anthropometric characteristics such as age, sex proportion, weight, heart rate and blood pressure (Table 1). However, patients with MVP were taller and had a larger body surface area, which is common for young adults with this disease (16).

Echocardiographic data

There were no significant differences in LV dimensions and volumes or in global systolic function between the MVP group and the control group (Table 2). Other chamber dimensions and volumes (right ventricular end-diastolic dimension and left atrial volume index) also did not differ between groups. Global diastolic LV function, evaluated by transmitral and tissue Doppler echocardiography, did not vary between MVP and healthy subjects.

MVP subjects, when compared with the control group, had larger aortic root dimensions at the sinus level of the Valsalva and ascending aorta, but the Z-score was the same in both groups because of the higher body surface area in MVP subjects. By contrast, the pulmonary artery diameter was similar in both groups. Subjects with MVP had significantly longer and thicker mitral valve leaflets and a larger mitral annulus diameter than the healthy subjects. MR was absent to mild in both groups, and mostly late systolic in the MVP subjects (P=0.013). Sixteen subjects from the MVP group exhibited classic MVP and 42 subjects exhibited nonclassic MVP. These two subgroups did not differ in anthropometric and echocardiographic data, except for the thickness of their mitral valve leaflets (anterior leaflet 4.7±1.3 mm (classic) versus 2.3±0.6 mm (nonclassic); posterior leaflet 5.0±1.1 mm (classic) versus 3.1±0.8 mm (nonclassic).

TABLE 2
Comparison of echocardiographic data in mitral valve prolapse (MVP) and control groups

	MVP group	Control group	P
EDD, mm	46.9±5.0	45.6±4.5	0.32
ESD, mm	29.5±4.6	28.1±3.6	0.20
EDV, mL	92.6±22.9	89.3±19.2	0.55
ESV, mL	34.5±11.6	33.9±8.9	0.82
LVEF, %	62.7±6.6	62.0±5.4	0.66
E, m/s	0.89±0.19	0.90±0.16	0.83
E/A	1.66±0.41	1.74±0.42	0.46
E-DT, ms	167±34	164±42	0.76
e′, cm/s	15.2±1.2	15.4±1.4	0.56
E/e′	5.9±1.7	5.8±1.2	0.83
LV mass index, g/m^2	82.5±21.4	83.5±15.9	0.84
LAVI, mL/m^2	22.1±2.7	21.6±2.9	0.49
RVEDD, mm	23.5±3.7	24.5±3.7	0.30
Aortic root, mm	28.6±2.9	26.7±2.9	0.015
Z-score, cm/m^2	1.59±0.12	1.59±0.17	0.94
Ascending aorta, mm	26.0±4.4	23.7±2.9	0.02
Pulmonary artery, mm	19.4±2.6	19.9±2.8	0.48
Anterior leaflet length, mm	25.6±3.3	21.8±2.3	<0.0001
Anterior leaflet thickness, mm	3.4±1.1	2.6±0.6	0.001
Posterior leaflet length, mm	14.2±2.8	11.3±2.0	<0.0001
Posterior leaflet thickness, mm	3.5±1.2	2.8±0.6	0.006
Mitral annular diameter, mm	31.3±3.7	26.0±3.6	<0.0001
Mitral regurgitation, n (%) none/ n (%) mild	12 (21)/46 (79)	20 (33)/40 (66)	0.27
Late-systolic mitral regurgitation, %	59	26	0.013

Data presented as mean ± SD unless otherwise indicated. E Peak early diastolic velocity; e' Early diastolic mitral annular motion velocity; E/A Ratio of early and atrial diastolic velocities; EDD End-diastolic diameter; E-DT Peak E deceleration time; EDV End-diastolic volume; ESD End-systolic diameter; ESV End-systolic volume; LAVI Left atrial volume index; LV Left ventricular; LVEF Left ventricular ejection fraction; RVEDD Right ventricular end-diastolic diameter; Z-score Aortic root diameter, standardized to body surface area

Myocardial deformation indexes

Of 4012 segments, only 3101 (73.3%) were accepted for deformation analysis. There were no differences in the global longitudinal peak systolic strains and SR between the MVP and control groups (Table 3). However, a significant decrease in inferoseptal longitudinal strains and SR in MVP subjects was observed when compared with the control group. In other segments, there were no significant differences in longitudinal deformation indexes. Circumferential SR in the MVP group also showed a significant decrease only in anteroseptal segments, with a preserved global value. In contrast, the global and segmental circumferential peak systolic strain was decreased in subjects with MVP. Radial, global and segmental systolic deformation indexes did not differ between the MVP and control groups, except for the anteroseptal radial peak systolic strain, which was significantly lower in the MVP group.

There were also no differences in the twist and rotation at basal and apical levels between MVP and control groups. However, anteroseptal basal segments rotated significantly more clockwise in MVP subjects compared with the control group.

Global myocardial indexes in the MVP group positively correlated with the aortic root diameter (longitudinal strain r=0.46; P=0.001, circumferential SR r=0.42; P=0.003). The same correlation was found in the septal segment deformation indexes (inferoseptal longitudinal strain r=0.49; P=0.0009, anteroseptal circumferential SR r=0.45;

P=0.001). None of the deformation indexes correlated with the maximal depth of mitral leaflet prolapse.

DISCUSSION

We found typical changes in mitral valve and aortic root morphology in our young subjects with MVP. It is known that MVP is associated with aortic root enlargement in patients with inherited connective tissue disorders. MVP is also an independent predictor of greater aortic size in a large population with otherwise normal echocardiographic parameters (17). The relationships between the measures of LV morphology and the myocardial strain and SR have been reported previously in healthy subjects (18). However, there were no data on correlations between regional, longitudinal and circumferential peak systolic strain and SR and aortic root size in patients with MVP.

Global systolic (calculated using Simpson's rule) and diastolic LV functions (evaluated using transmitral and tissue Doppler echocardiography), as expected, did not change in asymptomatic young MVP subjects without significant MR. Most global myocardial systolic and diastolic deformation indexes in the MVP group were also not reduced. Only global circumferential strain was decreased in MVP subjects. In the present study, the global strain and SR in the control group did not differ from reference values in a large young adult cohort examined in previous studies (19).

The present study also revealed a decrease in the longitudinal and circumferential peak systolic strain and SR in septal segments, as well as a decrease in the radial strain, which has not previously been described in patients with MVP. In genetic diseases, such as Friedreich's ataxia, Fabry disease or Duchenne cardiomyopathy, the first regional deformation change occurs in the inferolateral segment; as fibrosis develops first in this area, the reduction of local strain rates becomes apparent (20). We cannot suggest that the local reduction of myocardial indexes – identified in asymptomatic MVP subjects – is associated with septal fibrosis; further studies using magnetic resonance imaging are needed. However, these changes of deformation may be the first signs of future deterioration of the LV systolic function resulting from MVP progression.

Study limitations

Several limitations of the present study should be addressed. The results of the present study were obtained from a relatively small group of young adults with MVP. There was also a greater proportion of males than females in both the MVP and control groups, and this difference could affect the magnitude of myocardial deformation indexes, which are normally higher in women (21).

Circumferential and radial strain and SR, in contrast with longitudinal, are not yet validated and accepted for use in a wide clinical setting. The 2-D strain software used in the present study, similar to other commercially available tools, has limited capability to change preferences, and the technology behind the analyses is hidden from the user due to the program's simplistic nature (21).

TABLE 3
Global and septal myocardial systolic deformation indexes

	MVP group	Control group	P
Longitudinal systolic strain			
Global	–19.6±2.5	–20.5±2.6	0.18
Anteroseptal	–18.7±2.5	–19.8±2.4	0.09
Inferoseptal	–19.3±2.9	–20.7±3.1	0.04
Longitudinal peak systolic strain rate			
Global	–1.27±0.18	–1.32±0.16	0.26
Inferoseptal	–1.07±0.14	–1.18±0.19	0.01
Circumferential systolic strain			
Global	–17.2±2.5	–19.9±3.7	0.002
Anteroseptal	–21.3±2.4	–24.8±5.1	0.001
Anterior	–15.2±4.1	–18.9±5.2	0.004
Anterolateral	–12.8±4.5	–15.8±5.3	0.02
Inferolateral	–13.9±4.5	–16.5±5.3	0.05
Inferior	–16.2±5.3	–19.5±5.1	0.02
Inferoseptal	–21.3±3.5	–23.6±4.6	0.02
Circumferential peak systolic strain rate			
Global	–1.35±0.22	–1.39±0.29	0.55
Anteroseptal	–1.48±0.29	–1.68±0.39	0.03
Radial systolic strain			
Global	41.7±14.0	44.5±10.6	0.39
Anteroseptal	31.8±14.7	40.7±16.4	0.03
Radial peak systolic strain rate			
Global	1.57±0.37	1.60±0.44	0.78
Rotation			
Mean basal	–5.3±2.5	–6.0±2.3	0.27
Anteroseptal basal	–5.0±2.0	–6.1±2.1	0.04
Mean apical	6.8±2.5	6.8±2.6	0.96
Septal apical	6.6±2.7	6.9±3.0	0.69

Data presented as mean ± SD unless otherwise indicated. MVP Mitral valve prolapse

CONCLUSION

Septal myocardial deformation indexes were decreased in young subjects with MVP when compared with a healthy control group. These changes in deformation may be the first signs of deterioration of the LV systolic function and the existence of primary cardiomyopathy in asymptomatic young subjects with MVP. However, this fact needs to be further confirmed in larger studies.

CONFLICT OF INTEREST: The authors have no conflicts of interest to declare.

REFERENCES

1. Grau JB, Pirelli L, Yu PJ, et al. The genetics of mitral valve prolapse. Clin Genet 2007;72:288-95.
2. Freed LA, Levy D, Levine RA, et al. Prevalence and clinical outcome of mitral-valve prolapse. N Engl J Med 1999;341:1-7.
3. Freed LA, Benjamin EJ, Levy D, et al. Mitral valve prolapse in the general population: The benign nature of echocardiographic features in the Framingham Heart Study. J Am Coll Cardiol 2002;40:1298-304.
4. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2006;48:3:e1-148.
5. Hayek E, Gring CN, Griffin BP. Mitral valve prolapse. Lancet 2005;365:507-18.
6. Kiotsekoglou A, Saha S, Moggridge JC, et al. Impaired biventricular deformation in Marfan syndrome: A strain and strain rate study in adult unoperated patients. Echocardiography 2011;28:416-30.
7. Alpendurada F, Wong J, Kiotsekoglou A, et al. Evidence for Marfan cardiomyopathy. Eur J Heart Fail 2010;12:1085-91.
8. Pope AJ, Sands GB, Smaill BH, LeGrice IJ. Three-dimensional transmural organization of perimysial collagen in the heart. Am J Physiol Heart Circ Physiol 2008;295:H1243-H1252.
9. Delhomme C, Casset-Senon D, Babuty D, et al. A study of 36 cases of mitral valve prolapse by isotopic ventricular tomography. Arch Mal Coeur Vaiss 1996;89:1127-35.
10. Lumia FJ, LaManna MM, Atfeh M, Maranhao V. Exercise first-pass radionuclide assessment of left and right ventricular function and valvular regurgitation in symptomatic mitral valve prolapse. Angiology 1989;40:443-9.
11. Casset-Senon D, Babuty D, Philippe L, et al. Fourier phase analysis of SPECT equilibrium radionuclide angiography in symptomatic patients with mitral valve prolapse without significant mitral regurgitation: Assessment of biventricular functional abnormalities suggesting a cardiomyopathy. J Nucl Cardiol 2000;7:471-7.
12. Marciniak A, Claus P, Sutherland GR, et al. Changes in systolic left ventricular function in isolated mitral regurgitation. A strain rate imaging study. Eur Heart J 2007;28:2627-36.

13. Lancellotti P, Cosyns B, Zacharakis D, et al. Importance of left ventricular longitudinal function and functional reserve in patients with degenerative mitral regurgitation: Assessment by two-dimensional speckle tracking. J Am Soc Echocardiogr 2008;21:1331-6.
14. Leung DY, Ng AC. Emerging clinical role of strain imaging in echocardiography. Heart Lung Circ 2010;19:161-74.
15. Lancellotti P, Moura L, Pierard LA, et al. European Association of Echocardiography recommendations for the assessment of valvular regurgitation. Part 2: Mitral and tricuspid regurgitation (native valve disease). Eur J Echocardiogr 2010;11:307-32.
16. Flack JM, Kvasnicka JH, Gardin JM, et al. Anthropometric and physiologic correlates of mitral valve prolapse in a biethnic cohort of young adults: The CARDIA study. Am Heart J 1999;138:486-92.
17. Matos-Souza JR, Fernandes-Santos ME, Hoehne EL, et al. Isolated mitral valve prolapse is an independent predictor of aortic root size in a general population. Eur J Echocardiogr 2010;11:302-5.
18. Oxborough D, Batterham AM, Shave R et al. Interpretation of two-dimensional and tissue Doppler-derived strain (epsilon) and strain rate data: Is there a need to normalize for individual variability in left ventricular morphology? Eur J Echocardiogr 2009;10:677-82.
19. Marcus KA, Mavinkurve-Groothuis AM, Barends M, et al. Reference values for myocardial two-dimensional strain echocardiography in a healthy pediatric and young adult cohort. J Am Soc Echocardiogr 2011;24:625-36.
20. Bijnens BH, Cikes M, Claus P, et al. Velocity and deformation imaging for the assessment of myocardial dysfunction. Eur J Echocardiogr 2009;10:216-26.
21. Dalen H, Thorstensen A, Aase SA, et al. Segmental and global longitudinal strain and strain rate based on echocardiography of 1266 healthy individuals: The HUNT study in Norway. Eur J Echocardiogr 2010;11:176-83.