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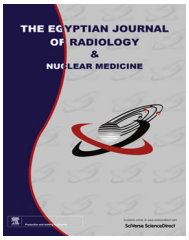

ORIGINAL ARTICLE

Evaluation of left ventricle diastolic dysfunction in ischemic heart disease by CMR: Correlation with echocardiography and myocardial scarring

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KEYWORDS

Cardiac magnetic resonance;
Left ventricle diastolic function;
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Diastolic heart failure

Abstract *Objective:* To detect the value of cardiac MR imaging in assessment of left ventricle diastolic function in patients with ischemic heart disease compared to echocardiography and to correlate the degree of dysfunction to the extent of myocardial scarring.
Patients and methods: We examined 40 patients with known coronary artery disease. Mean patient's age was 48 ± 10. All patients were subjected to 2D echocardiography and CMR including transmitral flow and left atrial planimetry. The degree of diastolic dysfunction was detected and correlated with the echocardiographic results and the extent of myocardial scarring.
Results: On CMR, 35% of the cases had grade I diastolic dysfunction, 35% showed grade II, 15% had grade III while 15% showed normal diastolic function. CMR showed 94.12% sensitivity, 100% specificity and 95% accuracy. Excellent agreement with echocardiography was detected (Kappa coefficient 0.931). There was a significant correlation between the degree of diastolic dysfunction and the extent of myocardial scarring with Spearman's correlation coefficient of 0.492 and $p = 0.028$.
Conclusion: CMR has comparative results to echocardiography in assessment of diastolic dysfunction. We found a significant correlation between the degree of diastolic dysfunction and the extent of myocardial scarring.

1. Introduction

The interest in diastolic dysfunction, which is present in various heart diseases, has been growing for many years. Over

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the past 2 decades, the concept of heart failure with preserved ejection fraction has emerged (1).

Ischemic heart disease is one of the main causes of diastolic heart failure. The presence of diastolic dysfunction predicts a poor prognosis in patients with coronary artery disease (2). Heart failure with preserved ejection fraction has become a diagnostic and therapeutic challenge, since its morbidity and mortality are similar to those of heart failure with deteriorated left ventricular ejection fraction (3). Echocardiography is the method of choice for diastolic function testing in clinical practice. Cardiac MR imaging (CMR) is often limited to evaluation of systolic function, including analysis of regional wall motion, measurement of mass and volume and estimation of ejection fraction. However, CMR offers a variety of applications for evaluation of diastolic function, moreover, it has much more superiority to echocardiography in myocardial assessment (4). The aim of this study is to evaluate the value of cardiac MR imaging in assessment of left ventricular diastolic function in ischemic heart disease (using transmitral flow and atrial size parameters) compared to echocardiography and to correlate the degree of dysfunction to the extent of myocardial scarring detected by delayed myocardial enhancement.

2. Patient and methods

2.1. Study population

Forty patients with known ischemic heart disease were enrolled in this study. Patient's mean age was 48 ± 10 years, 30 were males. Patients were diagnosed clinically, laboratory, ECG and by CT coronary angiography ± coronary catheterization. Exclusion criteria were the presence of atrial fibrillation, mitral regurge or stenosis as well as other known contraindications to CMR eg. claustrophobia and pace makers. All participants gave informed written consent. The study was approved by the Institutional Ethics Committee.

2.2. Echocardiography acquisition and analysis

Standard echocardiographic and Doppler recordings were performed by an experienced sonographer. Echocardiography was done using a Philips IE-33 machine equipped with 2.5 MHz transducer. Mitral diastolic inflow was interrogated using pulsed-wave Doppler from the apical 4-chamber view with the sample volume placed at the level of the mitral leaflet tips. Mitral early diastolic peak (E wave), late peak (A wave) velocities, E/A ratio, and deceleration time (DT) were measured. Planimetry for left atrial size was also performed.

3. CMR acquisition and analysis

All patients were imaged by a 1.5 *T* super conducting magnet (Gyroscan Achieva, Philips Medical Systems, Best, The Netherlands) using 5 channel phased-array cardiac coil.

The CMR protocol included cine imaging of the left ventricle using an ECG-gated, breath-hold balanced turbo field echo sequence (b-TFE) in two, four chamber and short axis views with the following parameters: repetition time (TR)/echo time (TE), 4.4/2.5; 25 cardiac phases; matrix 128 × 128; FOV 300, NSA 1, flip angle 15; slice thickness 8 mm and scan time of 7–12 s.

Transmitral flow was assessed via through-plane phase contrast images positioned at the top of the opened mitral valve perpendicular to the left ventricular inflow tract with the following parameters: repetition time (TR)/echo time (TE), 7/3.2; matrix 256 × 192; FOV 38, flip angle 20; slice thickness 8 mm. A region of interest (ROI) was placed at the center of the mitral valve orifice in the phase contrast images and then propagated to the other phases to obtain the transmitral flow (TMF) curve, early diastolic peak/late peak velocities ratio (E/A ratio) and deceleration time (DT).

For delayed contrast enhancement imaging, intravenous gadolinium-DTPA was given (0.2 mmol/kg) followed 10–15 min later by breath-hold segmented inversion recovery balanced turbo field echo (IR-b-TFE) in 4chambers, 2chambers and short axis images, optimizing the inversion time for adequate myocardial suppression and scar visualization by using the Look Locker sequence. The following parameters were used: TR/TE, 3.8/1.86; inversion time (TI), 260–350; FOV 300; matrix 128 × 128; flip angle 15; slice thickness, 8 mm and scan time of 9–15 s.

All images were interpreted by two experienced radiologists who were blinded to patient′s echocardiographic data.

3.1. Analysis of LV function

The 17-segment model according to the AHA (American Heart Association) definition for the left ventricle was used to analyze left ventricular function and delayed enhancement per segment.

LV global function was calculated by the Philips extended work station (EWS) View Forum 2.6, after the manual tracing of the endocardial and epicardial contours of the left ventricular wall at end diastole and end systole on the short axis cine images. Images were analyzed for wall thickness and wall motion abnormality and EDV, ESV, CO, SV, EF and CI were calculated.

3.2. Analysis of LV diastolic dysfuntion

Diastolic function was considered normal if E/A was 1–1.5 and $DT > 200$ ms; grade I dysfunction if E/A decreased below 1; grade II dysfunction if E/A 1–1.5 with DT 160–200 ms; grade III dysfunction if E/A above 2 and $DT < 160$ ms. (Fig. 1).

Left atrial size was assessed at end systole by manual endocardial delineation (planimetry) in the four chamber or two chamber views (Fig. 2). LA was considered dilated if planimetry showed an area $> 24\ cm^2$.

3.3. Analysis of delayed enhancement

Segmental enhancement was quantified by the Philips (EWS) View Forum 2.6 in all 17 segments. The presence of enhancement in each segment was scored by visually assessing the area showing late gadolinium enhancement as compared with LV myocardium in each segment. The presence, distribution, extent and pattern of enhancement were detected.

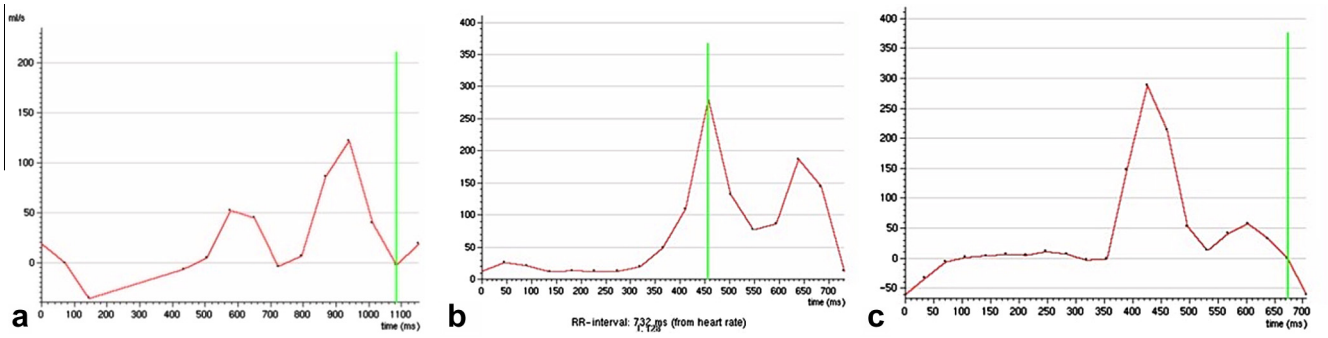

Fig. 1 Through-plane one-directional velocity-encoded MRI results in a time–flow rate graph, which revealed reversed E/A ratio denoting grade I diastolic dysfunction (a), pseudo-normal E/A ratio with decreased *DT* below 200 ms denoting grade II diastolic dysfunction (b) E/A ratio more than two denoting grade III diastolic dysfunction (c).

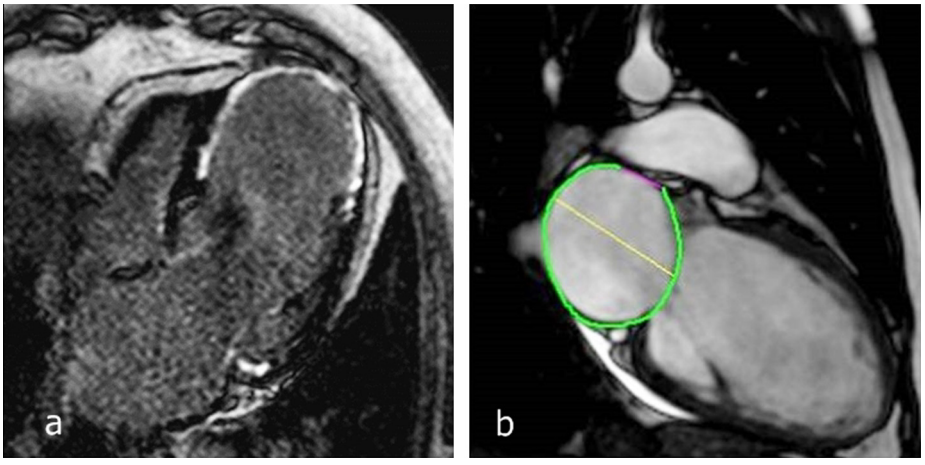

Fig. 2 Delayed myocardial enhancement image shows transmural and subendocardial enhancement at the apex of the heart (a) planimetry of the left atrium by manual tracing of the atrial wall denoting dilated left atrium of 26 cm^3.

3.4. Statistical analysis

Continuous variables were described as mean ± *SD*. Categorical data were presented with absolute frequencies and percentages. Comparison between study diagnostic tools was done using McNemar test. Agreement was tested using kappa statistic. Correlation between categorial variables was done using Spearman rank correlation. Accuracy was presented in terms of sensitivity, specificity, +ve predictive value, −ve predictive value and overall accuracy. p values < 0.05 was considered statistically significant. All statistical analyses were done using SPSS version 15.0 software for Windows (SPSSInc. Chicago, IL).

4. Results

All cardiac examination was diagnostically satisfactory by both CMR and echocardiography. Overall patients had mean end diastolic value of 176 ml, end systolic value of 101 ml, stroke value of 75 ml and mean ejection fraction was 43%.

We had 26 patients with systolic and diastolic heart failure. Eight patients had isolated diastolic heart failure while none had isolated systolic heart failure. Six patients did not have heart failure.

4.1. Transmitral flow and left atrial size

Transmitral flow by echocardiography showed that 14/40 patients (35%) had grade I diastolic dysfunction, 12/40 (30%) showed grade II diastolic dysfunction, 8/40 (20%) had grade III diastolic dysfunction, while 6/40 patients (15%) showed normal diastolic function. (Table 1) (Fig. 3)

Table 1 Showing grades of diastolic dysfunction and dilated LA by both echocardiography and CMR.

	Echocardiography	CMR
Grade I diastolic dysfunction	14 (35%)	14 (35%)
Grade II diastolic dysfunction	12 (30%)	14 (35%)
Grade III diastolic dysfunction	8 (20%)	6 (15%)
Normal diastolic function	6 (15%)	6 (15%)
Dilated LA	24 (60%)	30 (75%)

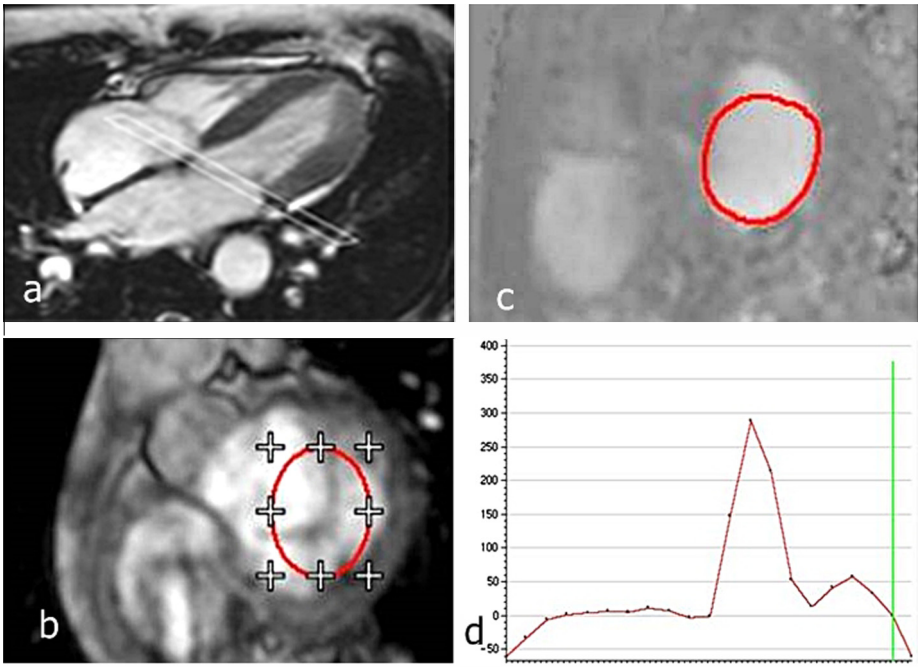

Fig. 3 At end-systole, an acquisition plane is positioned at the mitral valve (a). Through-plane one-directional velocity-encoded MRI magnitude image (b) and velocity image (c) time–flow rate graph (d) of the same patient in Fig. 2 shows grade III diastolic dysfunction.

On CMR, 14/40 patients with chronic ischemic heart disease (35%) had grade I diastolic dysfunction, 14/40 (35%) showed grade II diastolic dysfunction, 6/40 (15%) had grade III diastolic dysfunction while 6/40 patients (15%) showed normal diastolic function. (Table 1)

There was no statistically significant difference ($p = 0.000$) between CMR and echocardiography in assessing grades of diastolic dysfunction. CMR showed 94.12% sensitivity, 100% specificity and 95% accuracy. Excellent agreement with echocardiography was detected (Kappa coefficient 0.931).

Thirty patients (75%) showed dilated left atrium by CMR while 24 patients (60%) had dilated left atrium by echocardiography. Echocardiography showed 80% sensitivity, 100% specificity and 85% accuracy. MRI showed 94.12% sensitivity, 100% specificity, and 95% accuracy with a good Kappa agreement of 0.667 and $p = 0.002$.

4.2. Scarred myocardial segments

We had 142 total scarred myocardial segments in our study with a minimum of zero, maximum of 22 segments (mean 3.55 *SD* 3.517). All patients (with +ve delayed enhancement) showed subendocardial enhancement within the territory of one or more coronary arteries, 18 patients showed transmural enhancement pattern.

LGE (late gadolinium enhancement) as indicator of myocardial scarring was seen in 38 myocardial segments in patients with grade I diastolic dysfunction ($n = 14$), 70 segments in grade II diastolic dysfunction patients ($n = 14$), 32 segments in grade III dysfunction patients ($n = 6$) and no LGE in patients with normal diastolic function ($n = 6$). There was a significant correlation between the degree of diastolic dysfunction and the extent of myocardial scarring with Spearman's correlation coefficient 0.492 and $p = 0.028$. (Table 2).

5. Discussion

Heart failure with preserved ejection fraction represents approximately 40–50% of all cases of heart failure, and its prevalence is increasing (1). Diastolic dysfunction and coronary artery disease are interrelated. The complications of coronary artery disease, myocardial ischemia or infarction, are major causes of diastolic dysfunction. Diastolic dysfunction refers to abnormal mechanical diastolic properties of the left ventricle (relaxation and filling dynamics). Left ventricular ejection fraction may be normal or decreased (5,6).

Table 2 Correlation between the degree of diastolic dysfunction and the extent of myocardial scarring.

Grades of diastolic dysfunction	No of scarred myocardial segments	No of patients
Grade I diastolic dysfunction	38 segments	14
Grade II diastolic dysfunction	70 segments	14
Grade III diastolic dysfunction	32 segments	6
Normal diastolic function	0 segments	6

Spearman's correlation coefficient 0.492 and $p = 0.028$.

In this study we had eight cases (20%) of heart failure with preserved left ventricle ejection fraction (EF 57–64%) and abnormal diastolic function (grade I–III) while 26 cases (65%) showed decreased left ventricle ejection fraction (EF 32–51%) with abnormal diastolic function. Six cases (15%) did not have heart failure.

Echocardiography is the method of choice for diastolic function testing in clinical practice with the mitral flow pattern and left atrial size having predictive value of future heart failure hospitalization and mortality (7,8). However, TTE has important disadvantages, including limited field of view, dependence on sample volume location, cosine θ errors relative to the flow direction and an inability to image approximately 15–20% of patients (9).

Transmitral flow is an instantaneous marker of the LV filling pressure gradient between the LA and LV (1). In our study, assessment of E/A ratio for diastolic function testing was done by phase contrast MR technique across the mitral valve in addition to echocardiography. This showed excellent agreement between CMR and echocardiography regarding the patterns of diastolic dysfunction ($p < 0.0001$) in agreement with previous studies (9,10).

LA size is a chronic marker of diastolic dysfunction and cardiovascular risk (1). Our study showed that echocardiography underestimated the left atrial size compared to CMR with overall sensitivity of 80%, specificity of 100% and accuracy of 85% ($p = 0.002$) which was in line with a study carried out by Tobias et al. (11) that showed that echocardiography underestimates LA size with up to 32% compared with CMR and MSCT ($p < 0.001$).

Late gadolinium enhancement (LGE) using cardiac magnetic resonance (CMR) has emerged as the gold-standard technique for imaging of myocardial scar. With appropriate settings, normal myocardium appears nulled or black, whereas nonviable regions appear bright or enhanced (12).

LGE-CMR is a well-established technique to non-invasively detect foci of collagen deposition in vivo. Importantly, it has been documented that LGE results show a good correlation with direct histological findings (13,14).

In our study, the most benign alteration in diastolic function, termed impaired relaxation (grade I) and characterized by prolonged deceleration time of early diastolic filling and decreased E/A, is associated with delayed relaxation in the presence of normal LV filling pressures. At the other end of the spectrum, a restrictive filling pattern (grade III) is characterized by shortened deceleration time, increased E/A, and shortened relaxation time, and reflects high LV filling pressures. The pseudonormal filling pattern (grade II) is considered a condition of intermediate severity. Our data showed a significant correlation between the extent of myocardial scarring; as number of scarred segments by LGE-CMR according to the 17-segment model of the left ventricle proposed by the American Heart Association (AHA) and the degree of left ventricular diastolic dysfunction with a correlation coefficient of 0.492 and ($p = 0.028$).

This could be explained by the effect of increased tissue collagen deposition on altering the viscoelasticity of the myocardium impairing relaxation, diastolic recoil and passive stiffness (15,16). In addition, it has been documented that the size and distribution of a myocardial infarction from late gadolinium enhancement are of significant prognostic value for post-infarction patients (17) and that there is a direct relationship between the amount of remote myocardial scarring determined with nonstress DE-MRI and baseline resting systolic functional impairment in chronic ischemic heart disease (18).

Diastolic dysfunction and LGE myocardial scarring were previously studied in a broad range of cardiac conditions as well as patients without structural heart disease. Those studies showed that subjects with normal diastolic function exhibited no or minimal fibrosis. In contrast, the majority of patients with cardiomyopathy (regardless of etiology) had abnormal diastolic functional indices and substantial fibrosis with LGE remained significantly correlated with degree of diastolic dysfunction ($p = 0.0001$) (19–21).

Although, Heymon et al. (22) stated that the extent of myocardial scarring was weakly or not significantly correlated with LV myocardial and chamber diastolic functional indices. This contradiction with our results could be explained by the difference in study groups as Heymon studied patients with early reperfused acute myocardial ischemia in whom non-infarcted myocardial circumferential strain had high influence on LV diastolic functional indices while myocardial scarring has more contribution to LV diastolic dysfunction in chronic ischemia.

CMR has comparative results to echo in assessment of diastolic dysfunction, in addition, CMR has a very low intraobserver and interobserver variability, not limited by the body habitus. CMR allows comprehensive left ventricular assessment particularly detection of myocardial scarring that showed a significant correlation with the degree of diastolic dysfunction in ischemic heart disease.

Conflict of interest

We have no conflict of interest to declare.

References

(1) Caudron J, Fares J, Bauer F, Dacher JN. Evaluation of left ventricle diastolic function with cardiac MR imaging. Radio Graph 2011;31:239–61.
(2) Ren X, Na B, Ristow B, et al. Usefulness of diastolic dominant pulmonary vein flow to predict hospitalization for heart failure and mortality in ambulatory patients with coronary heart disease (from the heart and soul study). Am J Cardiol 2009;103(4):482–5.
(3) Tribouilloy C, Rusinaru D, Mahjoub H, et al. Prognosis of heart failure with preserved ejection fraction: a 5-year prospective population-based study. Eur Heart J 2008;29(3):339–47.
(4) Antonella M, Giuseppe A, Benedetta D, et al. Myocardial fibrosis severity and location: influence on diastolic dysfunction. Eur Heart J 2013;4:320–90.
(5) Owan T, Hodge D, Herges R, et al. Trends in prevalence and outcome of heart failure with preserved ejection fraction. N Engl J Med 2006;355(3):251–9.
(6) Bursi F, Weston S, Redfield M, et al. Systolic and diastolic heart failure in the community. J Am Med Assoc 2006;296(18):2209–16.
(7) Ristow B, Ali S, Whooley M, et al. Usefulness of left atrial volume index to predict heart failure hospitalization and mortality in ambulatory patients with coronary heart disease and comparison to left ventricular ejection fraction (from the heart and soul study). Am J Cardiol 2008;102(1):70–6.
(8) Stevens S, Farzaneh-Far R, Na B, et al. Development of and echocardiographic risk-stratification index to predict heart failure in patients with stable coronary artery disease: the heart and soul study. J Am Coll Cardiol 2009;2(1):11–20.
(9) Vikas K, Mark D, June Y, et al. Routine evaluation of left ventricular diastolic function by cardiovascular magnetic reso-

nance: a practical approach. J Cardiovasc Magn Reson 2008;8(10):36.
(10) Hartiala J, Mostbeck G, Foster E, et al. B: velocity-encoded cine MRI in the evaluation of left ventricular diastolic function: measurement of mitral valve and pulmonary vein flow velocities and flow volume across the mitral valve. Am Heart J 1993;125(4):1054–66.
(11) Tobias K, Jacob L, Fuchs A, et al. Assessment of left atrial volume and function: a comparative study between echocardiography, magnetic resonance imaging and multi slice computed tomography. J Am Coll Cardiol 2012;5:1061–71.
(12) Raymond Y, Afshin F. Measuring myocardial scar by CMR. J Am Coll Cardiol 2011;4(2):157–60.
(13) Papavassiliu T, Schnabel P, Schroder M, et al. CMR scarring in a patient with hypertrophic cardiomyopathy correlates well with histological findings of fibrosis. Eur Heart J 2005;26:2395.
(14) Moon J, Sheppard M, Reed E, et al. The histological basis of late gadolinium enhancement cardiovascular magnetic resonance in a patient with Anderson-Fabry disease. J Cardiovasc Magn Reson 2006;8:479–82.
(15) Kass D, Bronzwaer J, Paulus W. What mechanisms underlie diastolic dysfunction in heart failure? Cir Res 2004;94:1533–42.
(16) Burlew B, Weber K. Cardiac fibrosis as a cause of diastolic dysfunction. Herz 2002;27:92–8.
(17) Tao Q, Milles J, Zeppenfeld K, et al. Automated segmentation of myocardial scar in late enhancement MRI using combined intensity and spatial information. Magn Reson Med 2010;64(2):586–94.
(18) Srichai M, Schvartzman P, Sturm B, et al. Extent of myocardial scarring on nonstress delayed-contrast-enhancement cardiac magnetic resonance imaging correlates directly with degrees of resting regional dysfunction in chronic ischemic heart disease. Am Heart J 2004;148(2):342–8.
(19) Suk T, Edwards C, Hart H, et al. Myocardial scar detected by contrast-enhanced cardiac magnetic resonance imaging is associated with ventricular tachycardia in hypertrophic cardiomyopathy patients. Heart Lung Cir 2008 Oct;17(5):370–4.
(20) Paban S, Aya K, Kalyani B, et al. Diastolic function and myocardial scarring in hypertrophic cardiomyopathy. J Am Coll Cardiol 2011;57(14):311.
(21) Antonella M, Giuseppe A, Benedetta D, et al. Influence of myocardial fibrosis on left ventricular diastolic function: non invasive assessment by cardiac magnetic resonance and echo. Circ Cardiovas Imaging 2009;2(6):437–43.
(22) Heymon C, Ji-Hyun Y, Young W, et al. Different contribution of extent of myocardial injury to left ventricular systolic and diastolic function in early reperfused acute myocardial infarction. Cardiovasc Ultrasound 2014;12:6.