Role of Cardiac MR Imaging in Evaluation of Left Ventricular Diastolic Function in Ischemic Heart Disease

Ali Abd Elhady Elsayed, Mamdouh Helmi Eltahan, Ahmed Mohamed Abou Elfotouh, Mahmoud Mohamed Abou Mandour

Department of Diagnostic Radiology, Faculty of Medicine, Al-Azhar University

***Corresponding author:** Mahmoud Mohamed Abou Mandour**,**

E-mail: dr.mandour1985@gmail.com**, Mobile:** (+20) 01090114543

ABSTRACT

Background: Diastolic dysfunction and coronary artery disease (CAD) are interrelated. The complications of CAD, myocardial ischemia or infarction, are major causes of diastolic dysfunction.

Objective: The aim of this study was to determine the accuracy of CMR in assessment of left ventricular diastolic function in ischemic heart disease patients by using a combination of left atrium size measurement and phase-contrast evaluation of transmitral flow. Also, to evaluate the extent of myocardial scarring in these patients and to correlate between the degree of myocardial scarring and the degree of left ventricular diastolic dysfunction.

Patients and methods: In the current study a total number of 22 patients with known ischemic heart disease were enrolled for contrast enhanced CMR examination between January 2019 and October 2019. All patients underwent CMR and echocardiography. Two of the 22 patients were excluded from the study because of technical difficulties or failure of data acquisition (patient did not hear or did not obey breathing instructions). So, 20 patients were included in the present study.

Results: our study showed feasibility of routinely performing evaluation of MV flow to assess diastolic function using CMR. We were able to obtain clinical variables including E:A ratios and deceleration times, which agreed with those obtained using TTE.

Conclusion: In patients with CAD, extent of myocardial scarring reliably predicts the degree of diastolic dysfunction. LGE-CMR provides a powerful means to noninvasively assess the degree of myocardial scarring.

Keywords: Cardiac MR imaging, Left ventricular diastolic function, Ischemic heart disease, CAD, CMR.

INTRODUCTION

The interest in diastolic dysfunction, which is present in various heart diseases, has been growing for many years. Over the past 2 decades, the concept of heart failure with preserved ejection fraction has emerged. It was previously described as “diastolic heart failure” because diastolic dysfunction was thought to be its main mechanism. Heart failure with preserved ejection fraction represents approximately 40%–50% of all cases of heart failure, and its prevalence is increasing [(1)].

Moreover, 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 (LV) ejection fraction (LVEF) [(2)].

Ischemic heart disease is the leading cause of death worldwide as it accounts for 22% of all deaths [(3)]. Also, ischemic heart disease is one of the main causes of diastolic heart failure and the presence of diastolic dysfunction predicts a poor prognosis in patients with coronary artery disease (CAD) [(4)].

Assessment of left ventricular (LV) function with cardiac magnetic resonance (MR) imaging is often limited to evaluate systolic function, including analysis of regional wall motion, measurement of mass and volume, and estimation of ejection fraction. Currently, echocardiography is the method of choice for diastolic function testing in clinical practice. Various applications are in use and recommended criteria are followed for classifying the severity of dysfunction. Cardiovascular magnetic resonance (CMR) offers a variety of alternative applications for evaluation of diastolic function; moreover CMR has much more superiority to the echocardiography in myocardial assessment [(5)].

AIM OF THE WORK

The aim of this study was to determine the accuracy of CMR in assessment of left ventricular diastolic function in ischemic heart disease patients by using a combination of left atrium size measurement and phase-contrast evaluation of transmitral flow. Also, to evaluate the extent of myocardial scarring in these patients and to correlate between the degree of myocardial scarring and the degree of left ventricular diastolic dysfunction.

PATIENTS AND METHODS

Study population:

A total number of 22 clinically diagnosed patients as ischemic heart disease were enrolled for contrast enhanced MRI examination of the heart from January 2019 to October 2019. All patients underwent cardiac MRI and echocardiography.

Two patients were excluded from the study due to unsatisfactory images. So, 20 patients were included in the present study.

Patients presented with ischemic chest pain (defined as a retro-sternal or precordial diffuse burning, heaviness, or squeezing

Received:8/08/2019
Accepted:8/09/2019

sensation that may radiate to the left arm, neck or lower jaw and is precipitated by effort & relived by rest or nitrates) or suspected progression of known coronary artery disease.

The major inclusion criterion was presence of ischemic heart disease. Patients enrolled in this study had to fulfill the following criteria; sinus heart rhythm, able to hold breath for accepted time (10-20 seconds) and normal serum creatinine.

Exclusion criteria were; hemodynamic instability, atrial fibrillation, presence of severe mitral regurge or stenosis, contra-indications for MR imaging; claustrophobia, patients with pacemaker or metal implants, contraindication for contrast material including known allergy and renal insufficiency.

Ethical approval:

The study was approved by the medical ethics committee of Al-Azhar University Hospitals and a written informed consent is obtained from all patients.

Methods

Patient preparation and set up:

No special instructions were required prior to the examination. Medications were not discontinued.

First, a short medical history was taken. Patients were then screened for contraindication to MR imaging. All undergarments containing nylon or metal were removed. The former may cause artifacts because of static electricity and the latter can cause image degradation.

Before the examination; the heart rate and rhythm were evaluated. All steps of the study were explained in details for each patient. To evaluate patient's ability of breath-with holding for relatively long time; they were required to perform a deep inspiration and to continue to hold their breath without pushing (i.e., Valsalva maneuver).

Magnetic Resonance Imager:

A Philips (1.5 Tesla) magnet was used at Radiology Department, Al-Hussein University Hospital.

Patient position:

All patients were examined in the supine position, head first. The patient's knees and legs can be elevated to help relieve back strain and secure the patient's comfort.

Head phones supplied with the MRI machine are used to reduce repetitive gradient noise and in the same time allow the patient to hear the breath hold instructions.

ECG Lead positioning:

Four ECG pads were placed on the anterior chest wall, the first is placed 1 cm to the left of the xiphisternum, the second and the third are places in such a way that they are aligned at 90° to each other where the first electrode forms the right angle and the distance between the electrodes 15 cm. The fourth electrode is placed below the first electrode.

The ECG leads were attached. The green lead to the first pad, the red lead to the second pad, the white lead to the third pad, and the black lead to the fourth pad.

The QRS complex is then checked on the MRI monitor, adjustments of the site of the leads is done accordingly. The patient's heart rate is also detected on MRI monitor, it is used to determine the cardiac frequency as it should be close to the patient's heart rate.

The Respiratory Sensor:

The respiratory sensor is placed over the maximum area of respiratory movement (abdomen or thorax) under the coil. A strap is used to fix the sensor. The respiratory signal is then checked as the respiratory wave appears on the monitor and used to detect the patient's respiratory rhythm and synchronize breath hold instructions to the patient abilities.

Cardiac MR Examination:

Imaging protocol: All patients received 18-gauge intravenous line to allow administration of the contrast agent. The patients underwent a standard MR examination that included the following steps:

1. Scout images were acquired in orthogonal orientations for planning of the final long-axis and short-axis views.

2. Functional cine images: were acquired using electrocardiographic gated, breath hold balanced turbo field echo (b-TFE) sequences in short axis view, two and four chamber views.

3. Trans-mitral flow assessment (Q-flow):

TMF was determined from through-plane phase-contrast images obtained with retrospective or prospective electrocardiographic synchronization, breath holding was employed, and velocity of 130 cm/sec was used to avoid temporal aliasing.

To define the acquisition plane, the two- and four-chamber views were used during diastole. The section was positioned at the top of the opened mitral valve perpendicularly to the LV inflow **(Figure 1)**.

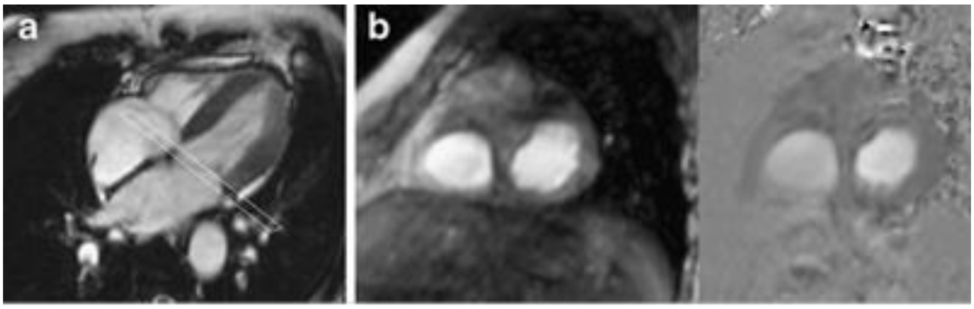

Figure 1: Q-flow acquisition plane" **Jos et al., 2011"**

4. Standard delayed gadolinium enhancement imaging was performed after using look locker to determine the best time of delay by using Segmental inversion recovery balanced turbo field echo (IR-b-TFE), starting 10–15 min after intravenous infusion of gadolinium chelate contrast material (0.1– 0.2 mmol/kg). Contrast-enhanced images were acquired in the same orientation as the cine images (short axis plane) and at least one of the long axis planes.

Assessment of left atrial dimensions: Assessment of left atrial dimensions was done at the end systole (just before opening of the mitral valve). In the four-chamber or two chamber views, planimetry was performed with manual endocardial delineation. The LA was considered dilated if planimetry shows an area greater than 24 cm^2.

Echocardiography: All patients were scheduled for transthoracic echocardiogram "TTE" is the same day. The exam was performed with the subject supine in the left lateral position. In the four-chamber view, the MV inflow was localized and the Doppler sample volume was placed at the level of the tip of the MV leaflets and the pulsed wave Doppler was recorded under free breathing conditions.

Statistical methodology:

Data were statistically described in terms of mean ± standard deviation (± SD), and range, or frequencies (number of cases) and percentages when appropriate. Comparison between the study diagnostic tools was done using McNemar test. Agreement was tested using kappa statistic. Correlation between various variables was done using Spearman rank correlation. Accuracy was represented using the terms sensitivity, specificity, +ve predictive value, -ve predictive value, and overall accuracy. p values less than 0.05 was considered statistically significant. All statistical calculations were done using computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

RESULTS

The study group consisted of 20 patients and the results were analyzed as follows:

Patients' characteristics:

Patient sex: Twenty patients were included in this study,15 males (75%) and 5 females (25%) **(Figure 2).**

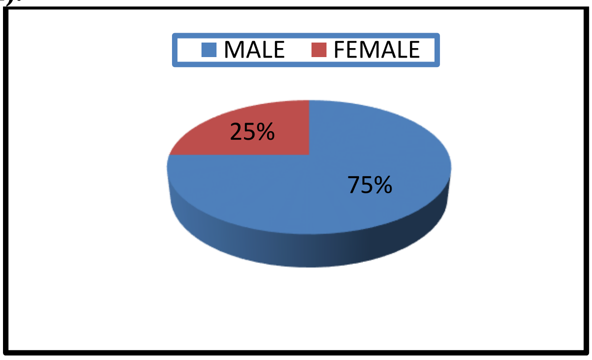

Figure (2): Sex distribution in our study.

Patient age: The patient's age was ranged between 43 and 68 years with mean age of **57.75** years.

A- CMR versus echo in assessment of left ventricular diastolic function Table 1.

Table 1: Comparison between echo and CMR findings in assessment of left ventricular diastolic function.

			Echo diastolic function "DF"				Total
			Grade I	Grade II	Grade III	Normal	
MRI diastolic function "DF"	Grade I	Count	7	0	0	0	7
		% with MRI DF	100.0%	0.0%	0.0%	0.0%	100.0%
		% within Echo DF	100.0%	0.0%	0.0%	0.0%	35.0%
		% of Total	35.0%	0.0%	0.0%	0.0%	35.0%
MRI diastolic function "DF"	Grade I	Count	0	6	1	0	7
		% with MRI DF	0.0%	85.7%	14.3%	0.0%	100.0%
		% within Echo DF	0.0%	100.0%	25.0%	0.0%	35.0%
		% of Total	0.0%	30.0%	5.0%	0.0%	35.0%
MRI diastolic function "DF"	Grade I	Count	0	0	3	0	3
		% with MRI DF	0.0%	0.0%	100.0%	0.0%	100.0%
		% within Echo DF	0.0%	0.0%	75.0%	0.0%	15.0%
		% of Total	0.0%	0.0%	15.0%	0.0%	15.0%
MRI diastolic function "DF"	Grade I	Count	0	0	0	3	3
		% with MRI DF	0.0%	0.0%	0.0%	100.0%	100.0%
		% within Echo DF	0.0%	0.0%	0.0%	100.0%	15.0%
		% of Total	0.0%	0.0%	0.0%	15.0%	15.0%
Total		Count	7	6	4	3	20
		% with MRI DF	35.0%	30.0%	20.0%		100.0%
		% within Echo DF	100.0%	100.0%	100.0%	100.0%	100.0%
		% of Total	35.0%	30.0%	20.0%	15.0%	100.0%

Comparison between echo findings and CMR findings in assessment of left ventricular diastolic function showed no statistically significant difference **"Tables 1 and 2."** with overall sensitivity 94.12% and specificity 100% and accuracy 95% **"Table 5."**

Table 2: Symmetric measures.

Symmetric Measures					
		Value	Asymp. Std. Error(a)	Approx. T(b)	P value
Measure of Agreement	Kappa	0.931	0.067	6.926	0.001
n. of valid cases		20			

B- TTE versus CMR in assessment of left atrial size:

Table 3: Comparison between CMR and TTE findings in assessment of left atrial size.

			Echo LA		Total
			Dilated	Normal	
CMR LA	Dilated	Count	12	3	15
		% within CMR LA	80.0%	20.0%	100.0%
		% within Echo LA	100.0%	37.5%	75.0%
		% of Total	60.0%	15.0%	
	Normal	Count	0	5	5
		% within CMR LA	0.0%	100.0%	100.0%
		% within Echo LA	0.0%	62.5%	25.0%
		% of Total	0.0%	25.0%	25.0%
Total		Count	12	8	20
		% within CMR LA	60.0%	40.0%	100.0%
		% within Echo LA	100.0%	100.0%	100.0%
		% of Total	60.0%	40.0%	100.0%

Table 4: Symmetric measures.

Symmetric Measures					
		Value	Asymp. Std. Error(a)	Approx. T(b)	P value
Measure of Agreement	Kappa	0.6676	0.167	3.162	0.002
N. of valid cases		20			

Comparison between CMR findings and echo findings in assessment of left atrial size shows overall sensitivity80% and specificity 100% and accuracy 85% **"Tables 3, 4 and 5."**

Table 5: Comparison between CMR findings and echo findings in assessment of left atrial size

	Sensitivity	Specificity	(+) ve PV	(-) ve PV	Accuracy
CMR in assessment of DF	94.12	100.00	100.00	75.00	95.00
Echo in assessment of LA size	80.00	100.00	100.00	62.50	85.00

C- Correlation between degree of myocardial scarring and diastolic dysfunction:

In our study, the total number of scarred segments in the 20 patients was 71 with minimum number 0 segments and maximum number 11 segments with mean number 3.55 **"Table 6".**

Table 6: Correlation between degree of myocardial scarring and diastolic dysfunction.

	N	Minimum	Maximum	Mean	Std. Deviation
Scarred segments	71	0	11	3.55	3.517
Valid N (listwise)	20				

Also there was significant correlation between the degree of diastolic dysfunction and degree of myocardial scarring with correlation coefficient of 0.492 **"Table 7"**

Table 7: Correlation between the degree of diastolic dysfunction and degree of myocardial scarring

			Diastolic dysfunction by CMR
Spearman's RHO	Scarred segments	Correlation coefficient	0.492
		P value	0.028
		N	20

DISCUSSION

In the current study a total number of 22 patients suffering from ischemic heart disease were enrolled for contrast enhanced CMR examination between January 2019 and October 2019. All patients underwent CMR and echocardiography.

Two of them were excluded from the study because of technical difficulties or failure of data acquisition (patient did not hear or did not obey breathing instructions). And the other 20 patients were included in the study.

The age of the patients ranges between 43 and 68 years old with mean age 57.75 years. There were a total number of 15 males and 5 females.

Eighty five percent of our patients were suffering from diastolic heart failure and 65% of them had systolic heart failure.

One hundred percent of our patient with systolic heart failure found to have also diastolic heart failure, while isolated diastolic heart failure "**HFpEF**" was present in 20% of our patients.

Transthoracic echocardiography (TTE) provides noninvasive measure of diastolic left ventricular (LV) function by assessing mitral inflow and mitral annular motion. Phase contrast CMR provide an alternative method in assessment of LV diastolic function.

Our study showed that there is excellent agreement between CMR and TTE in assessment of LV diastolic function with overall sensitivity 94.12% and specificity 100% and accuracy 95% ($p < 0.0001$), which was in line with study carried by **Rathi *et al.*** [(6)] including 31 patients (21 males and 10 females)with mean age of 60 ± 14years and 10 controls with mean age of 33 ± 9 years which showed excellent agreement between CMR and TTE with sensitivity 100% ($p < 0.001$).

Despite excellent correlations, E and A measured by CMR were systematically lower compared to TTE. This may reflect the differences in the nature of acquisition by each technique. TTE obtains data within each cardiac cycle and is thus influenced by changes that occur over short time scales, whereas CMR data are effectively averaged over several cycles, thus damping sensitivity to intra-cycle variation. Importantly, this did not result in significant misclassification of diastolic flow abnormalities between modalities.

Also our results were in concordance with the previous, but limited comparative study between CMR and TTE for diastolic function evaluation which was performed by **Hartiala *et al.*** [(7)]. They studied 10 normal individuals and achieved modest correlations between TTE and CMR-PC. The MV was imaged by CMR-PC using both 2D and 3Dvelocity encoding were both lower than the TTE measured velocities. The study was performed on early generation scanners and since then the imaging technique has evolved to allow better temporal resolution and faster imaging. Recently, powerful gradients and faster computing power has led to shorter echo time and repetition time, which has led to better results.

A similar approach was used by **Karwatowski *et al.*** [8], studying 19 patients with known coronary artery disease. The study was not designed to correlate diastolic patterns but showed that CMR and TTE E values were similar, but A values were slightly lower by CMR. Recently, **Lin *et al.*** [9] compared mitral valve area using pressure half time assessed independently by CMR-PC and echocardiography methods. They obtained E and A velocities similar to echocardiography.

In our study we imaged MV in the short axis orientation, perpendicular to the major direction of flow, and using 2D encoding of velocity, allowing interrogation of the complete cross-section of the plane to comprehensively assess diastolic flow, irrespective of the location and vector. The velocity window of 130 cm/s was used to avoid aliasing of the E and was not significantly different to values used in prior studies.

Also, our study showed feasibility of routinely performing evaluation of MV flow to assess diastolic function using CMR. We were able to obtain clinical variables including E:A ratios and deceleration times, which agreed with those obtained using TTE.

Left atrial (LA) size represents the integration of LV diastolic performance over time and is considered a reliable indicator of the duration and severity of diastolic dysfunction [10], regardless of whatever loading conditions are present at the time of the examination.

It provides significant prognostic information both in the general population and in patients with heart disease including CAD [11]. Recently CMR is considered the gold standard investigation for assessment of LA size [12].

Our study showed that TTE underestimate the left atrial size compared CMR with overall sensitivity 80% and specificity 100% and accuracy 85%($p = 0.002$)which was in line with study carried by **Kühl *et al.*** [13] who studied 54 patients 3 months post myocardial infarction with echocardiography and CMR and MSCT, **Kühl *et al.*** [13] showed an overall good agreement between CMR and MSCT while TTE underestimates LA size with up to 32% compared with CMR and MSCT ($P < 0.001$).

Myocardial scarring is a common endpoint of CAD, and may alter myocardial relaxation properties leading to diastolic heart failure.

Recently late post gadolinium myocardial enhancement cardiac magnetic resonance (LGE-CMR) is considered the gold standard tool in assessment of myocardial scarring.

By measuring degree of myocardial scarring by LGE-CMR and diastolic function by phase contrast CMR, we sought to define the influence of myocardial scarring on left ventricular (LV) diastolic function.

In our study there was significant correlation between the degree of myocardial scarring and the degree of left ventricular diastolic dysfunction with correlation coefficient of 0.492 and ($p=0.028$),which was in line with study carried by **Moreo *et al.*** [5] who studied 252 patients which 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 function indices and substantial fibrosis, Prevalence of LGE-positivity by diastolic filling pattern was 13% in normal,48% in grade I, 78% in grade II and 87% in grade III($p<0.0001$), and after multivariate analysis, LGE remained significantly correlated with degree of diastolic dysfunction ($p=0.0001$).

Moreo *et al.* [5] studied 282 patients with a broad range of cardiac conditions. Patients were classified into 4 groups according to presence/location of LGE: 1-LGE negative (N=120); 2-LGE in anterior or lateral or inferior wall (N=23); 3-LGE in septum (N=56), 4-LGE in septum and any other site (N=83). LGE scored 0 in group 1, 3.8±3.1 in group 2, 2.5±1.3 in group 3 and 10.3±5.4 in group 4 ($p<0.0001$ vs all other groups).

Correlation between degree of diastolic dysfunction and site of LGE was beyond our study.

Also our study was in line with studies done by **Burlew and Weber** [14], who studied effect of cardiac fibrosis "regardless of the etiology" on diastolic dysfunction, **Weber *et al.*** [15]**,** who studied the significance of myocardial fibrosis "regardless of the etiology" on the cardiac function, and **Querejeta *et al.*** [16] who studied myocardial fibrosis in hypertensive heart disease.

All of the above mentioned studies had shown a significant relationship between degree of cardiac fibrosis and diastolic dysfunction; however, those studies relied on evaluation of collagen deposition as assessed by histological examination of tissue specimens. While accurate, those investigations were obviously limited with respect to number of patients.

In summary: In patients with CAD, extent of myocardial scarring reliably predicts the degree of diastolic dysfunction. LGE-CMR provides a powerful means to noninvasively assess the degree of myocardial scarring.

CONCLUSION

In conclusion, we found that there is good agreement between the CMR and TTE evaluation of left ventricular diastolic function and there was significant correlation between the degree of myocardial scarring and the degree of left ventricular diastolic dysfunction in CAD patients.

REFERENCES

1. **Maeder MT, Kaye DM (2009):** Heart failure with normal left ventricular ejection fraction. J Am Coll Cardiol., 53(11):905–918**.**
2. **Tribouilloy C, Rusinaru D, Mahjoub H *et al.* (2014):** Prognosis of heart failure with preserved ejection fraction: a 5-year prospective population-based study. Eur Heart J., 29:339–347.
3. **American Heart Association (2017)**: Heart disease and stroke statistics, 2017 update. American Heart Association, 135:146–603.
4. **Ren X, Na B, Ristow B *et al.* (2012):** 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., 103:482–485.
5. **Moreo A, Ambrosio G, Chiara BD *et al.* (2014):** Myocardial fibrosis severity and location: influence on diastolic dysfunction. European Heart Journal, 4:320-90**.**
6. **Rathi VK, Doyle M, Yamrozik J *et al.* (2013):** Routine evaluation of left ventricular diastolic function by cardiovascular magnetic resonance: A practical approach. Journal of Cardiovascular Magnetic Resonance, 10:36-42.
7. **Hartiala JJ, Mostbeck GH, Foster E *et al.* (2003):** 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., 125(4):1054-66.
8. **Karwatowski SP, Brecker SJ, Yang GZ *et al.* (2005):** Mitral valve flow measured with cine MR velocity mapping in Patients with ischemic heart disease: comparison with Doppler echocardiography. J Magn Reson Imaging, 5(1):89-92.
9. **Lin SJ, Brown PA, Watkins MP *et al.* (2009):** Quantification of stenotic mitral valve area with magnetic resonance imaging and comparison with Doppler ultrasound. J Am Coll Cardiol., 44(1):133-7.
10. **Simek CL, Feldman MD, Haber HL *et al.* (2005):** Relationship between left ventricular wall thickness and left atrial size: comparison with other measures of diastolic function. J Am Soc Echocardiogr., 8:37-47.
11. **Melenovsky V, Borlaug BA, Rosen B *et al.* (2012):** Cardiovascular features of heart failure with preserved ejection fraction versus nonfailing hypertensive left ventricular hypertrophy in the urban Baltimore community: the role of atrial remodeling/dysfunction. J Am Coll Cardiol., 49:198-207.
12. **Rossi A, Cicoira M, Florea VG *et al.* (2011):** Chronic heart failure with preserved left ventricular ejection fraction: diagnostic and prognostic value of left atrial size. Int J Cardiol., 110:386-92.
13. **Kühl JT, Lønborg J, Fuchs A *et al.* (2016):** Assessment of left atrial volume and function: a comparative study between echocardiography, magnetic resonance imaging and multi slice computed tomography. J Am Coll Cardiol., 5: 1061-1071.
14. **Burlew BS, Weber KT (2007)**: Cardiac fibrosis as a cause of diastolic dysfunction. Herz., 27:92–98.
15. **Weber KT, Brilla CG, Janicki JS (2003):** Myocardial fibrosis: functional significance and regulatory factors. Cardiovasc Res., 27:341–348.
16. **Querejeta R, Varo N, Lopez B *et al.* (2010):** Serum carboxy-terminal propeptide of procollagen type I is a marker of myocardial fibrosis in hypertensive heart disease. Circulation, 101:1729–1735.