Turkish Journal of Medical Sciences

http://journals.tubitak.gov.tr/medical/

Research Article

Turk J Med Sci
(2013) 43: 118-124
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doi:10.3906/sag-1205-21

Assessment of left-ventricular diastolic function in diabetic patients: the role of cardiac MR imaging

İhsan YÜCE[1], İbrahim Halil TANBOĞA[2], Ümmügülsüm BAYRAKTUTAN[1], Enbiya AKSAKAL[2], Hayri OĞUL[1], Ahmet YALÇIN[1], Yeşim KIZRAK[1], Abdülmecit KANTARCI[1,]*

[1]Department of Radiology, Faculty of Medicine, Atatürk University, Erzurum, Turkey

[2]Department of Cardiology, Faculty of Medicine, Atatürk University, Erzurum, Turkey

Received: 08.05.2012 • **Accepted:** 20.06.2012 • **Published Online:** 18.01.2013 • **Printed:** 18.02.2013

Aim: To evaluate the reliability of cardiac magnetic resonance (CMR) imaging in diabetic patients with clinically suspected cardiomyopathy and to compare the consistency of CMR imaging with 2-dimensional echocardiography (2DE).

Materials and methods: Twenty-one diabetic patients with clinically suspected cardiomyopathy were evaluated with CMR imaging and 2DE. Two observers for each modality performed the evaluation. Quantitative data (the ejection fraction, end-systolic volume, end-diastolic volume, left-ventricular mass index, and left-atrial volume index) were acquired from both observers. The data were compared for statistical agreement using the Bland–Altman test between the modalities.

Results: The CMR examination and 2DE results were consistent with each other. There was strong agreement between the 2 methods. The intraclass correlation-coefficient comparison of the data from the 2 observers of each modality showed that the CMR observers' measurements were more consistent than the 2DE observers' measurements.

Conclusion: This study demonstrates that compared with CMR, 2DE has much poorer reproducibility and much higher interobserver variability. Although 2DE is currently the noninvasive imaging technique used to assess diastolic function in diabetic patients, CMR imaging is emerging as a valuable alternative, having the unique potential of function analysis.

Key words: Cardiac magnetic resonance imaging, diastolic heart failure, diabetic cardiomyopathy

1. Introduction

Cardiovascular disease, a common complication of diabetes mellitus, is responsible for 80% of the mortality in the diabetic population. Coronary artery disease is the leading cause of increased cardiovascular morbidity and mortality in diabetes, and atherosclerosis of the coronary vessels is a hallmark of pathogenesis. However, postmortem, experimental, and observational studies also provide evidence for a specific cardiomyopathy in diabetes, called diabetic cardiomyopathy, that may contribute to myocardial diastolic dysfunction in the absence of coronary artery atheroma (1). Diastolic dysfunction is a common finding in healthy and asymptomatic diabetic patients and is thought to be the earliest detectable functional abnormality in diabetic cardiomyopathy (2). Thus, detection of diastolic function gains importance in the course of chronic cardiovascular disease.

Assessment of diastolic dysfunction can be performed with noninvasive techniques (Doppler echocardiography, radionuclide ventriculography) and invasive techniques (micromanometry, catheter angiography, the conductance method). Two-dimensional echocardiography (2DE) is the most useful tool for routinely measuring diastolic function. However, echocardiography has a limited role due to its poor acoustic windowing in the chest. Quantifying global left ventricular (LV) function requires geometric assumptions, and its ability to provide specific tissue characterization is modest. On the other hand, cardiac magnetic resonance (CMR) imaging is a new and promising technology that is increasingly being used for imaging cardiac chambers and the myocardium in patients with heart failure. To our knowledge, no study in the literature compares echocardiography with CMR with regard to diastolic function in diabetic patients. In this article, we report on the availability and consistency of CMR imaging, compared with 2DE, for the diastolic functional evaluation of patients with diabetes.

* Correspondence: akkanrad@hotmail.com

2. Materials and methods

2.1. Patient population

Twenty-one diabetic patients diagnosed with LV diastolic dysfunction were referred to our department during their routine follow-up. Detailed echocardiography revealed diastolic dysfunction in all patients. All patients included in the study had ejection fraction (EF) values higher than 50%. Patients with coronary heart disease, hypertension, pericardial effusion, mitral and aortic valve pathologies, atrial fibrillation, and chronic obstructive pulmonary disease were excluded from the study. Three patients with metal implants (n = 1) and claustrophobia (n = 2) were excluded from the study due to contraindication to examination. The mean age was 47 ± 14 years (range: 18–72 years). The sex distribution was 7 males and 11 females. CMR imaging and 2DE were performed on the same day. All procedures used in this study complied with the Declaration of Helsinki and were approved by our local ethics committee; all patients gave their written, informed consent.

2.2. Imaging protocol

2.2.1. Echocardiography

We used an echocardiographic system (Vingmed, Vivid 7, GE Ultrasound; Horten, Norway) with a 2.5-MHz probe. All examinations were performed by 2 cardiologists. Echocardiographic studies were performed on the parasternal long and short axes of the apical 2-chamber and 4-chamber views, with patients in the left lateral decubitus position. End-diastolic and end-systolic diameters of the left ventricle were measured on the parasternal long axis. The 2DE LV EF, end-systolic volume (ESV), and end-diastolic volume (EDV) were obtained using Simpson's biplane method in 2DE. Left-atrial (LA) volume was measured using the biplane area length method (3). LV mass was calculated according to American Society of Echocardiography criteria. Both LA volume and LV mass were indexed to body surface area. Pulsed-wave Doppler (PWD) recordings were performed 1 cm above the mitral inflow to diagnose LV diastolic dysfunction. In addition, PWD recordings were acquired from the LV lateral and septal annulus. The presence and degree of LV diastolic dysfunction were evaluated as has been previously described (4).

2.2.2. CMR imaging

All CMR examinations were performed using a 1.5-T MRI scanner (Magnetom Avanto, Siemens Healthcare, Germany) with an 18-channel body coil and high performance gradients (maximum gradient: 45 mT/m; maximum slew rate: 200 T/m/s). Cine-CMR was used, a commercially available 2D steady-state free precession pulse sequence (SSFP). Images were acquired in contiguous short-axis slices from the mitral annulus through the LV apex. The following parameters were used: 3.5 ms repetition time, 1.6 ms echo time, 60° flip angle, 1.9 mm × 1.4 mm in-plane spatial resolution, 6 mm slice thickness, 4 mm interslice gap, and 36.5 ± 9.2 ms reconstructed temporal resolution.

2.3. Image analysis

Two radiologists with more than 8 years of experience in cardiovascular radiology independently reviewed the MR examinations on a commercially available CMR workstation with standard software (Argus, Siemens Workstation, Germany). For CMR images, data were also recorded for each of the 17 LV segments based on the recommended LV segmentation. Manual tracing of the endocardial and epicardial borders of successive short-axis slices at the end-diastole and end-systole was performed. The contour tracing was monitored by reviewing the movie with contours attached. Papillary muscles were included in the mass and excluded from the volume calculations.

LA volumes were calculated as follows. Short-axis sections were acquired from the LA base to the atrioventricular junction, and LA volume was determined from manual delineation of the LA endocardial borders at the end of the LV systole.

The resulting section provided the typical LV and LA volumetric and functional data, including the EDV, ESV, EF, LA volume, and LV mass index parameters. The calculation was done using the modified Simpson rule. Functional parameters and the normalized body surface area were also calculated.

2.4. Statistical analysis

Bland–Altman analysis was used to determine possible bias (the mean difference between the 2 methods) and the limits of agreement (±1.95 standard deviation [SD]). Agreement between the 2 modalities was analyzed, and plots were constructed. Interobserver agreement was also calculated between the analyses made by the observers, using an intraclass correlation coefficient. All statistical analyses were performed using MedCalc software (version 12.2.1.0, MedCalc, Mariakerke, Belgium).

3. Results

All CMR and 2DE studies were completed, and the data for 5 measurements (EF, ESV, EDV, LA volume index, and LV mass index) were acquired in both modalities by the observers. CMR data were analyzed at a workstation with computer-aided calculation of the parameters after the imaging session, whereas datasets given by 2DE were calculated during and after the examination (Figures 1 and 2).

The EF, EDV, ESV, LV mass index (Figure 3), and LA volume index (Figure 4) were automatically calculated with standard software.

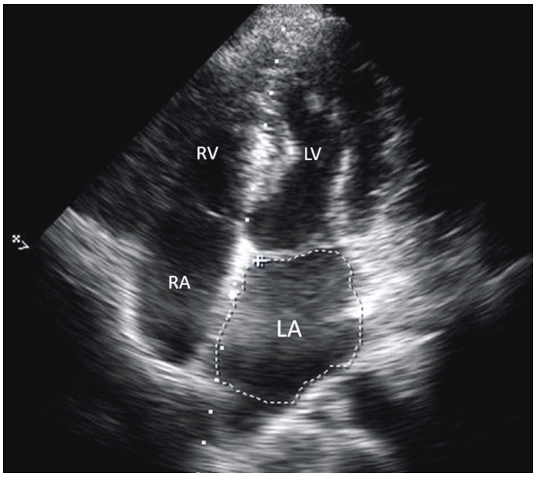

Figure 1. Left-atrial volumetric measurement from apical 4-chamber view. LV: left ventricle; RV: right ventricle, LA: left atrium; RA: right atrium.

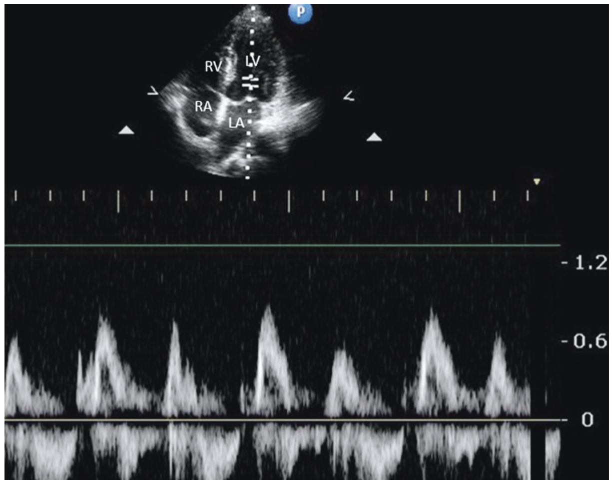

Figure 2. Pulsed-wave Doppler-derived transmitral E and A wave velocity. LV: left ventricle; RV: right ventricle, LA: left atrium; RA: right atrium.

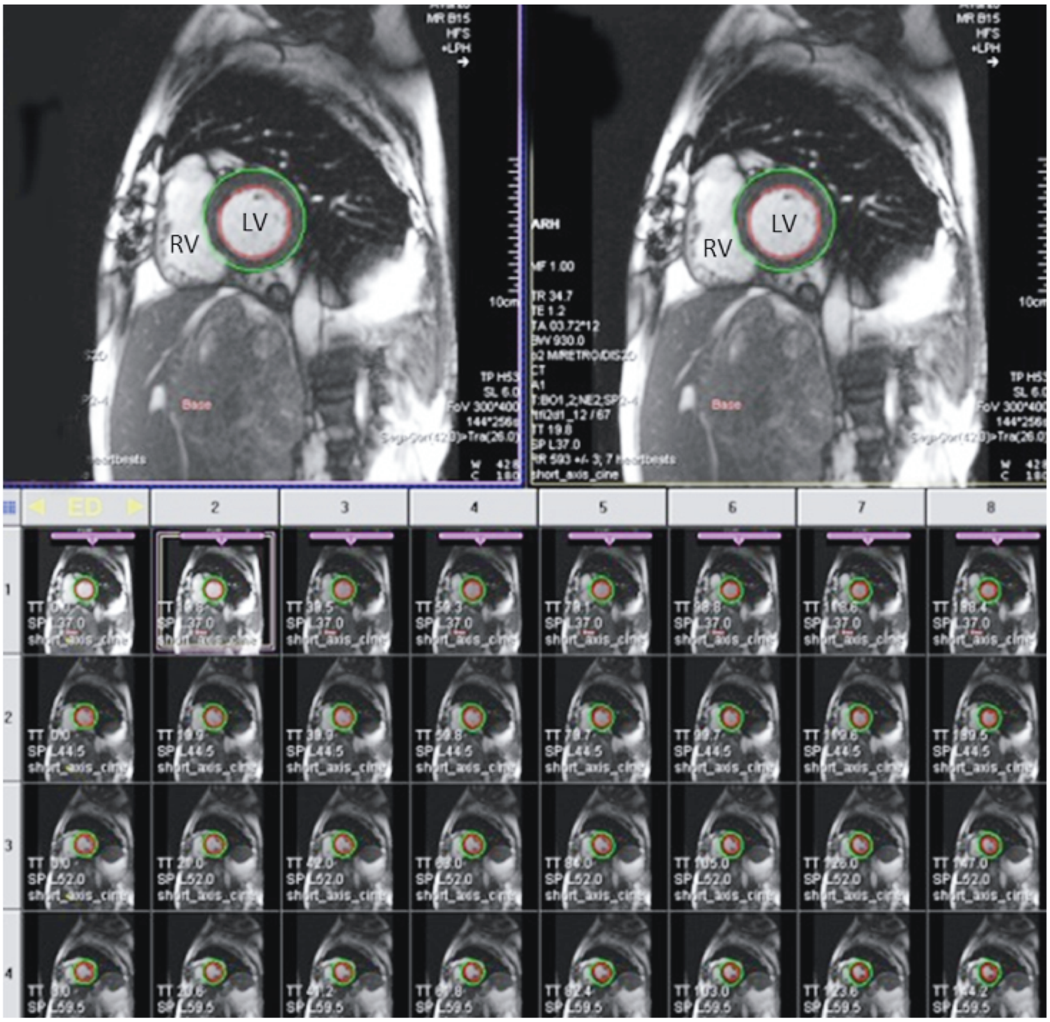

Figure 3. Left-ventricular function assessment. Successive manual tracing of the endocardial and epicardial borders of short-axis slices at the end-diastole and end-systole. LV: left ventricle; RV: right ventricle.

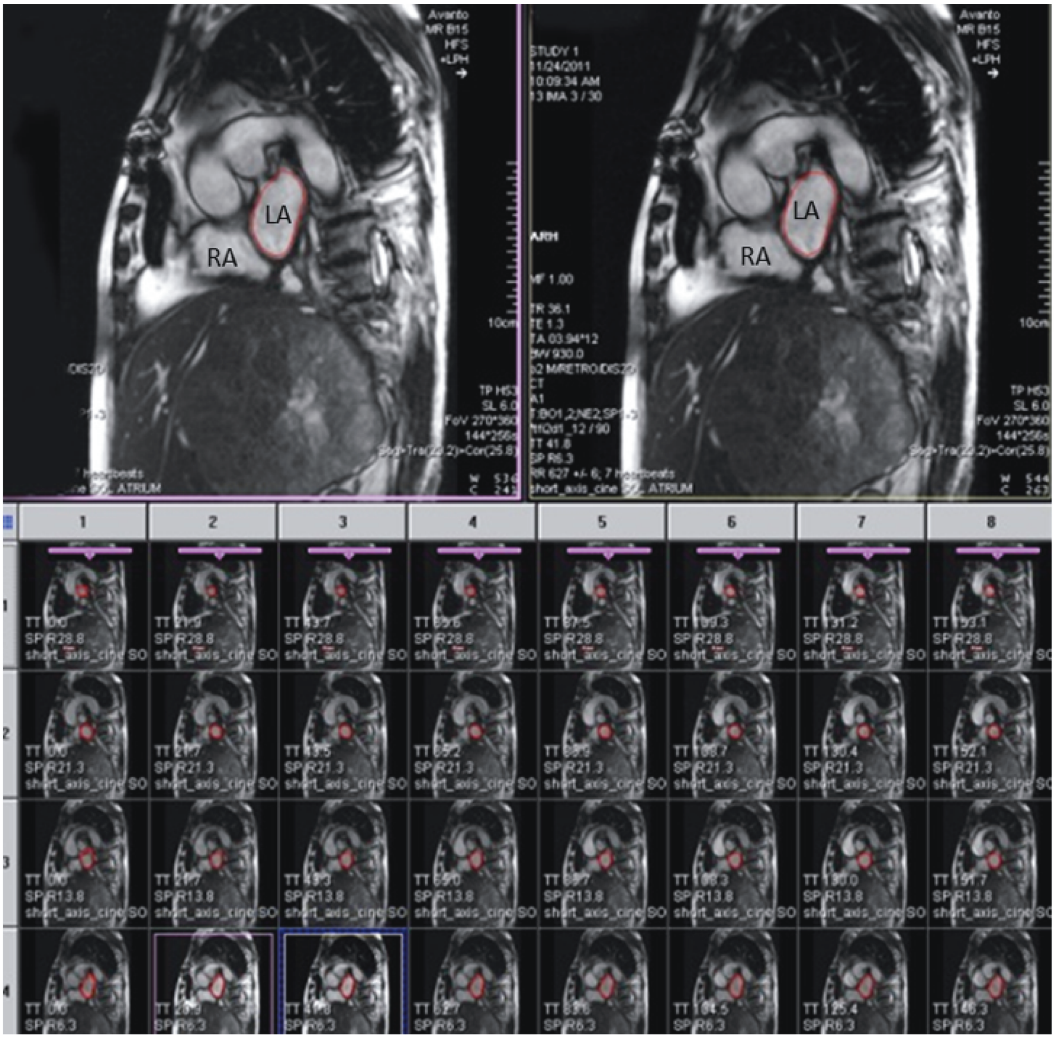

Figure 4. Left-atrial volume calculation. The left-atrial border was traced at the end left-ventricular systole. LA: left atrium; RA: right atrium.

Table 1 shows the average values of these 5 measurements based on the calculations of 2 observers in both modalities. Interobserver agreement was tested with an intraclass correlation coefficient. As shown in Table 2, agreement between observers on the 5 measurements was more powerful for CMR imaging than for 2DE.

Estimates of the 5 measurements by 2DE were analyzed and compared with the corresponding CMR measurements. Agreements between the 2 different modalities were evaluated with Bland–Altman analysis. The mean difference between the 2 methods (and the 2 SDs of the difference, which implies the limits of agreement) was also calculated, and Bland–Altman agreement plots were constructed. As a result derived from Bland–Altman curves, there was strong agreement between CMR and 2DE regarding measurements of the EF, EDV, ESV, and LV mass index, whereas this agreement was moderate for the LA volume index measurement.

4. Discussion

Diastolic dysfunction is commonly found in healthy and asymptomatic diabetic patients and is thought to be the earliest detectable functional abnormality in diabetic cardiomyopathy (2). Diastolic dysfunction is characterized by the impairment of the relaxation and passive filling of the left ventricle, and diastolic heart failure is said to exist when diastolic dysfunction is associated with an elevated end-diastolic pressure, clinical signs of heart failure with a normal EF. Functional abnormalities occur because of structural remodeling (concentric LV hypertrophy) and result in normal or near-normal EDV with elevated LV mass-to-volume and elevated wall thickness-to-chamber radius (5). In addition, the left atrium is directly affected by LV filling pressure during diastole when the mitral valve is opened. Thus, its enlargement suggests elevated LV filling pressure and chronic diastolic dysfunction.

Table 1. Average values of EF, EDV, ESV, LA volume index, and LV mass index based on the calculations of 2 observers in both modalities.

Measurements		Mean ± SD (range)
EF (%)	CMR	64.2 ± 10.0 (50.1–78.5)
	2DE	65.8 ± 10.2 (50.6–79.8)
EDV (mL)	CMR	126.5 ± 31.5 (75.4–168.8)
	2DE	123.2 ± 32.1 (73.2–165.7)
ESV (mL)	CMR	44.1 ± 14.6 (28.2–75.9)
	2DE	40.9 ± 13.7 (25.7–70.4)
LV mass index (g/m^2)	CMR	86.2 ± 18.1 (62.9–124.2)
	2DE	80.4 ± 18.3 (53.4–117.4)
LA volume index (mL/m^2)	CMR	35.6 ± 4.3 (28.5–42.4)
	2DE	28.4 ± 3.3 (23.6–34.2)

Table 2. Intraclass correlation coefficient intervals and 95% confidence intervals of observers in pairs.

Calculation parameters	Intraclass correlation		95% confidence interval	
	CMR	DE	CMR	DE
EF	0.9134	0.7498	0.7421 to 0.9709	0.2549 to 0.9160
ESV	0.9769	0.8766	0.9313 to 0.9923	0.6325 to 0.9586
EDV	0.9918	0.9750	0.9755 to 0.9972	0.9256 to 0.9916
LV mass index	0.9779	0.9154	0.9341 to 0.9926	0.7481 to 0.9716
LA volume index	0.7761	0.5152	0.3332 to 0.9248	0.5130 to 0.4913

Evaluating diastolic dysfunction and diastolic heart failure is still controversial due to the absence of acceptable indicators and due to its more complex mechanism. The ventricular relaxation process is difficult to assess by noninvasive means because imaging methods cannot directly measure cavity pressure changes. However, the assessment of diastolic dysfunction can be performed with several noninvasive techniques (Doppler echocardiography, radionuclide ventriculography) and invasive techniques (micromanometry, angiography, the conductance method).

Cardiac catheterization with simultaneous pressure and volume measurement is the gold standard for assessing LV diastolic function. The rate of LV relaxation and the rate and timing of diastolic filling, as well as myocardial and chamber stiffness, can thereby be determined (6). However, this diagnostic method is invasive and cannot be performed in all patients with suspected diastolic dysfunction.

Echocardiography is an excellent noninvasive, practical imaging tool for defining cardiac structure and function, and it allows real-time visualization of the cardiac cycle in diabetic cardiomyopathy. Quantitative and qualitative assessments of the heart can be made with regard to LV geometry, regional wall motion, and systolic and diastolic function, in addition to valvular anatomy and function (7).

PWD echocardiography is currently the most practical and commonly used method for assessing diastolic function. A detailed, comprehensive diastolic study is vital for diabetic patients, and it should include the measurement of transmitral and pulmonary venous flow/velocities and LA volume (8–10).

Tissue Doppler imaging (TDI) has been shown to identify global and regional abnormalities in myocardial properties, with a high level of temporal resolution. TDI differs from conventional Doppler in that it uses a filter that eliminates high-velocity and low-amplitude signals reflected from blood cells, thereby allowing low-velocity and high-amplitude tissue signals to be analyzed.

Despite its widespread use, echocardiography has important disadvantages, including a limited field of view and calculation errors related to flow direction. Interference with the acoustic window from bones or lungs limits echocardiography. Small changes in LA or LV volumes and mass can be detected by CMR imaging, as opposed to echocardiography; these small changes might be important when evaluating the progression of disease or response to therapy. CMR imaging, which is the criterion standard for measuring volumes and LV mass due to its image quality and high spatial and temporal resolution, has been compared with echocardiography for the diagnosis of diastolic dysfunction in a limited number of studies (11).

Radionuclide angiography may be used to study the rapid-filling phase of diastole, the duration of the isovolumic relaxation phase, and the relative contribution of rapid filling to total diastolic filling. However, this technique is not performed in routine clinical practice.

With its technological advancement in the past decade, CMR imaging, a noninvasive, nonionizing imaging procedure, has gained attention for its use in diagnosing cardiovascular diseases. The role of CMR in assessing systolic dysfunction has been well established. On the other hand, CMR is seldom used for assessing diastolic dysfunction. However, 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 a preserved EF (known as diastolic heart failure) has emerged.

CMR provides spot and in-motion images and sophisticated calculations that enable the accurate and reproducible assessment of global and ventricular regional function. The reproducibility of CMR measurements of the cardiac chamber volume, ventricular EF, and ventricular mass is very good. The functional information derived from cine-CMR includes global ventricular volumes and mass, without the need to make any geometrical assumptions, and therefore applies to ventricles of all sizes and shapes, even to those that have been extensively remodeled (12–14).

In our study, we evaluated the EF, EDV, ESV, LA volume, and LV mass index values obtained from both methods. For our results, we calculated the degree of agreement between observers from 2DE and CMR examinations. According to our results, these 5 values were measured more consistently by CMR observers than by 2DE observers. We also evaluated the agreement between the 2 modalities: our results showed that CMR measurements were compatible with the 2DE measurements.

To our knowledge, the literature includes no similar study comparing the use of CMR and 2DE in diabetic patients. However, a number of studies have determined diastolic parameters by using echocardiography, radionuclide ventriculography, and positron-emission tomography (15–18). A study by Krishnamurthy et al. calculated the isovolumic relaxation time and E/A ratio by using CMR, and compared these to conventional echocardiographic data from healthy volunteers (19). In another study, Sten et al. sought the different confounding factors influencing LV measurement results in diabetic patients, and they found that intra- and interreader variability, analyst experience, and different techniques for determining the boundaries of the left ventricle significantly affected the MRI parameters for cardiac function (20). Bollache et al. aimed to develop a robust process to automatically estimate the velocity- and flow-rate–related diastolic parameters from CMR data and to test the consistency of these parameters against echocardiography, as well as their ability to characterize LV diastolic dysfunction in patients with severe aortic stenosis. In addition, they evaluated the interoperator variability of the CMR measurements of a subgroup of 30 subjects (21).

Several limitations of our study should be recognized. First, breath-holding, along with long image-acquisition time, is needed for optimal-quality images. This is a major drawback, especially when testing the elderly population. Second, the patient population was relatively small. Our results will need to be confirmed in a larger prospective study.

In conclusion, this study demonstrated that 2DE has much higher interobserver variability than does CMR and that CMR is as reliable as 2DE. Although 2DE is currently the noninvasive imaging technique used to assess diastolic function in diabetic patients, CMR imaging is emerging as a valuable alternative, with its unique potential for function analysis.

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