Automated Evaluation of Diastolic Function from Phase-Contrast MRI in Healthy Subjects and Patients

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Abstract

Early detection of diastolic dysfunction is crucial for patients with incipient heart failure. Our goal was to develop a robust process to automatically estimate diastolic parameters from phase-contrast cardiovascular magnetic resonance (PC-CMR) data and to test their ability to characterize left ventricular (LV) dysfunction. We studied 53 subjects (35 controls and 18 patients with a severe aortic valve stenosis) who had PC-CMR and Doppler echocardiography on the same day. PC-CMR data were analyzed using custom software to extract diastolic parameters. Our technique was reproducible, as reflected by a small variability (<4.25 ± 5.89 %). The PC-CMR diastolic parameters significantly (p<0.0002) varied in patients as opposed to controls. Moreover, PC-CMR diastolic parameters were consistent with echocardiographic values (r>0.71) and were able to accurately separate patients from controls (accuracy>0.85). Of note, a superiority in terms of correlation with echocardiography and accuracy to detect LV abnormalities were found for flow-rate parameters. A fast and reproducible technique was proposed and was successfully used to extract consistent PC-CMR diastolic parameters. This technique provides a valuable addition to established CMR tools in evaluation of patients with diastolic dysfunction.

1. Introduction

Altered diastolic function, which is strongly related to the quality of left ventricular (LV) filling, is a source of heart failure: it has been shown that 40 to 50% of patients suffering from heart failure have a normal LV ejection fraction while their diastolic function is impaired [1]. Furthermore, diastolic impairment without global systolic dysfunction is related to poor outcome [2]. Thus, the early and robust detection and quantification of diastolic dysfunction is crucial for optimal patient management. In clinical routine, the evaluation of diastolic function is achieved using Doppler echocardiography [3]. Several conventional diastolic parameters are estimated: the early and late filling peak velocities of the transmitral flow (E and A) and E-wave deceleration time (DT), as well as the annular myocardial early longitudinal peak velocity (E'). It has been shown that the calculated ratios E/A and E/E', as well as DT, have a high prognostic value [3].

CMR with its recent developments in velocity encoding is increasingly used for the analysis of blood flow and myocardial velocities. Furthermore, several studies demonstrated the usefulness of PC-CMR in the measurement of some of the aforementioned conventional diastolic parameters [4]. However, these analyses were mostly based on manual positioning of regions of interest (ROIs) within transmitral flow area or myocardium on multiple phases [4]. This manual positioning of ROIs is time-consuming and operator-dependent.

Accordingly, our first goal was to develop a robust technique to automatically delineate the transmitral flow pattern, as well as the myocardium throughout the cardiac cycle, and to extract functional diastolic parameters from both velocity and flow rate curves. Our second aim was to test the consistency of these parameters by evaluating: 1) the correlation between CMR parameters and the echocardiographic indices, 2) the ability of both CMR and echocardiographic diastolic parameters to characterize LV dysfunction, and 3) the reproducibility of CMR measurements.

2. Methods

2.1. Study population and data acquisition

A group of 53 subjects had an echocardiographic exam for the evaluation of LV function and a CMR exam on the same day. This group included 35 controls free from

overt cardiovascular disease and 18 patients with severe aortic valve stenosis (AVS). The study protocol was approved by the institutional review board and informed consent was obtained from all participants.

Doppler echocardiography was performed by an experienced echocardiographer using a GEMS Vivid 7 system. The transmitral early filling and atrial filling peaks (E_{US} and A_{US}) velocities and deceleration time (DT_{US}), as well as the lateral annular early peak (E'_{US}) longitudinal velocity were measured.

CMR imaging was performed using a 1.5 T MRI system (Signa HDx, GEMS, Waukesha, WI, USA). Previously acquired 2-chamber and 4-chamber views allowed positioning of a retrospectively ECG-gated PC pulse sequences, in a plane perpendicular to the transmitral inflow and located below the mitral annulus at the level of the tips of the opened mitral leaflets. At this location, two dynamic PC series, corresponding to an entire cardiac cycle, were acquired during breath-hold: 1) the transmitral flow velocity sequence (encoding velocity Venc = 180 cm/s, echo time TE = 3.1 ms, repetition time TR = 7.6 ms, views per segment = 2, view sharing was used resulting in an effective temporal resolution of 15 ms), and 2) a myocardial longitudinal velocity sequence (Venc = 15 or 20 cm/sec, TE = 5 ms, TR = 9.5 ms, views per segment = 2, view sharing was used resulting in an effective temporal resolution of 20 ms). For both sequences, the following parameters were used: flip angle = 20°, slice thickness = 8 mm, pixel spacing = 1.9 x 1.9 mm, matrix 256 x 128.

2.2. Analysis of blood flow velocity images

PC-CMR modulus images were difficult to segment because of the flow-related contrast variations along time. We therefore preferred to process velocity images, which presented connected areas in terms of velocity sign.

Based on these connectivity properties, our segmentation algorithm comprised three main steps. First, a rough ROI was manually drawn on a single phase around the flow of interest. This cardiac phase was automatically set to the middle of the cardiac cycle for transmitral flow segmentation. The mean velocity curve was calculated within this ROI, and the cardiac phase corresponding to its highest absolute value was detected. In the second step, this latter cardiac phase was used to initialize the segmentation algorithm, by an automated detection of the biggest connected area, in terms of sign. The centre of mass of this area was calculated and reported on the neighbouring phases. In the third step, the biggest connected areas containing this centre of mass were detected on these neighbouring phases, and their centres of mass were used to repeat the process toward the beginning and the end of the cardiac cycle.

After transmitral orifice segmentation, curves of maximal and mean velocities, as well as flow rates, were derived. The transmitral flow maximal velocity curve was used to estimate velocity-related parameters (E_{MR} and A_{MR}), by automatically detecting the two highest local peaks during the diastolic period. Similar processing was applied on the transmitral flow rate curve to detect the peak filling rate (Ef_{MR}, in ml/s) and the peak atrial rate (Af_{MR}, in ml/s). The Ef_{MR}/Af_{MR} ratio, as well as the peak filling rate normalized by the filling volume Ef_{MR}/FV_{MR} (in s-1), were calculated. The filling volume (FV_{MR}, in ml) was defined as the area under the transmitral flow rate curve comprised between the beginning and the end of the filling period. Finally, the deceleration time, DT_{MR}, was calculated as the duration between the time to peak filling rate Ef_{MR} and the end of the Ef_{MR} wave (Figure 1).

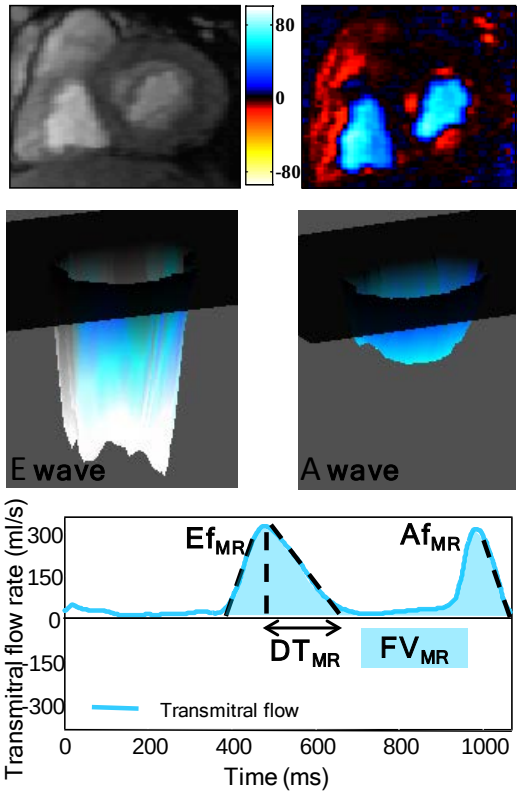

Figure 1. analysis of PC CMR transmitral flow data. Line 1: modulus and color-encoded through plane velocity images. Line 2: segmented transmitral flow represented at the time of the E and A waves. Line 3: extracted flow-rate curve and diastolic parameters.

2.3. Analysis of myocardial velocities

Again, velocity images were preferred for the longitudinal motion analysis. However, the connectivity process was not adapted because of the bi-directional (up and down) longitudinal motion of the mitral annulus during a single cardiac cycle, which implies changes in velocity sign. Accordingly, a classification based on the k-means algorithm was applied on temporal velocity

profiles of fixed pixels during a whole cardiac cycle, within a rough ROI manually drawn around the LV on a single phase. This classification allowed isolating the biggest connected cluster, defined as the "myocardial" cluster. Maximal and mean velocity curves can be calculated from the obtained myocardial global cluster. The myocardial maximal longitudinal velocity curve, corresponding to the whole myocardium, was used to derive the parameter E'_{MR}, which was the highest local peak occurring first during the filling period. This peak velocity was used to estimate the E_{MR}/E'_{MR} ratio.

2.4. Inter-operator variability

Inter-operator variability of our analysis in terms of functional velocity and flow rate parameters was studied on a sub-group of 30 subjects (20 controls and 10 AVS).

2.5. Statistical analysis

A non-parametric Mann-Whitney test was used to evaluate the significance of the differences between controls and patients functional parameters. A p value < 0.05 was considered as significant. In addition, Pearson correlation analysis was performed to compare CMR with Doppler echocardiography values. For both analyses, the ability of the calculated diastolic parameters to separate controls from patients, in terms of sensitivity, specificity, negative and positive predictive values (NPV and PPV) as well as the accuracy, was evaluated using a receiver operating characteristic (ROC) analysis to define optimal thresholds. For both blood flow and myocardial parameters, inter-operator variability was calculated for each subject as the absolute difference of the repeated measurements in the percentage of their mean.

3. Results

For each subject, the processing time was less than 5 minutes, on a personal computer (CPU 2.67 GHz, 3 Gb RAM). In addition, blood flow segmentation was reproducible, as reflected by an averaged percentage of variation < 1.96 ± 2.95% for the transmitral flow related parameters and of 4.25 ± 5.89% for mitral annulus longitudinal velocity.

3.1. Doppler *vs.* CMR parameters

Table 1 summarizes diastolic parameters values calculated from echocardiographic and CMR data on both controls and patients groups. All echocardiographic and CMR diastolic functional parameters significantly varied in patients when compared to the controls.

A stronger correlation and a slope closer to 1 were found for the comparison between the echocardiographic E_{US}/A_{US} and the CMR flow rate-related Ef_{MR}/Af_{MR} (r= 0.81, slope=0.90) than for the comparison with the CMR velocity-related E_{MR}/A_{MR} (r= 0.71, slope=0.55). In addition, although the CMR mitral annulus longitudinal velocities E'_{MR} were lower than echocardiographic values E'_{US}, a good correlation was found between these two velocities (r=0.75).

Table 1. Diastolic parameters for controls and patients

	Controls	AVS Patients	p value
Echocardiographic measurements			
E_{US}/A_{US}	1.39 ± 0.60	0.76 ± 0.27	<0.0001
DT_{US} (ms)	180 ± 56	261 ± 59	0.0001
E'_{US} (cm/s)	15.7 ± 4.2	8.0 ± 2.5	<0.0001
CMR measurements			
E_{MR}/A_{MR}	1.33 ± 0.40	0.74 ± 0.27	<0.0001
Ef_{MR}/Af_{MR}	1.44 ± 0.58	0.54 ± 0.23	<0.0001
Ef_{MR}/FV_{MR} (s^{-1})	4.26 ± 0.93	2.55 ± 0.61	<0.0001
DT_{MR} (ms)	185 ± 35	260 ± 40	<0.0001
E'_{MR} (cm/s)	11.3 ± 3.5	7.3 ± 1.6	<0.0002

3.2. Abnormality detection

Figure 2 summarizes the values of sensitivity, specificity, and the overall accuracy obtained from the ROC analysis performed for each echocardiographic and CMR diastolic parameter on the 35 controls and the 18 patients with AVS.

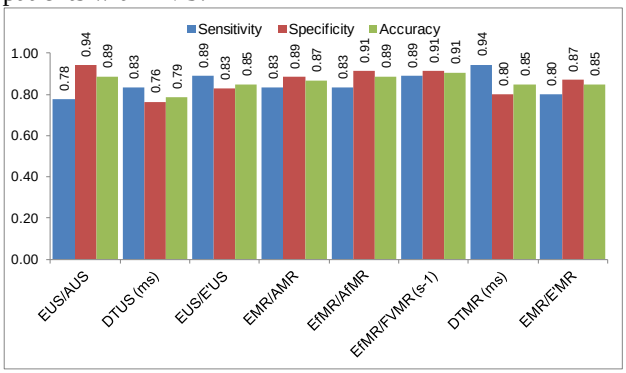

Figure 2. Ability of echocardiographic and CMR diastolic parameters to separate controls from patients.

4. Discussion

The early diagnosis of diastolic dysfunction has an important prognostic value and may impact the management strategy and the follow-up of patients with incipient heart failure. Although CMR is known as the modality of choice for the evaluation of global LV function, systolic function and myocardial viability, Doppler echocardiography remains the clinical reference for the evaluation of diastolic dysfunction [3]. Several CMR studies, based on velocity and flow rate curves extracted from PC images [4], reported capabilities of this modality for the assessment of diastolic function.

However, despite these methodological developments and the recent technological improvements in PC-CMR sequences, the use of CMR in clinical evaluation of diastolic function remains limited because of the lack of automated methods designed for the analysis of PC images. Indeed, most of the PC-CMR studies previously presented in the literature were based on manual positioning of ROIs on each phase of the cardiac cycle [4]. This manual positioning is time-consuming and subjective [4]. Accordingly, our primary goal was to minimize manual intervention to reduce variability and shorten the processing time. The final objective was to test the ability of the resulting CMR diastolic parameters to characterize LV diastolic dysfunction.

To achieve this aim, we first developed a connectivity-based technique for a semi-automated segmentation of the transmitral flows patterns on blood velocity PC series. Because of the connectivity property, our technique is not related to the geometrical shape of the flow, which is an important feature of our technique. Thanks to this property, our segmentation method can be easily used for the delineation of various flow patterns with high reproducibility. The automated analysis of the derived velocity and flow rate curves enabled the estimation of consistent diastolic parameters. Indeed, despite the underestimation of velocity values, the comparison between the CMR and the echocardiographic parameters revealed a good correlation. This correlation was higher and the slope of the linear interpolation between the CMR and the echocardiographic measurements was closer to one when considering the flow rate related parameters. This finding might be related to the fact that flow rates are less sensitive to the shape of the velocity profile and to the slight mismatch between the acquisition plane and the true perpendicular to the transmitral flow.

In addition, the proposed flow rate-related parameters Ef_{MR}/Af_{MR} and Ef_{MR}/FV_{MR} resulted in a higher accuracy than the other CMR parameters, when used for LV diastolic dysfunction characterization (Figure 3).

Secondly, a clustering technique enabled isolating the myocardial cluster from tissue velocity PC-CMR and the corresponding maximal velocity curve during the cardiac cycle. To the best of our knowledge, the estimation of myocardial longitudinal velocities in the setting of diastolic function was previously presented in only few PC-CMR studies [4] and the positioning of myocardial ROIs was always done manually. In the present study inter-operator variability of the myocardial annular early peak longitudinal velocity E'_{MR} was very small (4.25 ± 5.89%). This variability was significantly lower than the 10% variability previously reported in a CMR study [5].

Despite the underestimation of CMR tissue measurements, E'_{MR} was significantly reduced in patients with severe AVS and the resulting ratio E_{MR}/E'_{MR} characterized LV dysfunction with high accuracy.

The differences in diastolic parameters found between echocardiography and CMR can be explained by the differences in imaging principles of the two techniques, including the difficulties of plane or beam positioning, but also by technical limitations inherent to the CMR acquisitions. These limitations included the limited temporal resolution of PC-CMR imaging as opposed to Doppler echocardiography. Despite these technical limitations, high correlations were found between CMR and echocardiographic parameters and, more importantly, PC-CMR parameters were able to characterize LV diastolic dysfunction with the same accuracy than the echocardiographic indices.

Our semi-automated method was fast, reproducible and was successfully used on PC-CMR data of 53 subjects, including controls and patients with severe AVS and a preserved ejection fraction. This application enabled the estimation of velocity and flow rate-related diastolic parameters, which were highly correlated with echocardiographic measurements. In addition, significant differences were found between PC-CMR diastolic parameters estimated in controls and in patients with AVS, resulting in a high accuracy of the CMR characterization of LV diastolic dysfunction. Importantly, equivalent accuracy was found for both echocardiographic and CMR parameters, indicating a potential clinical usefulness of CMR for the evaluation of diastolic function, which should be confirmed in larger populations with subtle to severe diastolic dysfunction.

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