Reproducible Evaluation of Diastolic Function Using Phase-Contrast Magnetic Resonance Data

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Abstract

The evaluation of diastolic function from phase-contrast (PC) Magnetic Resonance (MR) data in clinical routine is not yet established. Thus, our goal was to develop a reproducible process to analyze PC data. These developments were used to estimate mitral flow and myocardial velocities from PC data of 40 controls. Besides, the reproducibility was assessed on a sub-group of 20 subjects. Transmitral flow and myocardial patterns were successfully delineated on each cardiac phase, resulting in conventional diastolic parameters, consistent with echocardiographic literature. Moreover, new proposed parameters correlated strongly (r>0.8) with those with high prognostic value. Finally, the flow segmentation was reproducible (99.5±2.1% of overlap between two segmentations), and a low inter-operators variability (<3.65%) in diastolic parameters measurements was obtained. Our technique provides a valuable addition to established cardiac MR tools.

1. Introduction

Diastolic dysfunction is an early sign of heart failure. Indeed, it has been shown that 40 to 50% of patients suffering from heart failure have a normal left ventricular (LV) ejection fraction while their diastolic function is impaired [1]. Accordingly, the early detection of diastolic dysfunction is crucial for an optimal patient management. In clinical routine, this evaluation is achieved using Doppler echocardiography, which enables estimating several conventional diastolic parameters, such as: the transmitral flow-related early peak (E) and late peak (A) velocities and deceleration time (DT), as well as the myocardial annular early peak (E') longitudinal velocity. The high prognostic value of the E/A and E/E' ratios, as well as DT, has been demonstrated in several studies [2].

Magnetic Resonance Imaging (MRI), with its recent developments in velocity encoding, is increasingly used for the analysis of through-plane velocities. Furthermore, several studies demonstrated the usefulness of phase-contrast (PC) MRI in the measurement of the aforementioned conventional diastolic parameters [3-4]. However, these analyses were mostly based on manual positioning of regions of interest (ROIs) within the transmitral flow or the myocardium on multiple phases, which is time-consuming and operator-dependent.

Accordingly, our primary goal was to develop a robust and reproducible technique to delineate the transmitral flow pattern, as well as the myocardium, throughout the cardiac cycle, with minimal manual interventions. In addition, an automated process was developed to analyze velocity and flow rate curves derived after this delineation. We hypothesized that the excellent quality of PC images, combined with the aforementioned processing techniques, would allow the estimation of consistent conventional and additional diastolic parameters. These latter were: 1) the isovolumetric relaxation time (IVRT), previously described in echocardiography but, to our knowledge, never assessed in MRI, and 2) filling flow rate-related parameters, such as the peak filling rate (Ef, in ml/s) and the peak atrial filling rate (Af, in ml/s), as well as the filling volume (FV, in ml). Our technique was tested on a group of 40 controls and its reproducibility was evaluated on 20 subjects.

2. Methods

2.1. Study population

A group of 40 controls (23 women, 17 men, age: 33 ± 12 years), free from overt cardiovascular disease, was studied. Each subject underwent imaging using a GE 1.5 T MRI system (Signa HDx, General Electric Medical Systems, Waukesha, WI, USA). Previously acquired 2-chamber and 4-chamber views allowed positioning of a

plane perpendicular to the transmitral inflow and located below the mitral annulus at the level of the tips of the opened mitral leaflets. Two dynamic PC series, corresponding to an entire cardiac cycle, were acquired in this plane: 1) the transmitral flow velocity sequence (velocity encoding Venc = 180 cm/s, repetition time TR = 7.6 ms, echo time TE = 3.1 ms), and 2) a myocardial longitudinal velocity sequence (Venc = 15 cm/s, TR = 9.5 ms, TE = 5 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. The number of phases varied between 43 and 89 images per cardiac cycle. Velocity PC images were transferred for off-line analysis using our custom software.

2.2. Segmentation of flow velocity images

Each PC dataset included a modulus and a velocity-encoded dynamic series (Figures 1.A and 1.B). The modulus images were difficult to segment because of the flow-related contrast variations during the cardiac cycle, as well as the variable shapes of the mitral orifice. We therefore preferred to process velocity images, which presented connected areas in terms of pixel sign, defined by the local direction of the blood flow.

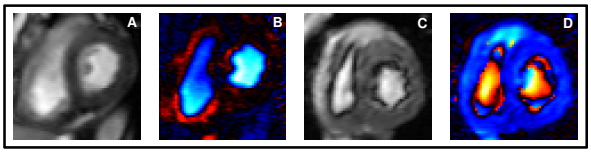

Figure 1. Examples of A: a transmitral flow modulus image; B: a transmitral flow velocity-encoded image; C: a myocardial modulus image; D: a myocardial velocity-encoded image.

Based on connectivity properties, our segmentation comprised three main steps. First, a rough ROI was manually drawn on a single phase around the flow of interest (Figure 2.A). 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 velocity sign. The center of mass of this area was calculated and reported on the neighboring phases. In the third step, the biggest connected areas containing this center of mass were detected on these neighboring phases, and their centers of mass were used to repeat the process toward the beginning and the end of the cardiac cycle. The propagation of the center of mass, while looking for the biggest connected area, constrained the segmentation process to track the flow of interest. This segmentation process provided a refined delineation of the blood flow pattern in each phase of the PC velocity series (Figure 2.A).

2.3. Myocardial detection

Similar to blood flow PC data, myocardial PC datasets contained a modulus and a velocity-encoded series (Figures 1.C and 1.D). Because of the extreme basal position of the imaging plane and of the low contrast between the myocardium and the neighboring structures, myocardial detection on modulus images is even more challenging than on conventional cine MR images. Again, velocity images were preferred for the longitudinal motion analysis.

Accordingly, a classification based on the k-means algorithm was applied on temporal velocity profiles, within a rough ROI manually drawn around the LV on a single phase (Figure 2.B). This classification allowed isolating the biggest connected cluster, defined as the "myocardial" cluster, which contained pixels with a similar temporal velocity profile (Figure 2.B).

2.4. Functional parameters

After transmitral orifice segmentation, curves of maximal velocity and flow rate (mean velocity x segmented area for each phase), were derived (Figure 2.C). The aortic orifice was delineated from PC series acquired for transmitral flow analysis, using the above flow segmentation technique. It resulted in ejection flow rate curve, used to estimate the end of the ejection phase. This time enabled the delimitation of the diastolic period. The transmitral flow maximal velocity curves were used to estimate the conventional parameters E and A, by automatically detecting the two highest local peaks during the diastolic period. Similar processing was applied on the transmitral flow rate curves to detect the additional parameters Ef and Af. The Ef/Af ratio, as well as the peak filling rate normalized by the filling volume Ef/FV (in s-1), were calculated, FV being defined as the area under the transmitral flow rate curves comprised between the beginning and the end of the filling period. Finally, IVRT was estimated as the difference between the beginning of the filling period and end of the ejection, and DT was calculated as the duration between the time to peak filling rate Ef and the end of the Ef wave. Of note, all times were defined as the intersection between the time axis and the linear interpolation of the ascending or descending slope, automatically calculated on the part of the curve comprised between 40% and 70% of its maximal value.

The myocardial longitudinal maximal velocity curve (Figure 2.C) on the lateral wall was used to derive the parameter E', which was the first and highest local peak during the diastolic period. This maximal longitudinal velocity calculated on the lateral wall was used to estimate E/E'.

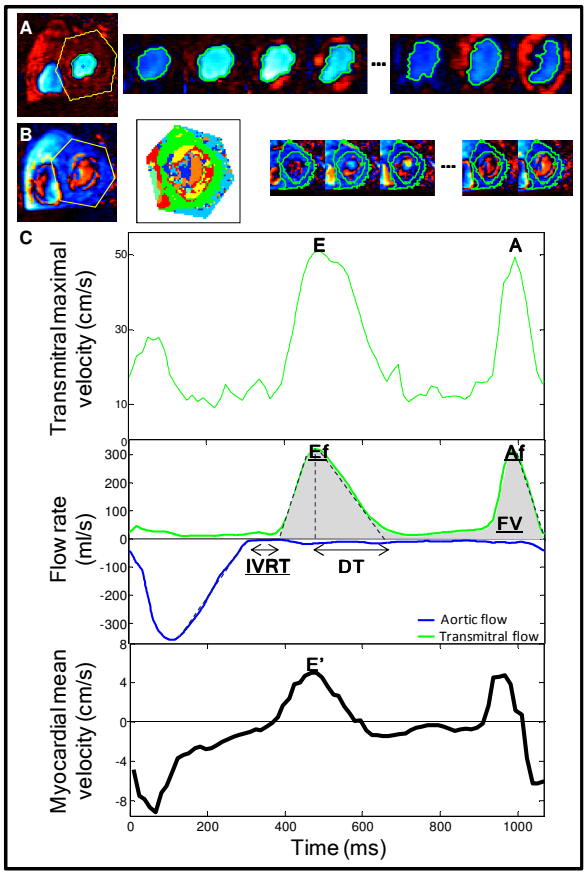

Figure 2. A: example of transmitral flow delineation on PC velocity data. B: example of myocardial cluster detection on PC velocity data. C: parameters automated extraction from velocity and flow rate curves.

2.5. Inter-operators variability

Since both flow segmentation and myocardial clustering needed a manual initialization on a single phase, the inter-operators variability of our analysis, in terms of blood flow segmentation, as well as functional velocity and flow rate parameters estimation, was studied. For this evaluation, the whole process developed for flow and myocardial PC data analysis was repeated by two independent operators on a sub-group of 20 controls.

2.6. Statistical analysis

Mean values and standard deviations of conventional diastolic parameters (E, A, E/A, DT, E' and E/E'), obtained with our automated process, were calculated and compared against values previously described in the echocardiographic literature. The additional parameters proposed in the present study (IVRT, Ef/Af and Ef/FV) were compared against values previously presented in the echocardiographic literature, when available, or were correlated using a Pearson analysis to the conventional parameters obtained in our study, such as E/A and DT.

To evaluate inter-operators variability in terms of blood flow segmentation, the percentage of overlap between the two segmentations was calculated for each cardiac phase. The mean and standard deviation of these percentages were calculated for the whole sub-group, on the diastolic period for the transmitral flow and on the systolic period for the aortic flow. Moreover, inter-operators variability in terms of diastolic parameters measurements was calculated for each subject as the absolute difference of the repeated measurements in the percentage of their mean. Mean and standard deviation of these percentages on the whole sub-group were provided.

3. Results

All developments, including blood flow and myocardial detection and the automated extraction of functional parameters from velocity and flow-rate curves, were integrated in a user-friendly interface developed on Matlab (Mathworks, Natick, MA, USA). This software was used to analyze PC data of the 40 controls. For each subject, the processing time was less than 5 minutes, on a personal computer (CPU 2.67 GHz, 3 Gb RAM).

Conventional parameters derived from the PC data were averaged over the 40 subjects and presented in Table 1. The E/E' ratio mean value was 5.9 ± 2.3.

Table 1. Comparison of parameters with literature.

Transmitral flow-related parameter	Present study (n = 40)	Echocardiographic study [5] (n = 61)
Age (years)	33 ± 12	21-49
E (cm/s)	62 ± 16	72 (44-100)
A (cm/s)	44 ± 11	40 (20-60)
E/A	1.5 ± 0.5	1.9 (0.7-3.1)
DT (ms)	179 ± 33	179 (139-219)
Myocardial parameter	**Present study (n = 40)**	**Echocardiographic study [6] (n = 29)**
Age (years)	33 ± 12	29 ± 5
E' (cm/s)	11.7 ± 4.0	10.8 ± 3.1

Regarding the additional parameters: 1) IVRT mean value was 73 ± 27 ms, 2) the mean flow rate ratio Ef/Af was 1.7 ± 0.7 and its comparison with the conventional velocity ratio E/A resulted in a correlation coefficient of r = 0.95, and 3) FV mean value was 69 ± 19 ml and Ef/FV mean value was 4.5 ± 0.8 s-1. The comparison of this latter ratio with DT resulted in a correlation coefficient of r = 0.80.

Blood flow segmentation was reproducible, as reflected by an averaged percentage of overlap between the segmentations performed by two independent operators of 99.8 ± 0.94% for the transmitral flow and 99.5 ± 2.07% for the aortic flow. Table 2 summarizes the

inter-operators variability for each diastolic parameter averaged over the sub-group of 20 subjects.
Table 2. Inter-operators variability in measurements.

Parameter	Inter-operators variability
E	0.00 ± 0.00%
A	0.00 ± 0.00%
DT	0.92 ± 2.51%
E'	2.37 ± 3.22%
IVRT	3.65 ± 8.42%
Ef	0.04 ± 0.12%
Af	0.07 ± 0.21%
FV	0.16 ± 0.40%

4. Discussion

Early diagnosis of diastolic dysfunction is an important prognostic factor and may impact the management strategy and the follow-up of patients with incipient heart failure. Although MRI 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 [5]. Several MRI studies, based on volume curves extracted from cine images or on velocity and flow rate curves extracted from PC images [4], showed the usefulness of this modality for the assessment of diastolic function. However, despite these methodological developments and the recent technological improvements in cardiac PC MR sequences, the use of MRI in the clinical evaluation of diastolic function remains limited because of technical issues, such as the lack of automated methods designed for the analysis of PC images. Accordingly, our primary goal was to minimize manual intervention to reduce variability and shorten the processing time.

To achieve this aim, we first developed a connectivity-based technique for a semi-automated segmentation of the transmitral flow pattern on blood flow velocity PC series. Because of the connectivity properties, our technique is not related to the geometrical shape of the flow, which is an important feature since it enables its application to various flow patterns. In the present study, this segmentation was successfully used on the transmitral and the aortic flows of 40 subjects and was shown to be reproducible in a sub-group of 20 subjects, in terms of area overlap and functional parameters. The combination of this robust segmentation with an automated analysis of the derived velocity and flow rate curves enabled the estimation of consistent diastolic parameters. Indeed, our conventional parameters were very close to those previously described on groups of controls of two echocardiographic studies [5-6] (Table 1). Studies used for this comparison were selected on the basis of participant ages because of the known relation between diastolic parameters and aging [5]. Regarding the additional parameters: the isovolumetric relaxation time (IVRT) compared favorably with the values previously described in the echocardiographic study [5] (IVRT = 76 ms (54-98 ms)); comparisons of the ratios Ef/Af and Ef/FV against conventional parameters with known prognostic value (E/A and DT, respectively) resulted in high correlations. These flow rate-related parameters are specific to MRI data and are, by definition, less sensitive to data noise than the conventional maximal velocity-related parameters, since they are estimated from the averaged velocity throughout the blood flow surface.

Secondly, a clustering technique was used for a classification of velocity profiles from tissue velocity PC data. It enabled isolating the myocardial cluster. The only manual intervention was the positioning of a rough ROI around the LV, resulting in a low inter-operators variability in the measurement of E'.

Our semi-automated software was fast, reproducible and was successfully used on PC blood flow and myocardial data of 40 controls. This application enabled the estimation of conventional diastolic parameters, which were consistent with previous echocardiographic findings. Robust additional flow rate-related parameters, which may prove clinically useful, were proposed and compared favorably with diastolic parameters with known prognostic value. Our process may provide a valuable addition to the standard MRI tools already used in the clinical settings for the diagnosis of heart disease.

References

[1] Zile MR, Baicu CF, et al. Diastolic heart failure--abnormalities in active relaxation and passive stiffness of the left ventricle. N Engl J Med 2004; 350:1953-1959.

[2] Nagueh SF, Appleton CP, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. J Am Soc Echocardiogr 2009, 22:107-133.

[3] Karwatowski SP, Mohiaddin R, et al. Assessment of regional left ventricular long-axis motion with MR velocity mapping in healthy subjects. J Magn Reson Imaging 1994; 4:151-155.

[4] Paelinck BP, de Roos A, et al. Feasibility of tissue magnetic resonance imaging: a pilot study in comparison with tissue Doppler imaging and invasive measurement. J Am Coll Cardiol 2005; 45:1109-1116.

[5] Cohen GI, Pietrolungo JF, et al. A practical guide to assessment of ventricular diastolic function using Doppler echocardiography. J Am Coll Cardiol 1996; 27:1753-1760.

[6] Nikitin NP, Witte KK, et al. Longitudinal ventricular function: normal values of atrioventricular annular and myocardial velocities measured with quantitative two-dimensional color Doppler tissue imaging. J Am Soc Echocardiogr 2003, 16:906-921.

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