Parameters for Characterizing Diastolic Function with Cardiac Magnetic Resonance Imaging

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Abstract

23 healthy subjects and 23 patients with isolated diastolic dysfunction were examined with cine magnetic resonance imaging to find new markers for the diastolic heart function. A single mid-ventricular short axis slice in the true cardiac axis was used and endo- and epicardial borders were hand drawn. Five features were applied to characterize isolated diastolic function: Irregularity marker of contraction calculated as the sum of the standard deviations of corresponding points across all frames (IRREG); slope of a linear fit to the diastolic area change (SLOPE); slope of the minimal and mean wall thickness (MINWTH/MEANWTH); shift parameter of the least-squares fit of the sigmoid Fermi-function (SHIFT). The parameters were corrected for through-plane motion. MINWTH, MEANWTH, and SHIFT differed significantly in both groups. These features represent promising objective parameters to discriminate patients with diastolic dysfunction from healthy subjects.

1. Introduction

The full heart cycle is characterized by contraction (systole) and relaxation (diastole). Relaxation is as important for global ventricular performance as systolic function but more difficult to assess. Relaxation speed and duration for example measured by echocardiography are accepted parameters for the diastolic function of the left ventricle [1]. Primary diastolic heart failure can be observed in patients with left ventricular hypertrophy (due to pressure overload as it occurs with hypertension or obstruction of the outflow tract) and restrictive cardiomyopathy. Impairment of the diastolic function is also an early sign of myocardial ischemia.

All current methods for the detection of diastolic dysfunction have major drawbacks [2] and there is no robust parameter like the ejection fraction for the systolic function.

The evaluation of the heart function by magnetic resonance imaging (MRI) as a non-invasive tool with a good spatial and temporal resolution has become feasible in the last years. Current dedicated cardiovascular MRI scanners provide excellent demarcation of the endocardial border in nearly all patients. There are different approches to determine diastolic function by MRI. Flow velocity and volume measurements across the mitral valve are possible [3] but hampered by a systematic error due to the movement of the valve plane during the heart cycle.

In an earlier feasibility study [4] we found promising new markers in a patient group with both diastolic and systolic dysfunction. Aim of this study was the examination of the previously described and new parameters in patients with isolated diastolic dysfunction.

2. Methods

2.1. Subject data

Twenty-three healthy subjects (control) and 23 consecutive patients with isolated diastolic dysfunction (diadys) were examined with magnetic resonance imaging. All of the diadys patients had an elevated left ventricular end-diastolic pressure (>16mmHg), measured invasively by cardiac catheterization. Hypertension treated with drugs was present in 14 patients, the remaining had valvular disease or other conditions leading to diastolic dysfunction.

2.2. Imaging

Imaging was performed on a 1.5T whole body scanner (Intera CV, Philips Medical Systems) with Master Gradients (slew rate 150 T/m/s, amplitude 30 mT/m) and software Release 8.1. A 5-element phased-array cardiac coil was used. Three short survey scans were performed to define the position and true axis of the left ventricle. Afterwards, wall motion was imaged during breath holding with long and short-axis slices using a steady-state free precession (balanced fast-field echo) sequence, which provides an excellent endocardial contrast. Cardiac synchronization was achieved by prospective gating. The cine images were recorded with 23 heart phases (23 frames per heart cycle). Septal wall thickness was measured in a basal short axis slice.

2.3. Image analysis

A single mid-ventricular short axis slice was chosen for the analysis. Short axis slices are more representative for the cardiac function than long axis views and planimetry results in a nearly circular area. In addition, partial-volume-effects are lower in short-axis-slices compared to the long axis. Endocardial and epicardial contours for each of the 23 heart phases were hand-drawn on a Sun Ultra 60 workstation using the Easy Vision Software Release 5.1 (Philips, Best, The Netherlands). The papillary muscles were assigned to the ventricular cavum (Fig. 1). Movie sequences of the contours were then exported as MPEG files. From these image sequences the cross sectional mid-ventricular area with and without cardiac muscle was determined across all frames with a computer algorithm resulting in binary image sequences. On the preprocessed images five types of features were applied to characterize isolated diastolic function. The previously described irregularity marker of contraction calculated as the sum of the standard deviations of corresponding points across all frames (IRREG; see Fig. 2), the slope of a linear fit to the diastolic area change (SLOPE), and the shift parameter of the least-squares fit of the sigmoid Fermi-function (SHIFT) were tested in this new setting. As new parameters the slope of the minimal wall thickness change (MINWTH) and the slope of the mean wall thickness change (MEANWTH) were used.

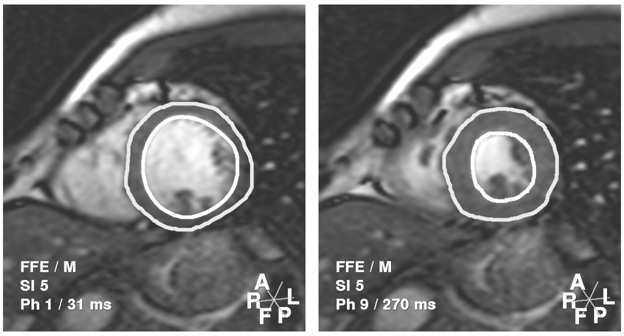

Figure 1. A MR short axis slice acquired from a patient with posterior infarction. The left image is end-diastolic, the right image end-systolic. The hand-drawn endocardial (outer) and epicardial (inner) contour is shown.

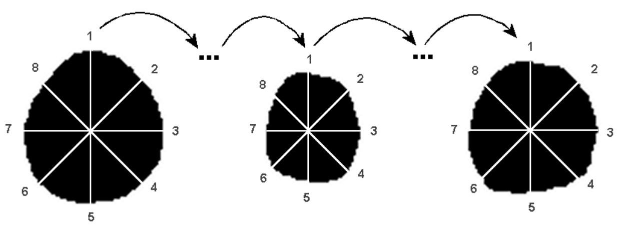

Figure 2. Illustration of the irregularity marker of contraction. The crossing point of the four lines is the center of gravity. Eight points on each frame were traced and described by their standard deviations.

All parameters except for IRREG were corrected for through-plane motion by a frame by frame division through the myocardial area (see Fig. 3). This is based on the assumption that the myocardial wall area should be constant over the whole heart cycle and a difference will occur (apart from imprecision of the contour drawing) due to through-plane motion.

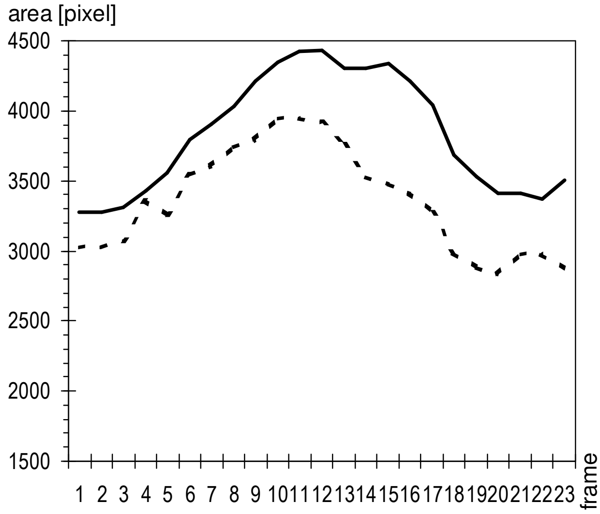

Figure 3. Median over time of the wall area in the control group (dashed line) and the patients with diastolic dysfunction (solid line), used as a surrogate for through-plane motion. The area was calculated as the difference of the endocardial and epicardial area. The patients with diastolic dysfunction had a significantly larger area. Due to the cone-shaped form of the left ventricle there will be an increase in the area if there is movement to the base and a decrease in case of movement to the apex.

2.4. Statistics

Data are presented as median and interquartile ranges. For analysis of the differences between groups, the Mann-Whitney U-test was used. A statistical probability of $p<0.05$ was considered to be significant. A one-sided t-test was used for a paired comparison of each control with every patient.

3. Results

Median left ventricular ejection fraction was 65% in the control group, there was no significant difference compared to the control group (median 67%). The control group had a median age of 34 yrs (interquartile range 34 to 42 yrs), the diadys group was significantly older with age 54 yrs [49;64 yrs], $p<0.01$. Heart rate, which influences relaxation, did not differ between the both groups (median 70 bpm). Septal wall thickness was normal in the control group (median 10.0 mm [8;10 mm]). In the group with diastolic dysfunction most patients had significant left ventricular hypertrophy (median 12.0 mm [10.0;14 mm], $p<0.01$).

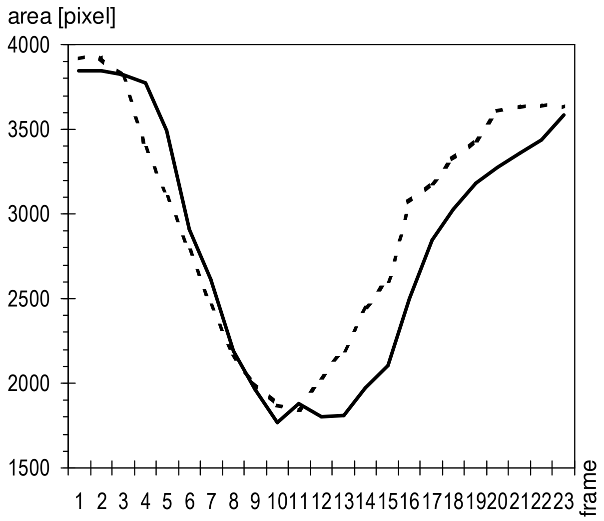

Figure 4. Median over time of the cross-sectional area in pixels of the control group (dashed line) and the patients with diastolic dysfunction (solid line). There is a shift towards late heart phases in the diadys group.

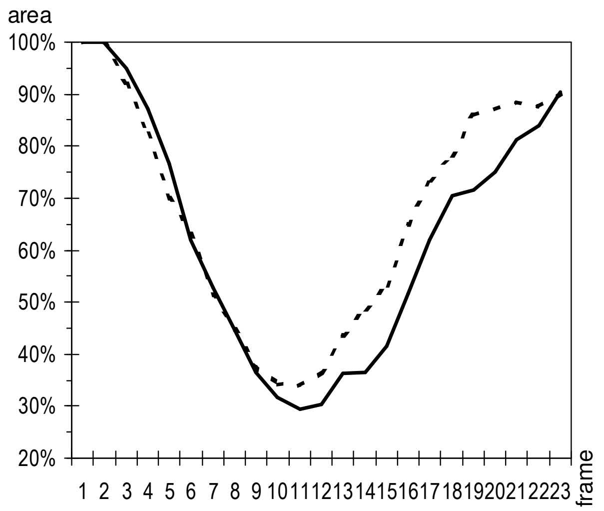

Figure 5. Median over time of the cross-sectional area in pixels of the control group (dashed line) and the patients with diastolic dysfunction (solid line). The area was corrected for through-plane motion and normalized by the maximum

Median change of the area across the heart cycle is shown in Fig. 4, and, corrected for through-plane motion on Fig. 5. A shift of the diastolic slice area enlargement towards later frames in the diadys group can be observed n the figures. The features used refelcted this:

SHIFT differed in both groups (-74 vs. -34, p=0.02). SLOPE (p=0.19) and IRREG (p=0.10) did not differ in both groups. MINWTH (p=0.03) and MEANWTH (p<0.01) were significantly lower in the group with diastolic dysfunction. If no correction for through-pane motion was applied, only MINWTH was significantly lower in the diadys group (p<0.01, MEANWTH p=0.05). Paired comparisons of the area change (summed squares) during the relaxation phase revealed a highly significant difference between both groups (mean=0.224, 95% CI= 0.204 to 0.243; p<0.01). The functions obtained from the median slope and SHIFT for both groups are shown on Fig. 6.

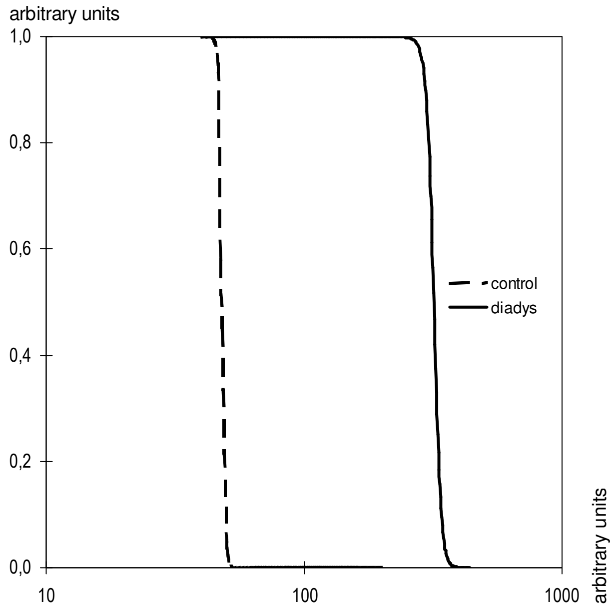

Figure 6. Fermi functions obtained from the median slope and shift for both groups:

$$\frac{1}{1+e^{(-ax+SHIFT)}}$$ (*a* depicts the slope).

4. Discussion

This paper scrutinizes the previously described markers for the diastolic function in a more selective setting. New markers using the information of the epicardial border and therefore regional wall thickness are introduced. Patients with isolated diastolic dysfunction were compared with a control group of normal subjects.

Diastolic dysfunction includes delayed relaxation, increased stiffness and/or impaired filling. The slope of the function that depicts the diastolic increase of the short axis slice area reflects relaxation speed. This parameter was addressed in a MRI study [5]. In contrast to our previous findings in patients with both regional systolic and diastolic dysfunction [4], the slope did not differ significantly between the two groups in this study. Fig. 4 and 5 show that the relaxation curve is shaped differently and there are more than one possible point to start a linear least squares fit. This indicates that the slope of a fit to the curve may not be a robust parameter and may be influenced by systolic performance.

The second previously described feature, the shift parameter of the least-squares fit of the sigmoid Fermi-function can be visually observed in Fig. 6 and reflects a delay of the relaxation and differed clearly in the two groups.

The irregularity index, which did not differ between the two groups, reflects regional wall motion abnormality that was not present in these patients. In our study with patients after myocardial infarction [4] there was a significant difference compared to the control group.

The two new parameters directly reflecting the global (MEANWTH) and regional (MINWTH) contraction and relaxation speed were significantly lower in the group with isolated diastolic dysfunction as compared to the control persons. Since these parameters are using the myocardial wall area, a correction for through-plane motion appears to be necessary, and the difference of MEANWTH between the two groups was only statistically significant after correction for total wall area.

In some individuals the initial area at the beginning of the heart cycle is not fully attained in the last frame. This can be explained by the heart synchronization used in the this study. Prior to scanning, an estimated heart frequency and a gating window (5% in this study) has to be entered. That means the last five percent of the heart cycle are used for r-wave detection and cannot be utilized for data acquisition. If the actual heart rate is slower than the entered heart rate, the full heart cycle will not be used for scanning. Since there are only minor changes of the area in the last frames this should not alter the general diastolic area change. This problem might be overcome by using other synchronization methods such as retrospective gating.

5. Conclusion

We conclude that this study provides a first step towards a more objective characterization of diastolic dysunction by means of non-invasive cardiac MRI.

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