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Heart deformation analysis for automated quantification of cardiac function and regional myocardial motion patterns: a proof of concept study in patients with cardiomyopathy and healthy subjects

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Abstract

Objective—To test the performance of HDA in characterizing left ventricular (LV) function and regional myocardial motion patterns in the context of cardiomyopathy based on cine cardiovascular magnetic resonance (CMR).

Materials and methods—Following the approval of the institutional review board (IRB), standard cine images of 45 subjects, including 15 healthy volunteers, 15 patients with hypertrophic cardiomyopathy (HCM) and 15 patients with dilated cardiomyopathy (DCM) were retrospectively analyzed using HDA. The variations of LV ejection fraction (LVEF), LV mass (LVM), and regional myocardial motion indices, including radial (Drr), circumferential (Dcc) displacement, radial (Vrr) and circumferential (Vcc) velocity, radial (Err), circumferential (Ecc) and shear (Ess) strain and radial (SRr) and circumferential (SRc) strain rate, were calculated and compared among subject groups. Inter-study reproducibility of HDA-derived myocardial motion indices were tested on 15 volunteers by using intra-class correlation coefficient (ICC) and coefficient of variation (CoV).

Results—HDA identified significant differences in cardiac function and motion indices between subject groups. DCM patients had significantly lower LVEF ($33.5 \pm 9.65\%$), LVM ($105.88 \pm 21.93\text{g}$), peak Drr ($0.29 \pm 0.11\text{cm}$), Vrr-sys ($2.14 \pm 0.72\text{cm/s}$), Err (0.17 ± 0.08), Ecc (-0.08 ± 0.03), SRr-sys ($0.91 \pm 0.44\text{s}^{-1}$) and SRc-sys ($-0.64 \pm 0.27\text{s}^{-1}$) compared to the other two groups. HCM patients demonstrated increased LVM (171.69 ± 34.19) and lower peak Vcc-dia

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(0.78 ± 0.30 cm/s) than other subjects. Good inter-study reproducibility was found for all HDA-derived myocardial indices in healthy volunteers (ICC = 0.664 - 0.942, CoV = 15.1% - 37.1%).

Conclusion—Without the need for operator interaction, HDA is a reproducible method for the automated characterization of global and regional LV function in the context of cardiomyopathy.

Keywords

Heart deformation analysis; Cardiovascular magnetic resonance; Cardiomyopathy; Strain analysis

Introduction

Cardiovascular magnetic resonance (CMR) has become a standard tool that is able to noninvasive characterization of global and regional cardiac function for the assessment of cardiovascular disease (CVD). At the global level, left ventricular ejection fraction (LVEF) and mass (LVM) is routinely calculated based on balanced steady-state free precession (bSSFP) cine images. As a result, bSSFP acquisition has become a standard part in most clinical CMR protocols. On the other hand, in order to assess the subtle progression of CVD at the regional level, indices that present motion patterns of local myocardial areas can be acquired with various CMR techniques, including myocardial tagging, tissue phase mapping (TPM), strain-encoded (SENC) or *Displacement encoding with stimulated echoes* (DENSE) (1-4). Unfortunately, current CMR methods for the quantification of regional myocardial motion patterns usually require a dedicated image acquisition, data analysis tools, and variable processing time.

Based on deformable image registration (DIR) algorithms, heart deformation analysis (HDA) is a post-processing method for tracking myocardial motion on conventional bSSFP images (5). Using an inverse consistent DIR algorithm to recover deformation fields (forward and backward), the HDA is able to assess variations of target deformation areas over time. From this process, global LV function and morphological changes (LVEF and LVM), as well as regional LV motion patterns (displacement, velocity, strain and strain rate), can be measured by calculating deformation fields through the cardiac cycle (6). In addition, myocardial segmentation of the LV, including the identification of landmark anatomical structures can now be automatically performed with this technique. Comparing to existing methods for tracking myocardial motion on cine CMR, such as feature tracking (FT), HDA can further reduce the processing time and while simultaneously eliminating the intra- and inter-observer influence in quantitative analysis. Therefore, HDA represents a valuable opportunity of acquiring myocardial motion information on existing cine CMR datasets without additional scan time.

Previous studies have evaluated HDA-derived indices in describing global LV function and regional myocardial velocity in healthy volunteers using existing methods as references (7). However, the capability and reproducibility of HDA in automated discriminating abnormal myocardial motion patterns in regionally and globally altered myocardial structure is unclear. In the present study, we compared cardiac function and myocardial motion indices derived from HDA in healthy volunteers, patients with hypertrophic cardiomyopathy (HCM), and patients with dilated cardiomyopathy (DCM). The aim of the present study was

to test the performance of HDA in characterizing LV functions and regional myocardial motion patterns in the context of cardiomyopathy.

Materials and Methods

Subject description

This study complied with HIPAA regulations. Following the approval of the institutional review board (IRB), cine bSSFP images of 45 subjects, including 15 healthy volunteers (9 men, group #1), 15 HCM patients (9 men, group #2) and 15 DCM patients (9 men, group #3) were retrospectively included for analysis (table 1). Inclusion criteria: 1) All subject age: 18 - 80 years old; 2) All patients with cardiomyopathy were diagnosed according to the clinical practice guidelines published by the American Heart Association (AHA); 3) HCM was defined as patients with thickened LV wall ($> 15\text{mm}$) using echocardiography, without a causative cardiac or systemic disorder, such as hypertensive heart disease (8); and 4) DCM was defined as systolic dysfunction with LVEF ($< 45\%$) accompanied with LV dilation measured with echocardiography (9). Exclusion criteria: 1) Patients with co-existing CVD, such as myocardial infarction (MI); and 2) Volunteers with documented CVD.

CMR scans

All participants underwent CMR examinations using the same cardiac cine protocol on a 1.5 T scanner (Avanto, Siemens AG, Germany). Certified clinical radiology technologists performed all CMR scans. At four-chamber, two-chamber, and short-axis views, segmented bSSFP cine sequences were run in the cardiac imaging planes under conditions of breath-holding. Imaging parameters were as follows: TR/TE = 2.8/1.1 ms; flip angle = 65° , voxel size = $2.1 \times 2.1 \times 8.0 \text{ mm}^3$, bandwidth = 930 Hz/pixel, parallel imaging (GRAPPA technique) with reduction factor $R = 2$. Ten to twelve short-axis myocardial slices were set to cover the entire LV from base to apex. Each cine acquisition was acquired with retrospective ECG-gating and reconstructed into 25 cardiac time frames.

Post processing using the HDA tool

Cine CMR images, including 2-chamber, 4-chamber and a stack of short-axis images were loaded to a dedicated image processing workstation (Dell, STUDIO, SPS 435T) and analyzed with prototype software programmed in Visual C++ (TruFiStrain, Siemens Corporation, Princeton, NJ) by an experienced analyzer (___, reader #1, with 9 years of experience in cardiovascular imaging). Different from an existing study, the improved HDA tool automatically detects anatomical landmarks in the heart, including the mitral valve anchor points and apex point in the long-axis images, aortic valve anchor points and the right ventricle [RV] insertion/lateral points on short-axis images (7). The myocardial borders (epicardial and endocardial) were automatically delineated using an existing DIR algorithm described before (5). Elastic image registration was then completed to calculate frame-to-frame motion deformation fields (5). Cardiac time frames are segmented using a shortest path algorithm and time consistency is enforced through the deformation fields (10). Global cardiac function (LVEF and LVM) and regional myocardial motion indices, including displacement, velocity, strain and strain rate, could therefore be derived from the variant deformation fields over time. Next, the in-plane time-resolved regional myocardial motion

vectors in radial and circumferential directions were generated for each myocardial segment (mapped on a standard 16-segment AHA LV model).

The reader #1 judged whether the HDA-generated contours were “reasonable” for each case. If not, the reader #1 would adjust contours manually. In order to test the inter-analysis variation, the reader #1 reloaded cine SSFP images of all subjects a week later and repeat the same automatic image analysis processing method (on a different workstation installed with the same version of the HDA tool). All 15 volunteers underwent a second cardiac cine CMR scan using the same imaging protocol 2 weeks later. The retest data was used to assess the inter-study reproducibility of the HDA tool.

Data processing and statistical analysis

All continuous variables were represented by mean $\pm$ one standard deviation (SD). The global LV parameters, including LVEF and LVM, were calculated for each subject. The variations of regional myocardial motion indices, including radial (Drr) and circumferential (Dcc) displacement, radial (Vrr) and circumferential (Vcc) velocity, radial (Err), circumferential (Ecc) and shear (Ess) strain and radial (SRr) and circumferential (SRc) strain rates, were recorded through the cardiac cycle (25 time points) and were mapped on an AHA LV model (16 segments). The difference in peak values among different subject groups was compared using independent *t*-tests. Inter-study reproducibility of HDA-derived indices was tested on 15 healthy volunteers by using intra-class correlation coefficient (ICC) and coefficient of variation (CoV). An ICC value > 0.75 or a CoV $< 20\%$ between duplicated measurements was considered as good reproducibility. Bland-Altman plots were also used to show inter-study variability of HDA-derived indices (peak values). Statistical analyses were two-tailed and were performed using SPSS statistical software (Version 13.0, SPSS, Inc, Chicago, IL). A *p* value < 0.05 was considered statistically significant.

Results

Cine CMR images were eligible for quantitative analysis in all 45 subjects. All contours that were automatically generated by the HDA tool were judged as “reasonable” by the reader #1. No manually adjustments for contours or landmark points were needed. Figure 1 shows examples of myocardial contours automatically generated by the HDA tool and typical LV images (short-axis view) of a healthy volunteer, an HCM patient and a DCM patient. Significant differences on multiple myocardial function and motion indices were found between subject groups, as detailed below.

DCM vs. HCM patients

HCM patients had higher LVEF ($59.2\% \pm 7.77$ vs. $33.5\% \pm 9.65$) and LVM ($171.69 \pm 34.19\text{g}$ vs. $105.88 \pm 21.93\text{g}$, $p < 0.001$) than DCM patients. DCM patients demonstrated significantly lower peak Drr (0.29 ± 0.11 vs. 0.57 ± 0.10 cm, $p < 0.001$), Vrr-sys (2.14 ± 0.72 vs. 3.41 ± 1.07 cm/s, $p = 0.001$), Err (0.17 ± 0.08 vs. 0.38 ± 0.12 , $p < 0.001$), Ecc (-0.08 ± 0.03 vs. -0.17 ± 0.03 , $p < 0.001$), SRr-sys (0.91 ± 0.44 vs. 1.85 ± 0.82 s⁻¹, $p = 0.001$) and SRc-sys (-0.64 ± 0.27 vs. -1.00 ± 0.29 s⁻¹, $p = 0.002$) than HCM patients. HCM

patients presented with lower peak Vcc-dia (0.78 ± 0.30 vs. 1.07 ± 0.38 cm/s, $p = 0.028$) than DCM patients.

DCM patients vs. healthy controls

DCM patients were found to have lower LVEF ($33.5\% \pm 9.65$ vs. 60.14 ± 7.29 , $p < 0.001$) and LVM (105.88 ± 21.93 g vs. 138.94 ± 42.50 g, $p < 0.001$) compared to healthy volunteers. DCM patients had significantly lower peak Drr (0.29 ± 0.11 vs. 0.58 ± 0.12 cm, $p < 0.001$), Vrr (2.14 ± 0.72 vs. 3.08 ± 1.07 cm/s, $p = 0.001$), Err (0.17 ± 0.08 vs. 0.31 ± 0.08 , $p < 0.001$), Ecc (-0.08 ± 0.03 vs. -0.17 ± 0.02 , $p < 0.001$), SRr (0.91 ± 0.44 vs. 1.39 ± 0.34 s⁻¹, $p = 0.003$) and SRc (-0.64 ± 0.27 vs. -0.95 ± 0.21 s⁻¹, $p = 0.002$) than healthy volunteers.

HCM patients vs. healthy controls

LVM was increased in HCM patients compared to healthy volunteers (171.69 ± 34.19 g vs. 138.94 ± 42.50 g, $p < 0.001$). There were no significant differences of LVEF, peak Drr, Dcc, Vrr, Err, Ecc, Ess, SRr and SRc in systole and diastole between HCM patients and healthy volunteers.

The group-specific magnitude of overall displacement, velocity, strain and strain rate for 25 time points within a cardiac cycle, covering both systolic and diastolic periods, is shown in figure 2.

Reproducibility

Since contour drawing and anatomic landmark selection were performed automatically by the HDA tool and no operator input was taken into account to calculate motion indices in the present study, intra- or inter-observer variability could be eliminated. Re-analysis of cine image datasets resulted in the same results of motion indices for all 45 subjects. Good inter-study reproducibility for measuring major function and motion indices were found between scans and rescans for all 15 volunteers (ICC = 0.664 - 0.942, CoV = 15.1 - 37.1). See table 2 for the list of ICCs and CoVs for the acquisition of myocardial indices between tests and retests. Bland-Altman plots demonstrating inter-study reproducibility of HDA tool in describing LV function and motion indices are shown in Figure 3.

Discussion

In the present study, we demonstrated significant differences of HDA-derived LVEF, LVM, displacement, velocity, strain and strain rate among healthy volunteers, HCM and DCM patients. Based on regular cine CMR, HDA has the potential to become a robust tool for the automatic description of myocardial function and motion patterns for the evaluation of existing CVD.

With various pathological mechanisms, cardiomyopathy comprises a group of diseases accompanied with heterogeneous myocardial damage result in diverse clinical expressions and affect clinical outcomes (11). Generally, mechanic and electric ventricular dysfunctions are two major life-threatening conditions affiliated with the progression of cardiomyopathy. With a thin LV wall and dilated LV, the major manifestation of DCM is congestive heart

failure (CHF), the most common cause of death in DCM patients. Caused by mutations on genes coded for the synthesis of sarcomere proteins, HCM is characterized with regional or global hypertrophic LV wall and at diagnosis the chamber size is often normal. HCM serves as the leading cause of sudden cardiac death (SCD) in youth people, an immediate consequence of fatal arrhythmia. In the present study, three subject groups could be discriminated by using HDA-derived myocardial indices. HCM patients have higher LVM than other two groups. However, HCM patients do not have lower LVEF than healthy volunteers. Although advanced stages of HCM can result in CHF, this is uncommon early in the disease process. DCM patients have lower LVEF and LVM than HCM patients and healthy volunteers. As expected, DCM patients have lower magnitudes in most motion indices than HCM patients and healthy volunteers, including peak systolic and diastolic displacement, velocity, strain and strain rate. HCM patients have lower peak diastolic circumferential velocity (V_{cc-dia}) than DCM patients. This exception can be explained by the fact that the thickened LV wall can become more rigid, which may affect ventricular dilation, in HCM patients.

Nevertheless, we need to point out that the concept of analyzing regional myocardial motion based on cine images has been existing for a long time and some similar techniques have already been developed for the same clinical purpose. For example, FT has been used to semi-automatically track the motion and deformation of the heart (12). With FT, visual features of an anatomical structure, including corner-, speckle-like or area features, can be extracted and tracked over multiple time frames based on the brightness and/or the shape. Currently, many individual FT algorithms, such as mean shift, particle filter (PF), and Kanade-Lucas-Tomasi (KLT) tracker, were developed based on a common principle that minimizes the sum of squared differences (SSD) (13). By matching special features cross frames, mechanical indices of the heart, including velocity and strain, can therefore be calculated. However, applying FT algorithms to clinical image data is challenging, as some features may change or disappear from time frame to time frame. As such, intra-, inter-observer and inter-study reproducibility of FT-derived myocardial strain measures are not high in healthy volunteers or clinical patients with left bundle branch block (LBBB) (14, 15). In addition, FT tracking needs a time consuming operation for manually tracing myocardial borders. Different from the algorithms that were used for the FT, DIR algorithms were applied to improve the description of heart motion/deformation. In previous publications, DIR algorithms were used to determine myocardial strains or lung motion (16, 17). For a given cardiac plane, DIR methods register all cardiac time frames to the starting time frame use an inverse consistent deformable registration. Then, a segmentation algorithm, which was based on automated gray scale analysis among various tissues, can be applied to any time frame and results in continuing contours reflecting the deformation of myocardium through the cardiac cycle (10). HDA can then generate a set of cardiac function and motion indices. We have proved that HDA had good agreement with ARGUS (a standard clinical device) for the measurement of LVEF and LVM in 160 older adults (6). In addition, HDA-derived regional myocardial velocity is comparable to its counterpart measured with tissue phase mapping (TPM), an existing phase contrast CMR method (7, 18). In the present study, we further demonstrated good inter-study reproducibility of global and regional myocardial indices measured with HDA, a prominent advantage of a

quantitative measurement for potential clinical use, as compared with existing methods. As an operator-independent image processing method, HDA has the potential to serve as a convenient and reliable tool for the comprehensive assessment of cardiac function and motion.

Our study has some limitations. First, we were unable to compare the accuracy of HDA in the measuring of multiple motion indices because there is not a single well-accepted clinical method that can serve as the “gold standard” for calibrating displacement, velocity, strain and strain rate. For the same reason, we did not compare HDA-derived indices to similar indicators acquired with current clinical methods or other similar image processing techniques, such as FT. Instead, we are currently assessing the predictive value of HDA-derived cardiac function and myocardial motion indices by using clinical outcomes as reference in another ongoing study. Second, limited by the small sample size, we were unable to validate the clinical application of the HDA tool in differential diagnosis of cardiomyopathy. The study was not designed as a comprehensive diagnosis test. Actually, the aim of this “proof of concept” study was to demonstrate the performance of the HDA tool for describing different cardiac function and regional myocardial motion patterns in patients with cardiomyopathy. Further studies are warranted to test the capability of HDA-derived measures for predicting clinical outcomes of CVD.

Conclusion

Without the need for operator interaction, HDA is a reproducible method for the automated characterization of global and regional LV function in the context of cardiomyopathy.

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List of abbreviations

HDA	Heart deformation analysis
CMR	Cardiovascular Magnetic Resonance
LVEF	Left ventricular ejection fraction
LVM	Left ventricular mass
Drr	Radial displacement
Dcc	Circumferential displacement
Vrr	Radial velocity
Vcc	Circumferential velocity
Err	Radial strain

Ecc	Circumferential strain
Ess	Shear strain
SRr	Radial strain rate
SRc	Circumferential strain rate

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Highlights

- Heart deformation analysis (HDA) can quantify global and regional cardiac function.
- HDA works based on cine CMR images without the needs of operator interaction.
- HDA-derived cardiac motion indices are reproducible.

Figure 1.

The succinct procedure of HDA (one click) for the analysis of global LV function, mass, displacement, velocity, strain and strain rate in healthy volunteers, HCM and DCM patients. The tool HDA can automatically trace myocardial borders through the entire cardiac cycle.

a The contours of the LV were automatically drawn by the HDA tool.

b A control case with normal LV wall. The LVEF is 63.5%.

c A HCM patient with a thickened LV wall (> 15mm). The LVEF is 55%.

d A DCM patient with a thin LV wall and an enlarged LV. The LVEF is 16.7%.

Figure 2.

The HDA tool automatically describes displacement, velocity, strain and strain rate at different cardiac time points for 3 subject groups. Curves with different colors represent variations of multiple cardiac indices within a cardiac cycle among healthy volunteers and patients with DCM and HCM. For each time point, motion indices were averaged from 16 myocardial segments of 15 controls.

Figure 3.

Bland-Altman plots demonstrate low inter-study variability on measuring peak displacement, velocity, strain and strain rate of individual myocardial segments. Duplicated measurements on 240 myocardial segments from 15 volunteers were included.

Table 1

Subject description

	Volunteers (N =15)	HCM patients (N =15)	DCM patients (N =15)
Male (%)	9 (60)	9 (60)	9 (60)
Age (years)	48.8±17.5	58.0±18.5	44.0±17.2
Height (cm)	175 ± 8	177 ± 13	174 ± 10
Weight (kg)	73 ± 15	75 ± 12	71 ± 11

Table 2

Summary of the reproducibility of HDA-derived global and regional myocardial indices

Values	Inter-study ICC	95%CI of ICC	CoV (%)	P value
LVEF (%)	0.754	0.691-0.809	18.9	< 0.001
LVM (g)	0.942	0.908 - 0.981	23.1	< 0.001
Drr (cm)	0.895	0.864-0.918	17.7	< 0.001
Dcc (cm)	0.858	0.814 - 0.891	22.1	< 0.001
Vrr-sys (cm/s)	0.830	0.777 - 0.866	23.0	< 0.001
Vrr-dia (cm/s)	0.795	0.733 - 0.842	24.7	< 0.001
Vcc-sys (cm/s)	0.664	0.561 - 0.743	31.6	< 0.001
Vcc-dia (cm/s)	0.687	0.587 - 0.762	33.5	< 0.001
Err	0.896	0.866 - 0.919	22.2	< 0.001
Ecc	0.838	0.791 - 0.874	15.1	< 0.001
Ess	0.884	0.851 - 0.910	37.1	< 0.001
SRr-sys (s-l)	0.829	0.779 - 0.827	25.5	< 0.001
SRr-dia (s-l)	0.851	0.807 - 0.886	27.2	< 0.001
SRe-sys (s-l)	0.794	0.734 - 0.840	32.5	< 0.001
SRe-dia (s-l)	0.698	0.610 - 0.765	30.4	< 0.001