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Comparison of strain measurement from multimodality tissue tracking with strain-encoding MRI and harmonic phase MRI in pulmonary hypertension

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ABSTRACT

Background: Pixel-based multimodality tissue tracking (MTT) is a new noninvasive method for the quantification of cardiac deformation from cine image of MRI. The aim of this study is to validate bi-ventricular strain measurement by MTT compared to strain-encoding (SENC) MRI and harmonic phase (HARP) MRI in pulmonary hypertension (PH) patients.

Methods: In 45 subjects (30 PH patients and 15 normal subjects), RV and LV peak global longitudinal strains (Ell) were measured from long axis 4 chamber view using MTT. LV peak global circumferential strains (Ecc) by MTT were measured from short axis. For validation, RV and LV Ell by MTT were compared to measures by SENC-MRI from short axis, and LV Ecc by MTT was compared to measures by short axis tagged MRI analysis (HARP). Reproducibility of MTT was also determined.

Results: MTT quantified RV Ell correlated closely to those of SENC ($r = 0.72$, $p < 0.001$), with good limits of agreement. LV Ell quantified by MTT showed moderate correlation with SENC ($r = 0.57$, $p = 0.001$), and LV Ecc by MTT also showed moderate correlation with HARP (-16.9 ± 4.1 vs -14.3 ± 3.5, $p < 0.001$ for all, $r = 0.60$, $p < 0.001$). RV Ell negatively correlated with RVEF ($r = -0.53$, $p = 0.001$) and also positively correlated with mean PAP in PH patients ($r = 0.60$, $p = 0.001$). Strain measurement by MTT showed high reproducibility.

Conclusions: We demonstrate that MTT is a reproducible tool for quantification of cardiac deformation using cine images in PH patients. Hence, it could serve as a new rapid and comprehensive technique for clinical assessment of regional cardiac function.

1. Background

Pulmonary hypertension (PH) is characterized by increased mean pulmonary artery pressure (PAP) ≥25 mm Hg at rest, which leads to right pressure overload, right heart failure, and ultimately premature death [1,2]. It has become increasingly evident that clinical improvement and prolonged survival in PH are highly dependent on preserved right ventricle (RV) function [3]. The RV and left ventricle (LV) share the interventricular septum (IVS) and are contained within the same pericardial sac, which leads to interventricular dependence; thus, RV pressure and volume loads cause leftward septal bowing, resulting in altered LV filling dynamics and function [4]. Recently, it has been reported that reduced biventricular regional function is associated with increased RV afterload [5,6]. Thus, biventricular assessment and follow-up in PH patients are critical.

Recent developed cardiovascular imaging modality such as echocardiography and cardiac magnetic resonance can allow for assessment for detailed cardiac structure and function [7,8]. LV and RV regional function can be assessed from cardiac magnetic resonance (CMR) imaging through myocardial tagging [9–11] as well as real-time myocardial strain encoding (SENC) [12,13] or direct tissue encoding sequences (DENSE) [14]. Myocardial tagging and SENC have quantitative value, but have not yet gained widespread clinical use, in part because of

Abbreviations: PH, pulmonary hypertension; RV, right ventricle; LV, left ventricle; HARP, harmonic phase analysis; MTT, multimodality tissue tracking; SENC, strain-encoding; Ell, longitudinal strain; Ecc, circumferential strain.

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expertise of specific sequences, additional scanning time and the need for complex post-processing analysis. In the current study, we assessed an alternative method of deformation assessment. Pixel based multimodality tissue tracking (MTT) utilizes tissue patterns obtained from cine CMR images and automatically tracks them frame to frame by an automated pattern matching technique. MTT can measure regional myocardial function of both the RV and LV from cine imaging. We validate biventricular strain measurements measured by MTT, by using the validated strain measures from SENC and HARP in PH patients.

2. Methods

2.1. Subjects

A total of 30 patients (27 females) with catheter-diagnosed PH (mean pulmonary artery pressure (mPAP) 40 mm Hg) were included. In addition, 15 healthy volunteers were also included in the study. Exclusion criteria for healthy volunteers included any evidence suggestive of systemic hypertension, diabetes mellitus, ischemic or non-ischemic heart disease, chest disease, and history of smoking. Exclusion criteria for both PH patients and healthy volunteers were contraindication to CMR studies (e.g. presence of metallic implants and inability to follow instructions for breath holding). The institutional review board approved the study protocol and all participants gave written informed consent.

2.2. Data acquisition

Imaging was performed using a 3 T whole-body MR system (Tim Trio; Siemens Medical Solutions, Erlangen, Germany) followed by SENC acquisition using a 3 T whole-body Philips MR system (Achieva 3 T; Philips Medical Systems, Best, The Netherlands). Vector electrocardiogram was used for R-wave triggering [15]. All participants were examined in the supine position.

2.2.1. Cine MRI

Assessment of resting LV and RV global function was performed using a stack of retrospectively gated fast gradient echo (FGRE) cine images acquired in the short-axis plane covering both ventricles from base to apes (9 to 12 slices), as well as two- and four-chamber long-axis views. Parameters for the cine acquisition were typically pulse repetition time = 72.9 ms, echo time = 3.3 ms, flip angle = 12°, slice thickness = 6.5 mm, slice gap = 4.5 mm, acquisition matrix = 256 × 146, and field of view = 350 × 350 mm.

2.2.2. Strain encoded MRI

To quantify RV and LV longitudinal strain (*EllRV* and *Ell* respectively), three short-axis slices were planned from the four-chamber view, orthogonal to the inter-ventricular septum, and with the planes at the basal, mid, and apical ventricular levels. Typical SENC imaging parameters were pulse repetition time = 25 ms, echo time = 0.8 ms, flip angle = 30°, slice thickness = 10 mm, slice spacing = 4 mm, field of view = 350 × 350 mm, reconstruction matrix = 96 × 96, and spatial resolution 2.5 × 2.5 mm. Temporal resolution was 25 ms. Each slice was acquired over 13 s (a breath hold of 13 heartbeats), with overall SENC scan acquisition time of 2 min, allowing for patient rest between each two consecutive breath holds.

2.2.3. MR tagging

Tagging images were prescribed using the spatial modulation of magnetization at the same locations prescribed for the short-axis strain-encoded images, using the following parameters: pulse repetition time = 32.8 ms, echo time 3.2 ms, flip angle = 10°, field of view = 350 × 350 mm, reconstruction matrix = 256 × 144, and tag spacing of 7 mm. Tagging images were used for quantification of LV circumferential strain (*Ecc*).

2.2.4. Catheterization of the right heart

All PH patients underwent catheterization of the right heart. Quantified hemodynamic variables in this study included mean PAP and pulmonary vascular resistance index (PVRI) as markers of RV afterload.

2.3. Data analysis

2.3.1. Global ventricular function analysis

Short-axis cine images were analyzed by using software (Qmass 6.2.1; Medis, Leiden, the Netherlands). Epicardial and endocardial ventricular borders were manually contoured at end diastole and end systole for quantification of myocardial function and ventricular volumes.

2.3.2. Myocardial strain quantification and data analysis

2.3.2.1. Strain encoded imaging and harmonic phase imaging analysis. Myocardial strain quantification from SENC, and MR tagging images was performed using the SENC and HARP software packages (Diagnosoft Inc., Palo Alto, CA). We measured *EllRV*, *Ell* and *Ecc*. If either of the FGRE, SENC, or tagged dataset was judged to be of inadequate quality, that participant was excluded from the analysis.

We analyzed peak systolic *EllRV* by SENC using the short-axis slices at the basal, mid, and apical ventricular levels. In each section, the RV wall was divided into five equal segments: anterior septal insertion point, anterior, lateral, inferior, and inferior septal insertion point [5], the total number of segments was 15. In each segment, two regions of interest were selected, and an averaged strain-curve was generated. By using these curves, peak systolic *EllRV* was determined. For LV strain analysis, a grid overlay was semi-automatically traced in the short-axis SENC and conventional tagging images for quantification of *Ell* and *Ecc*, respectively [5]. According to the American Heart Association (AHA) segmentation model [16], the LV was divided into six basal, six mid, and four apical segments, to yield a total of 16 segments. Peak systolic *EllRV*, *Ell* and *Ecc* were calculated from average of peak strains from each segment.

2.3.2.2. Multimodality tissue tracking. The multimodality tissue tracking software (MTT; version 6.0, Toshiba, Japan) is used to obtain *EllRV*, and LV *Ell* and *Ecc* derived from cine CMR images. MTT software utilizes a pixel-to-pixel matching technique by defining angle-independent motion vectors from multiple tracking points to find identical voxels in successive frame, as described in Hell-Valle et al. [17]. It has been reported that MTT can assess LV and left atrium deformation with high reproducibility [17–19]. RV and LV endocardial and epicardial borders were manually drawn at a reference frame, the ventricular end-diastolic frame (from long-axis images for *Ell*) or end-systolic frame (from short-axis images for *Ecc*). The software then propagated these borders across the cardiac cycle automatically using a template matching algorithm described as follows (Fig. 1). The software recorded a characteristic pixel pattern of each 10 × 10 mm square area in the reference frame; an area with identical pixel pattern was recognized in the next frame that maximized the similarity evaluated by cross-correlation between the square areas. This procedure was repeated for all pixels in each image and for each frame to track the borders throughout the whole cardiac cycle. After successful tracking, peak systolic segmental strains were extracted from the inner, mid and outer wall for circumferential strain. In case of inadequate tracking, the border delineation was manually adjusted to reflect visual interpretation. Manual correction was necessary on average up to 2 times for a study.

EllRV was measured from RV free wall of 4-chamber view cine CMR image. RV wall was automatically divided into 6 equal segments. LV *Ell* was measured from 4-chamber views, dividing into 6 equal segments; basal lateral, mid lateral, apical lateral, apical septum, mid septum, and basal septum. For LV *Ecc* measurement, cine CMR image short axis sections at the basal, mid, and apical levels which were similar levels to tagging image were used. The LV was divided into 16 segments described above for the tagging analysis. Mean peak systolic *Ell* and *Ecc* were calculated by means of segmental averaging (Fig. 2).

2.3.3. Reproducibility of the MTT method

To determine inter- and intra-observer variability in the measurements of RV and LV segmental strain by MTT, cine MRI of LV long- and short-axis recordings of 3 healthy controls and 7 PH patients was randomly selected. To assess intra-observer reproducibility, a single reader performed the analysis twice at interval of over two weeks. At the same time, a second independent reader performed analysis of the same data sets to assess inter-observer reproducibility. Reproducibility was expressed by intra-class correlation and mean difference.

2.4. Statistical analysis

Data are presented as mean ± standard deviation (SD) unless otherwise stated. Normality was evaluated by the Shapiro–Wilk W test. Strain measurements obtained by MTT, SENC or HARP were compared using the paired Student's t-test. Linear regression and Bland–Altman plots were used to observe correlation and bias. Comparison of peak systolic strain between healthy volunteers and PH patients was analyzed using Student's t test. Peak systolic strains were correlated with global ventricular function and indexes of catheterization of right heart by using the Pearson's correlation coefficient. Statistical difference was considered significant at $p < 0.05$.

3. Results

3.1. Study population

Of the 45 subjects that underwent CMR examination, 6 were excluded; 1 was excluded because of tagged MRI, and 5 were excluded for inadequate cine MRI quality. In total, 26 PH patients (24 females, age = 59.8 ± 9.8 years) and 13 age matched healthy volunteers (9 females, age = 53.7 ± 7.5 years) were evaluated. In PH patients, 6 patients had a final diagnosis of idiopathic pulmonary arterial hypertension and 20 were associated with connective tissue diseases. Clinical characteristics and global biventricular cardiac function parameters of PH patients and control subjects are presented in Table 1. PH patients had trends of higher end systolic and diastolic RV volumes indices and lower RV ejection fraction and stroke volume index. They also had lower LV mean