Quantification of Regional Left Ventricular Function by Real-Time 3D Echocardiography: Validation by Magnetic Resonance Imaging and Clinical Utility

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Abstract

Quantitative information on regional left ventricular (LV) function from real-time 3D echocardiographic (RT3DE) images has significant clinical potential, but needs validation. Our goals were to validate these measurements against cardiac magnetic resonance (CMR) and test the feasibility of automated detection of regional wall motion (RWM) abnormalities from RT3DE data. RT3DE and CMR images were obtained in 31 pts and analyzed using prototype software to calculate regional volumes and ejection fractions. Indices were compared between RT3DE and CMR. Additionally, CMR images were reviewed by an expert, whose RWM grades were used as a reference for the automated detection of RWM abnormalities. RT3DE measurements resulted in good agreement with CMR. Automated detection showed high levels of agreement with expert reading, similar for CMR and RT3DE. Analysis of RT3DE data provides accurate quantification of regional function and allows automated detection of RWM abnormalities.

1. Introduction

The limitations of the conventional echocardiographic evaluation of LV function have been attributed to its 2D nature, which reveals only partial information about cardiac anatomy and function contained in specific cross-sectional planes. Alternative techniques based on 3D reconstruction from multiple planes, albeit time-consuming and prone to artifacts, have shown promise for more accurate assessment of LV function. More recently, real-time 3D echocardiographic (RT3DE) technology, which allows fast acquisition of a dynamic pyramidal data structures that encompass the entire left ventricle, has become widely available. Several studies have since demonstrated the potential improvements in the evaluation of global LV function by using RT3DE data [1-4]. The information on RWM contained in RT3DE datasets has been only studied using visual interpretation of selected planes [5,6] or by measurements performed on model-based, interpolated endocardial surfaces [7]. To circumvent these limitations, an approach based on the detection of dynamic endocardial surface in 3D space and direct quantification of surface segments displacement throughout the cardiac cycle was recently developed and implemented in commercial software. This software allows tracking changes in segmental LV volume throughout the cardiac cycle and calculating regional ejection fraction (REF). Since the use of this methodology is rapidly gaining popularity, its thorough validation is imperative prior to widespread clinical use.

Cardiac magnetic resonance (CMR) methodology is increasingly recognized as a less than ideal reference for LV function measurements because of several limitations that include poor endocardial definition near the apex due to partial-volume artifacts and the use of spatially fixed slices that disregards LV systolic shortening. Analysis of radial long-axis CMR images can potentially eliminate these limiting factors. Accordingly, the commercial software for analysis of RT3DE data was recently adapted for analysis of radial long-axis CMR images. This software calculates values of REF from both RT3DE and CMR data and thus allows direct comparisons while eliminating analysis-related inter-modality differences as a source of error.

Accordingly, the aims of this study were: 1) to validate RT3DE-derived indices of regional LV function against radial long-axis CMR reference values obtained with the same analysis software, and 2) to determine the accuracy of the automated detection of RWM abnormalities based on RT3DE-derived REF values and compare it to the accuracy of the same technique when applied to CMR images.

2. Methods

Thirty-one patients (17 males, 14 females, age: 60±15 years) referred for CMR studies with transthoracic 2D acoustic windows that allowed adequate endocardial visualization were studied. RT3DE and CMR imaging were performed on the same day.

2.1. RT3DE and CMR imaging

RT3DE imaging was performed from the apical window with the patient in the left lateral decubitus position in the harmonic mode using a commercial scanner (SONOS 7500, Philips) equipped with a fully sampled matrix array transducer (X4), using the wide-angled acquisition mode, wherein four wedge-shaped sub-volumes (93°x21°) were acquired over 8 consecutive cardiac cycles during a single breath-hold.

CMR images were obtained using a 1.5 Tesla scanner (Siemens, Sonata) with a phased array cardiac coil. Steady-state free precession mode was used to acquire images during 10 to 15 second breath-holds. Imaging was performed at a temporal resolution of 20 frames per cardiac cycle in six planes, rotated around the long axis of the left ventricle at 30° steps, resulting in dynamic cine-loops of radial long-axis views of the ventricle.

2.2. RT3DE and CMR analysis

Both pyramidal RT3DE datasets and radial long-axis CMR images were analyzed using prototype 4D-LV Analysis software (TomTec). In every CMR slice and in six long-axis planes automatically selected from the RT3DE dataset (30° apart), LV endocardial contours were traced semi-automatically frame-by-frame, with the papillary muscles included in the LV cavity, and manually corrected when necessary to optimize the boundary position. All measurements were performed by an experienced investigator blinded to results of all prior measurements. Following segmentation, regional volumes were calculated throughout the cardiac cycle. Each volume curve was analyzed to obtain: regional end-diastolic and and-systolic volumes (REDV, RESV), REF ((REDV-RESV)/REDV), as well as regional volumes at half-ejection and half-filling times (RV(½et), RV(½ft)). All RT3DE-derived indices of regional LV function were compared with the CMR reference values using linear regression with Pearson correlation coefficients and Bland-Altman analyses.

In addition, dynamic CMR images were reviewed by an expert, who classified RWM in each LV segment as normal or abnormal. Based on this interpretation, study patients were divided into two groups: 16 patients with RWM abnormalities and 15 patients whose RWM was classified as normal in all segments. RT3DE and CMR data were used separately for automated detection of RWM abnormalities, which was performed as follows. REF obtained in the 15 patients with normal RWM were averaged to represent the normal values for each segment. In the remaining 16 patients, RWM was evaluated in each segment by comparing the calculated REF with a predetermined threshold value, which was initially set arbitrarily as the mean REF minus 1SD of the normal group. Assuming that REF value below the threshold could be used to classify RWM as abnormal, these automated classifications were compared with the expert interpretations. Receiver Operating Characteristic (ROC) analysis [8] was used to optimize the REF thresholds for automated detection of RWM abnormalities.

2.3. Statistical analysis

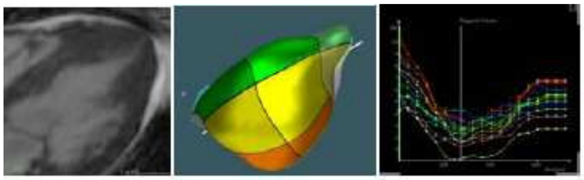
For each calculated index, significance of the biases between the RT3DE and CMR measurements was tested using paired t-tests ($p<0.05$). In addition, for each patient, the level of agreement between the automated technique and the expert interpretation was assessed by counting concordant grades (true positive and true negative) as well as discordant grades (false positive and false negative) assigned by the automated technique. The counts of concordant and discordant grades were used to calculate the sensitivity, specificity, positive and negative predictive values (PPV and NPV) and the overall accuracy, which were used for optimization of REF thresholds. REF thresholds for automated detection of RWM abnormalities varied by varying the number of SD below the mean REF of the normal group in each segment. The ROC curve was then constructed and used to determine the optimal REF thresholds.

3. Results

RT3DE imaging and analysis were feasible in all study subjects. The time required for image analysis, including data retrieval, surface detection and segmentation, and the computation of all indices of RWM, was ~30 minutes.

Figure 1 shows an example of a radial long-axis CMR image obtained at end-diastole in a patient with apical hypertrophic cardiomyopathy. The detected endocardial surface shows in 3D the typical LV morphology for this condition, in close correspondence with the 2D image. Regional LV volume curves demonstrated the expected ejection and filling phases of the cardiac cycle. Figure 2 shows in the same format the RT3DE data obtained in the same patient. The RT3DE-derived regional volume curves had similar shape despite the less detailed endocardial delineation, compared to the CMR images.

Table 1 shows the results of the comparisons between the RT3DE-derived indices of regional LV function against CMR reference values. Each index was calculated from measurements obtained in the 31 patients in each of



gure 1. Radial long-axis CMR image of the left ventricle btained at end-diastole in a patient with apical hypertrophic rdiomyopathy (left), the detected endocardial surface iddle), and the regional LV volume time curves (right).

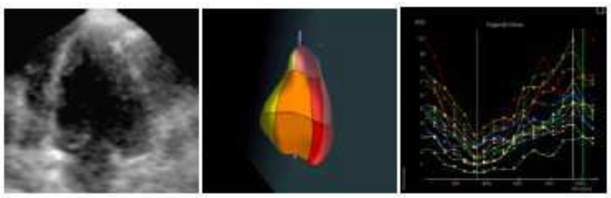


Figure 2. Example of cross-sectional view of the left ventricle extracted from the RT3DE dataset obtained in the same patient as in figure 1.

	RESV	REDV	REF	RV(½et)	RV(½ft)
r	0.82 ± 0.08	0.85 ± 0.04	0.71 ± 0.05	0.82 ± 0.09	0.79 ± 0.10
bias	0.2 ± 2.3 ml	0.0 ± 2.3 ml	-1.3 ± 9.5 %	-0.3 ± 2.7 ml	0.5 ± 2.7 ml
95% limits of agreement	6 ± 2 ml	7 ± 3 ml	23 ± 6 %	9 ± 3 ml	8 ± 2 ml

Table 1. Comparison of RT3DE-derived indices of regional LV function against CMR reference values. Values in the table are mean ± SD of the 16 segments.

the 16 endocardial surface segments. The agreement between the two techniques was reflected by high correlation coefficients, essentially zero biases and relatively narrow limits of agreement.

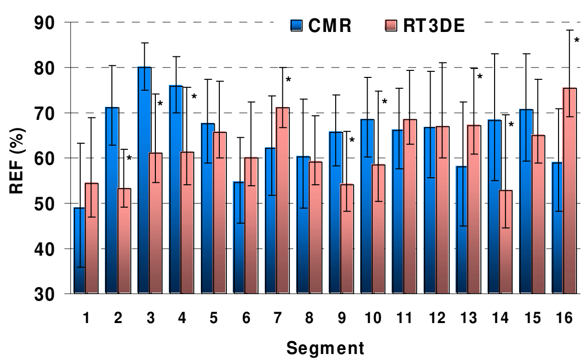


Figure 3. CMR- and RT3DE-derived mean REF values in 16 segments obtained in 15 patients with normal wall motion. The upward error bars represent the SD, while the tips of the downward error bars point at the optimized REF threshold values for each imaging modality (* p<0.05 vs CMR).

In the 15 patients with normal wall motion, REF values averaged over the 16 segments were not different between imaging modalities (CMR: 65±11%, vs. RT3DE: 62±13% NS). Nevertheless, significant differences were found on a regional basis. Figure 3 shows CMR- and RT3DE-derived mean REF values in each of the 16 segments.

In the remaining 16 patients, RWM abnormalities were noted in 206/256 segments (80%) based on expert interpretation of CMR images. Computer analysis resulted in automated detection of these abnormalities that reached maximum accuracy with thresholds at 0.9SD below mean value for CMR and 0.5SD below mean for RT3DE images. These values corresponded to a 16 segment-mean threshold of 56±7% for CMR and 55±10% for RT3DE images. The optimal segment-by-segment thresholds for the automated detection are also shown in figure 3. These threshold REF values allowed correct classification of 215/256 (84%) segments as normal or abnormal in the remaining 16 patients by analysis of either RT3DE or CMR images, in agreement with the expert wall motion scores. Importantly, the automated detection of RWM abnormalities from RT3DE data was as accurate as it was from the CMR data (Table 2).

	Sensitivity	Specificity	PPV	NPV	Accuracy
RT3DE	0.84	0.76	0.95	0.47	0.84
CMR	0.85	0.81	0.96	0.52	0.84

Table 2. Performance of the algorithm for automated detection of RWM abnormalities from CMR and RT3DE images against conventional visual interpretation by an expert reader.

Figure 4 shows the rates of agreement of both imaging modalities with the expert grades for each individual endocardial surface segment. Of note, for both imaging modalities, the highest rates of agreement were noted in

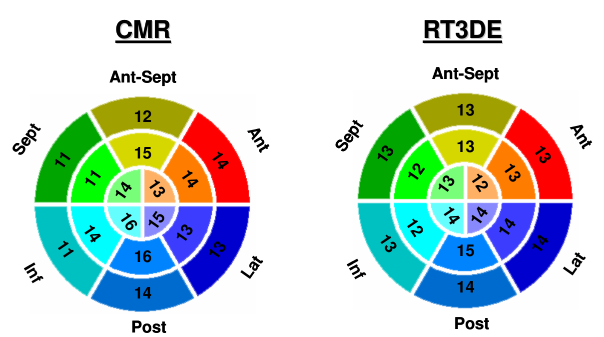


Figure 4. Rates of agreement with the expert grades for each individual endocardial surface segment calculated in 16 patients with RWM abnormalities for the automated interpretation of wall motion from CMR images (left) and RT3DE images (right).

the posterior wall segments, while the lowest rate of agreement were noted in the septal and inferior walls.

4. Discussion and conclusions

This is the first study to validate the frame-by-frame measurements of regional LV volumes against those obtained from radial long axis CMR images that offer significant advantages over the conventional short-axis images, including more uniform endocardial definition from base to apex and optimal visualization of LV systolic shortening within the imaging plane. The use of the same software to analyze both the RT3DE and the CMR images allowed us to eliminate possible analysis-related inter-modality differences as a source of error. In addition to validating volumetric indices of regional LV function against this improved CMR reference values, we successfully tested the feasibility of using REF values as a basis for objective automated interpretation of regional LV wall motion.

Despite the use of improved CMR reference values, the levels of agreement between RT3DE- and CMR-derived regional volumes were lower than those previously reported for global LV volumes and related indices [3,4,6]. This could be expected to occur with volume subdivision as a result of potential segmentation differences between imaging modalities. Nevertheless, correlations coefficients between 0.7 and 0.9 with no bias reflect high levels of concordance. The differences in REF measured by the two modalities (figure 3) could also be explained by the potential segmentation differences, since for both modalities, the segmentation requires the knowledge of the position of the junction between the right ventricular free wall and the interventricular septum [4,5]. This anatomic landmark may shift at different levels of the ventricle and also may be difficult to identify accurately on radial CMR images, since it may be located between imaging planes. The inter-segmental differences in the level of agreement with the CMR reference (figure 4) may probably be explained by the differences between the physics underlying the two imaging modalities, and how different factors such as fiber orientation affects the endocardial definition in different parts of the ventricle.

The ability to detect RWM abnormalities was tested to establish the clinical usefulness of segmental analysis of RT3DE data in patients with coronary artery disease, who are the ultimate target population of this methodology. The results demonstrated the clinical feasibility of this approach, albeit in a relatively small group of patients. However, the goal was feasibility testing, which was achieved as reflected by the high levels of agreement with the expert interpretation of regional wall motion.

One of the limitations of the technique we tested in this study is the relatively significant time commitment it requires. Also, one might suggest that subjective visual interpretation of wall motion is not the ideal standard for comparison.

Despite these limitations, our results proved that echocardiographic volumetric indices of regional LV function are accurate and that RT3DE-derived regional ejection fraction can be used as a basis for automated detection of regional wall motion abnormalities, which was found to be as accurate as that using CMR images, despite the inferior resolution of the ultrasound images.

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