Real-Time 3D Echocardiographic Quantification of Left Ventricular Volumes: Multicenter Study for Validation with Magnetic Resonance Imaging

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Abstract

Left ventricular (LV) volumes obtained from RT3DE datasets are underestimated compared to cardiac magnetic resonance (CMR). We sought to study the accuracy and reproducibility of this technique in a multicenter setting, the inter-institutional differences in these variables in relationship with investigators' experience, and the potential sources of underestimation. 92 patients underwent CMR and RT3DE imaging at 4 different institutions. End-systolic and end-diastolic LV volumes correlated highly with CMR values (EDV: r=0.91; ESV: r=0.93), but were 29 and 26% lower. This finding was consistent across participating institutions, with the magnitude of bias being related to experience. Exclusion of trabeculae and mitral valve plane from the CMR reference essentially eliminated the inter-modality bias. In conclusion, LV volumes are underestimated in most patients because RT3DE imaging cannot differentiate between the myocardium and trabeculae.

1. Introduction

The superiority of 3D measurements of LV volume measurements based on endocardial surface detection [1,2] was recently demonstrated for RT3DE imaging in terms of improved accuracy [3,4] and reproducibility of [2,4]. Although this methodology has been compared against CMR in single center studies, it has not been validated in a standardized protocol in a multicenter setting. Importantly, several recent studies have reported that RT3DE underestimates LV volumes [2,5] to a variable extent, but no consensus has been reached regarding the factors contributing towards this error. We hypothesized that this underestimation may be due to differences in spatial and contrast resolution between RT3DE and CMR imaging that determine the level of detail with which the LV endocardial surface is visualized. Also, the inter-modality discordance may be increased by analysis related differences.

This study was designed to: (1) validate volumetric analysis of the left ventricle from RT3DE datasets against the standard CMR reference technique in a multicenter setting, (2) compare the reproducibility of this analysis with CMR measurements, (3) study inter-institutional differences in accuracy and reproducibility of the RT3DE volume measurements in relationship with the level of the investigators' experience, and (4) to identify and evaluate the relative contributions of the potential sources of error.

2. Methods

2.1. Study design

Initially, aim 1, i.e. the accuracy of RT3DE volume measurements, was addressed by analyzing RT3DE and CMR images obtained in a large group of patients and comparing ESV and EDV between the two modalities. Aim 2, i.e. the reproducibility of both techniques, was achieved using repeated measurements.

To achieve aim 3, i.e. the experience-related inter-institutional differences, investigators in the participating institutions, were given different levels of instruction and training with the prototype software (QLAB, 3DQ-Advanced, Philips). The investigators were not informed that the level of experience was part of the study design. Accuracy and reproducibility were compared between institutions and correlated with the level of experience.

To achieve aim 4, i.e. identify potential sources of error, we performed several additional protocols. First, we obtained a series of RT3DE datasets from a phantom, which were used to rule out a calibration error and to calculate how much a minimal change in a boundary position would affect the measured volume.

In human hearts, one potential source of error that we investigated was the criteria for inclusion/exclusion of basal LV short-axis slices in the CMR reference technique. Previous studies have used different criteria

ranging from (1) including all slices below the mitral annulus to (2) the current convention used in this study that includes all slices in which at least 50% circumference of the LV cavity is surrounded by myocardial tissue. To determine how much this approach could have contributed to the inter-modality discordance, CMR LV volumes obtained at one site were recalculated using criterion (1) (figure 1).

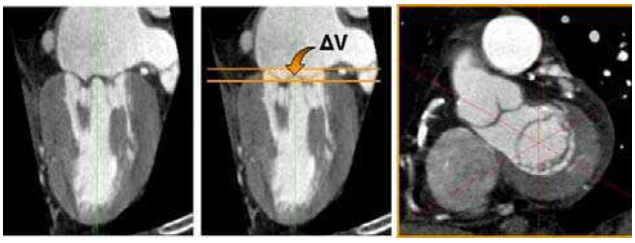

Figure 1. CT image depicting with great detail the LV anatomy (left). CMR images are generated by compacting information from slices of finite thickness (~1 cm). A slice that contains the mitral valve (middle, between horizontal lines) would provide a short axis view where most LV cavity is surrounded by myocardial tissue (right), and would be included in the calculation of LV volume.

Additional potential errors related to CMR analysis include tracing endocardial boundaries in short axis CMR slices (versus initializing in orthogonal long axis planes extracted from RT3DE datasets) as well as different algorithms used for volume calculations. To determine the magnitude of these errors, CMR images obtained in a subgroup of patients were interpolated into a 3D format identical to that of the RT3DE datasets and reanalyzed using the same volumetric analysis software.

Finally, since the visualization of the endocardial trabeculae by RT3DE imaging is limited in many patients (figure 2), they may be erroneously perceived as part of the myocardium. We hypothesized that this may also be an important source of error in the quantification of LV volumes. Accordingly, volumetric analysis of the reformatted CMR 3D datasets was repeated while excluding trabeculae from the LV cavity.

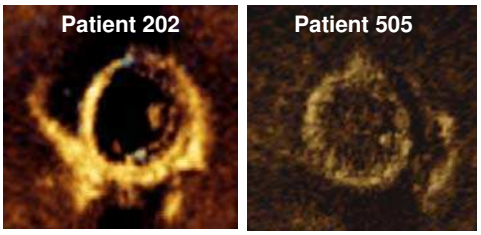

Figure 2. Example of short-axis cut-planes extracted from RT3DE datasets: while in one patient (left), trabeculae can be well visualized and clearly differentiated from the myocardium, in another patient, the spatial resolution of the RT3DE image is not sufficient to provide this kind of detail.

2.2. Population

We studied 92 patients (age 57±16 years, 69♂ and 23♀). Exclusion criteria were: prior cardiac surgery and contraindications to CMR imaging, including pacemakers or defibrillators, atrial arrhythmia, claustrophobia and dyspnea precluding a 10-15sec breath-hold.

2.3. CMR imaging and analysis

CMR images were obtained using a 1.5 Tesla scanner with a phased-array cardiac coil. Steady-state free precession dynamic gradient-echo cine-loops were obtained (8 mm thick short-axis slices with 2x2 mm in-plane spatial resolution) using retrospective ECG-gating during breath-hold at 30 frames per cardiac cycle. Images acquired at each site were analyzed using commercial software. LV endocardial boundary was semi-automatically traced with the papillary muscles and trabeculae included in the LV cavity in every slice at end-diastole and end-systolic. ESV and EDV were calculated using the disk-area summation method and used as a reference for comparison with the RT3DE data.

2.4. RT3DE imaging and analysis

RT3DE harmonic imaging was performed using the Philips iE33 system with X3-1 matrix array transducer. A wide-angled acquisition "full-volume" mode, in which 5 wedge-shaped sub-volumes are acquired over consecutive cardiac cycles, was used during a single breath-hold. Gain controls were optimized for endocardial visualization. Digital images were analyzed at each site using prototype software (QLAB, 3DQ-Advanced, Philips) by an investigator blinded to CMR measurements (figure 3).

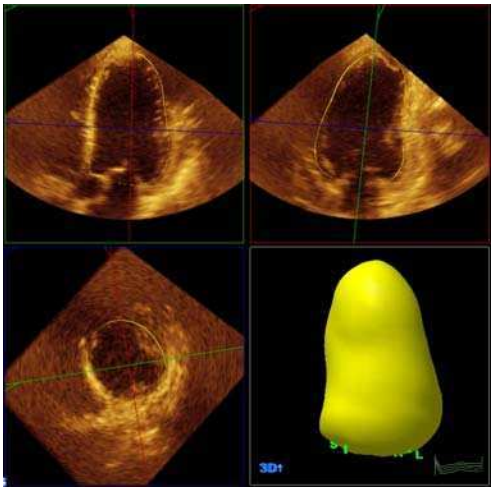

Figure 3. Example of apical 4- and 2-chamber and short-axis cut-planes obtained from a RT3DE dataset, shown with the endocardial contours. Optimization of the boundaries in multiple planes results in a cast of the LV cavity, from which EDV and ESV are calculated without geometric modelling.

To determine the reproducibility of LV volume measurements for each imaging modality, analysis was blindly repeated by an additional investigator as well as by the same primary reader. Inter- and intra-observer variability was calculated as an absolute difference of the corresponding pair of repeated measurements in percent of their mean.

2.5. Phantom imaging and measurements

An egg-shaped phantom was immersed in water and subjected to RT3DE imaging. The measured volume was compared with the manufacturer specified true volume. Then, custom software was used to expand the detected surface outwards exactly 1 mm and measure the volume increment in ml as well as in % of the true volume.

3. Results

3.1. Comparisons with CMR

Although RT3DE- and CMR-derived values of EDV and ESV correlated highly, as reflected by r-values of 0.91 and 0.93 respectively, Bland-Altman analysis revealed negative biases of -67 ml and -41 ml (-29% and -27% of the mean CMR-derived EDV and ESV values). Importantly, the SDs of the inter-technique differences were quite wide, reflecting the inconsistent nature of volume underestimation by RT3DE technique in individual patients.

3.2. Inter-institutional differences

Table 1 shows the results of regression and Bland-Altman analyses for each participating institution, which were arranged in the descending order of experience with the analysis software. Interestingly, measurements performed by the most experienced investigators (Site A) showed biases that were roughly half of those noted in the entire study group. Despite the high correlations with the CMR reference values for all sites, the biases progressively increased with the decreasing level of experience. Inter-site comparisons of tracing methodology revealed that the investigators most experienced with this technique traced the endocardium as far outwards as possible to include as much trabeculae as possible in the LV cavity. Conversely, less experienced users traced along what appeared to be the blood-tissue interface, i.e. the area of maximum intensity gradients.

Table 1.

	EDV		ESV	
	r	bias	r	bias
All patients	**0.91**	**-67 ± 47 ml (-29 ± 20 %)**	**0.93**	**-41 ± 46 ml (-27 ± 30 %)**
Site A	0.93	-37 ± 27 ml (-19 ± 13 %)	0.92	-18 ± 30 ml (-15 ± 25 %)
Site B	0.95	-63 ± 43 ml (-29 ± 20 %)	0.96	-31 ± 42 ml (-24 ± 32 %)
Site C	0.92	-72 ± 55 ml (-29 ± 22 %)	0.94	-44 ± 54 ml (-26 ± 32 %)
Site D	0.89	-89 ± 33 ml (-36 ± 13 %)	0.90	-63 ± 39 ml (-39 ± 24 %)

3.3. Reproducibility

Table 2 shows the reproducibility of LV volumes for CMR and RT3DE images. For both EDV and ESV, both inter- and intra-observer variability were higher for RT3DE than for the CMR. Not surprisingly, for both EDV and ESV, inter-observer variability was higher than intra-observer variability. Importantly, all variability values but one were below 10%. It is worthwhile noticing however, that in individual patients variability levels of both imaging modalities far exceeded the acceptable 10-15% levels (Table 2, ranges shown in parentheses). There were no clear experience related trends in variability data.

Table 2.

		Inter-observer (%)	Intra-observer (%)
EDV	**CMR**	5 ± 4 (0.0 -- 21)	4 ± 5 (0.0 -- 26)
	RT3DE	8 ± 8 (0.0 -- 38)	5 ± 5 (0.0 -- 20)
ESV	**CMR**	7 ± 7 (0.0 -- 36)	4 ± 4 (0.0 -- 19)
	RT3DE	13 ± 14 (0.0 -- 70)	10 ± 11 (0.0 -- 62)

3.4. Phantom studies

Figure 4A shows a long-axis cut-plane of the egg-shaped phantom extracted from a RT3DE dataset with the traced boundary superimposed. Volume measurements performed in the phantom yielded 68.7 ml. Expanding the surface only 1 mm outwards (figure 4B) resulted in volume of 76.1 ml. Of note, this barely visible difference in the surface position (figure 4C) resulted in volume difference of 7.4ml or 11% of the true volume of 73.3 ml.

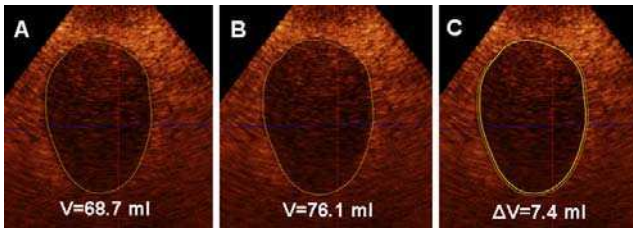

Figure 4. Long-axis cut-plane of the phantom extracted form a RT3DE dataset, shown with the boundary traced along the interface (A), after expanding the boundary 1 mm outwards (B) and with both boundaries (C). The small difference in boundary position resulted in an 11% difference in the measured volume.

3.5. Modifications to CMR reference

Excluding LV basal slices depicting the mitral annulus resulted in smaller CMR reference values, and thus reduced the biases in LV volumes only by ~20%. In addition, EDV and ESV measurements obtained from interpolated 3D CMR datasets were similar to those measured using the conventional CMR technique (r=0.997 for both volumes and small biases of -7±15 ml and -5±15 ml, respectively).

However, exclusion of endocardial trabeculae from the LV cavity during volumetric analysis of interpolated 3D

CMR datasets improved the agreement between the RT3DE-derived LV volumes and the CMR reference values, as reflected by regression slopes closer to 1.0 and smaller intercepts, higher correlation values and a decrease in the magnitude of the biases from -14 and -9% to -1 and 2% respectively.

4. Discussion and conclusions

The rationale behind our study design was to simulate as closely as possible the conditions under which this methodology would ultimately be used clinically. In this setting, the levels of training and experience with RT3DE evaluation of LV volumes vary widely. The main question we sought to answer was whether or to what extent average end-users of RT3DE equipment and volumetric analysis software could expect their LV volume measurements to be interchangeable with those performed with the current standard reference technique, namely CMR imaging.

Our results confirmed that RT3DE and CMR measurements do not yield identical LV volumes. First, RT3DE-derived volumes are underestimated compared to CMR reference for a variety of reasons, some of which are experience dependent and can be addressed by adequate training, while others are inherent to the technique and need to be taken into account while measurement results are interpreted. We found that the major source of error is that in most patients the spatial resolution of RT3DE imaging is insufficient to provide clear definition of endocardial trabeculae, which are as a result lumped together with the myocardium instead of being included in LV cavity, as during CMR analysis.

An additional source of inter-technique discordance includes the CMR criteria for inclusion of basal LV slices, which can significantly affect the reference values. This problem does not exist for RT3DE technique that uses mostly long-axis views for endocardial surface determination. Thus, this issue should not be regarded as an error of the RT3DE analysis, but rather its strength and the users need to be aware of these inter-modality differences while interpreting results of LV volume measurements.

Our phantom studies led us to rule out the possibility of calibration error, either in the imaging system or in the analysis software. These studies also demonstrated how crucial the exact boundary position is for accurate volume measurements, since a barely visible 1 mm difference in surface position resulted in considerable differences in the calculated volumes.

The use of interpolated 3D CMR datasets allowed us to first prove that the differences between analysis techniques normally used for CMR images and RT3DE datasets could not have biased the measurements to an extent found in our patients, since analysis of the same CMR images using the two techniques resulted in virtually the same volumes. Second, repeated analysis of these datasets while excluding endocardial trabeculae produced results very similar to those measured using the same analysis technique in RT3DE datasets. This finding allowed us to extrapolate our interpretation to state that, conversely, if trabeculae could be visualized on RT3DE images as well as on CMR images and thus be included in the LV cavity, one would expect RT3DE measurements to be very similar to the standard CMR reference.

In summary, this is the first study to test and validate volumetric quantification of LV volumes from RT3DE datasets against CMR standard reference in a multicenter setting wherein RT3DE data were analyzed by observers with variable levels of specific experience. Although in our patients RT3DE-derived LV volumes were underestimated compared to CMR reference values, this study provides information on the role of different potential sources of error and provides guidelines for future users on how to minimize these errors as well as how to interpret their findings.

References

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