

Rapid online quantification of left ventricular volume from real-time three-dimensional echocardiographic data

Lawrence D. Jacobs¹, Ivan S. Salgo², Sascha Goonewardena¹, Lynn Weinert¹, Patrick Coon¹, Dianna Bardo³, Olivier Gerard⁴, Pascal Allain⁴, Jose L. Zamorano⁵, Leopoldo P. de Isla⁵, Victor Mor-Avi¹, and Roberto M. Lang^{1*}

¹Noninvasive Cardiac Imaging Laboratory, University of Chicago Hospitals, 5841 S. Maryland Avenue, MC 5084, Chicago, IL 60637, USA; ²Philips Medical Systems, Andover, MA, USA; ³Department of Radiology, University of Chicago, Chicago, IL, USA; ⁴Philips Medical Systems, Paris, France; and ⁵University Clinic San Carlos, Madrid, Spain

Received 20 July 2005; revised 24 October 2005; accepted 3 November 2005; online publish-ahead-of-print 30 November 2005

KEYWORDS

Echocardiography;
Magnetic resonance;
Ventricular function;
Ejection fraction

Aims Determination of left ventricular (LV) volumes and ejection fraction (EF) from two-dimensional echocardiographic (2DE) images is subjective, time-consuming, and relatively inaccurate because of foreshortened views and the use of geometric assumptions. Our aims were (1) to validate a new method for rapid, online measurement of LV volumes from real-time three-dimensional echocardiographic (RT3DE) data using cardiac magnetic resonance (CMR) as the reference and (2) to compare its accuracy and reproducibility with standard 2DE measurements.

Methods and results CMR, 2DE, and RT3DE datasets were obtained in 50 patients. End-systolic and end-diastolic volumes (ESV and EDV) were calculated from the 2DE images using biplane method of disks. ES and ED RT3DE datasets were analysed using prototype software designed to automatically detect the endocardial surface using a deformable shell model and calculate ESV and EDV from voxel counts. 2DE and RT3DE-derived volumes were compared with CMR (linear regression, Bland-Altman analysis). In most patients, analysis of RT3DE data required <2 min per patient. RT3DE measurements correlated highly with CMR (r : 0.96, 0.97, and 0.93 for EDV, ESV, and EF, respectively) with small biases (–14 mL, –6.5 mL, –1%) and narrow limits of agreement (SD: 17 mL, 16 mL, 6.4%). 2DE measurements correlated less well with CMR (r : 0.89, 0.92, 0.86) with greater biases (–23 mL, –15 mL, 1%) and wider limits of agreement (SD: 29 mL, 24 mL, 9.5%). RT3DE resulted in lower intra-observer (EDV: 7.9 vs. 23%; ESV: 7.6 vs. 26%) and inter-observer variability (EDV: 11 vs. 26%; ESV: 13 vs. 31%).

Conclusion Semi-automated detection of the LV endocardial surface from RT3DE data is suitable for clinical use because it allows rapid, accurate, and reproducible measurements of LV volumes, superior to conventional 2DE methods.

Introduction

Left ventricular (LV) ejection fraction (EF) is an important predictor of morbidity and mortality in a wide range of patients and clinical scenarios.^{1,2} Despite its importance in prognosis and clinical decision making, most echocardiography laboratories currently determine EF primarily by visual estimation, which is highly experience-dependent and sensitive to intra- and inter-observer variability. A variety of more objective methods for two-dimensional estimation of LV volumes and EF are available but are inherently flawed because of foreshortening errors and reliance upon geometric models that may be inaccurate in diseased hearts. Three-dimensional echocardiography (3DE) is a relatively new tool that can mitigate the

errors inherent to two-dimensional echocardiography (2DE) because it has the potential to eliminate foreshortening and avoid geometric modelling. Indeed, LV volumes measured by tracing endocardial boundaries in multiple planes showed improved accuracy compared with 2DE.^{3–7} More recently, near-real-time three-dimensional echocardiographic (RT3DE) systems that utilize fully sampled matrix array transducers capable of acquiring volumetric data have been developed.^{8–10} In previous studies using RT3DE imaging, analysis of LV volumes and EF was cumbersome and time-consuming, because it was based on manual tracing of endocardial borders or semi-automated border detection in multiple planes extracted from the volumetric data. Moreover, these 3D analysis methods still required geometric modelling to translate the multiplanar measurements into volumes.

We previously suggested an alternative approach on the basis of detection of the 3D endocardial surface, which

* Corresponding author. Tel: +1 773 702 1842; fax: +1 773 702 1034.
E-mail address: rlang@medicine.bsd.uchicago.edu

allows direct quantification of LV volumes without multiplane tracing or geometric modelling.^{11,12} This approach was recently incorporated into commercial software for analysis of RT3DE data for online quantification of LV volumes and EF. As this new methodology is rapidly gaining widespread clinical use because of its high speed and ease of use and is poised to become part of the mainstream quantification of LV function, its thorough validation is imperative. Accordingly, the aims of this study were (1) to validate this online analysis software against cardiac magnetic resonance (CMR) determinations of LV volumes and EF, (2) to compare the accuracy of these measurements with that of the conventional 2DE technique, and (3) to prove that the mechanism by which this new tool provides incremental improvements over 2DE and multiplane 3DE methods is indeed its ability to eliminate the foreshortening errors and the need for geometric modelling.

Study design

To achieve these goals, we studied a group of patients with a variety of cardiac pathologies, who were recruited in two different institutions. To validate RT3DE measurements against CMR and compare them with 2DE measurements, each patient underwent 2DE, RT3DE, and CMR imaging, and each modality was used to measure LV volumes and EF. 2DE and RT3DE measurements were compared with the CMR reference values. In addition to performing these comparisons in the entire group of patients, RT3DE data acquired at the two institutions was analysed separately for each site, and the results were compared between the groups and with the entire cohort, as a way to confirm that RT3DE analysis can provide accurate measurements when applied to data acquired at different institutions.

To prove that the mechanisms by which the new RT3DE method improves the accuracy of LV volume measurements are its ability to eliminate foreshortening and its freedom from geometric assumptions, we studied a subset of patients in whom the 2DE results were least accurate. In these patients, an intermediate analysis step was performed in addition to the 2DE and RT3DE endocardial surface-derived measurements. RT3DE data were used to extract anatomically correct, non-foreshortened apical 2- and 4-chamber views, in which the endocardium was manually traced and LV volumes calculated using a biplane model. This intermediate step was designed to remove foreshortening while retaining an equivalent level of reliance on geometric modelling as the 2DE biplane method of disks (MOD), as a way to isolate the contribution of each of these sources of error.

Methods

Population

Fifty patients (27 males, 23 females, age: 58 ± 19 years) evaluated at the outpatient cardiology clinics of the University of Chicago Medical Center ($n = 29$) and University Clinic San Carlos, Madrid ($n = 21$), who were referred for CMR imaging, were studied. Of 58 patients screened for this study, eight were excluded because of transthoracic 2D acoustic windows that did not allow adequate endocardial visualization. Additional exclusion criteria were dyspnea precluding a 10–15 s breath-hold, atrial fibrillation or other cardiac arrhythmias, pacemaker or defibrillator implantation, and claustrophobia. Of the remaining 50 patients, 24 had coronary

artery disease, 18 dilated cardiomyopathy, four valvular disease, two aortic coarctation, and two right atrial masses. The study was approved by the regulatory committees of both institutions, and written informed consent was obtained from all patients prior to data acquisition.

Protocol

Data acquisition was performed using identical CMR and echocardiographic equipment and protocols in both institutions. The 2DE and RT3DE examinations were performed on the same day as the CMR study.

CMR imaging

CMR images were obtained with a 1.5T scanner (General Electric, Milwaukee, WI, USA) with a phased-array cardiac coil. Electrocardiogram-gated localizing spin-echo sequences were used to identify the long-axis of the heart to allow imaging of the left ventricle in anatomically correct short-axis planes. Steady-state free precession (FIESTA) dynamic gradient-echo cine-loops were obtained during 10–15 s breath-holds with a temporal resolution of 20 frames per cardiac cycle. In all patients, 6–10 short-axis cine-loops were obtained from the atrioventricular ring to the apex (9 mm slice thickness, no gaps).

2DE imaging

Transthoracic 2DE harmonic imaging was performed using a commercial ultrasound scanner (Philips 7500) equipped with an S3 transducer from apical windows in the harmonic mode with the patient in the left lateral decubitus position. Loops from five consecutive cardiac cycles were acquired from apical 4- and 2-chamber views during a breath-hold while taking care to avoid foreshortening. These loops were stored digitally for offline analysis.

RT3DE imaging

Harmonic RT3DE imaging was performed immediately following 2DE imaging using a fully sampled matrix array transducer (X4, 2–4 MHz), which utilizes 3000 active elements to obtain from a single apical window a pyramidal dataset that contains the entire LV cavity. The 3D images were optimized by modifying the gain, brightness, compression, and time-gain compensation controls. RT3DE datasets were then acquired using the wide-angle acquisition mode ($93^\circ \times 80^\circ$) in which four wedge-shaped subvolumes ($93^\circ \times 20^\circ$) were obtained over eight consecutive cardiac cycles during a breath-hold. Acquisition of each subvolume was triggered to the ECG R-wave of every second heartbeat to allow sufficient time for the probe to be recalculated and each subvolume stored.

Image analysis

CMR LV volume measurements

These loops were analysed offline using commercial software (MASS Analysis, General Electric). In every short-axis slice, endocardial contours were manually traced at end-systole and end-diastole, including the papillary muscles in the LV cavity. All tracings were performed by an investigator experienced in the interpretation of CMR images who had no knowledge of the echocardiographic measurements. The traced contours were used to calculate EDV and ESV, which served as the reference for comparisons against 2DE and RT3DE data.

2DE volume measurements

Analysis of 2DE images included manual tracing of the LV endocardial borders at end-systole and end-diastole in each apical view. EDV and ESV were then calculated using the biplane MOD, and EF was computed.

RT3DE volume measurements

3DQ Advanced software (Philips) was used for analysis of 3D data. First, non-foreshortened, anatomically correct apical 2- and 4-chamber views were extracted from the pyramidal dataset as described in detail previously,⁹ on the first frame in the loop, which corresponded to end-diastole. Then, five anatomic landmarks were manually initialized, including two points to identify the mitral valve annulus in each of the two apical views and one point to identify the apex in either view (Figure 1). Following manual identification of these points, the program automatically identified the three-dimensional endocardial surface using a deformable shell model.¹³ Adjustments to the automatic surface detection could be performed at this time, if necessary. EDV was then automatically computed directly from voxel counts. Then, end-systole was selected by identifying the frame with the smallest LV cavity cross-sectional area in both apical views. If the two frames appeared to have similar sizes, the end-systolic frame was selected as the last systolic frame before mitral valve opening. Surface detection, including initialization, was then repeated on this frame to obtain ESV. The EF was then calculated from these ED and ES volumes.

In the subset of 20 patients in whom the 2DE results were least accurate compared with CMR, data was analysed as follows. Instead of determining the volumes by surface detection, RT3DE datasets were used to extract the anatomically correct, non-foreshortened 2- and 4-chamber views and LV volume was calculated using a biplane MOD calculation on these views (Figure 2). The results of these measurements were compared with the 2D biplane MOD and the RT3DE direct surface detection volume determinations.

In addition, images obtained in a subgroup of eight patients were analysed using the TomTec software as described in detail by Kühl *et al.*⁸ The results of these analyses were compared with the results of our rapid online measurements.

Reproducibility

The reproducibility of the 2DE and RT3DE measurements of EDV and ESV was evaluated by calculating the intra- and inter-observer variability of both techniques. To achieve this, 10 of the 50 patients were selected at random. Analysis of the 2DE and RT3DE images obtained in these patients was repeated 1 week later by the primary reader and by an additional expert reader, who were both blinded to the previous measurements, and the CMR-derived volumes. Intra- and inter-observer variability was assessed for each technique by calculating the absolute difference between the corresponding repeated measurements, which was also expressed in per cent of their mean. Absolute differences between repeated measurements were subjected to Bland-Altman analysis. In addition, the inter-examination variability of the RT3DE technique was studied by repeating image acquisition 1 h later in a group of eight patients.

Statistical analysis

All LV volume and EF values were expressed as mean \pm SD. The relationship between each technique, 2DE and RT3DE with CMR, was evaluated using linear regression analysis with Pearson's correlation coefficient. The agreement between each, 2DE and RT3DE measurements and CMR reference values, was evaluated using Bland-Altman analysis¹⁴ by calculating the bias (mean difference) and the limits of agreement (2SD around the mean difference). The significance of the biases was tested using paired *t*-tests with a two-tailed distribution. *P*-values <0.05 were considered significant.

In addition, RT3DE data acquired at the two institutions were analysed separately, including comparisons with CMR, using linear regression and Bland-Altman analyses. The results of these analyses were compared between groups and with the entire cohort. Inter- and intra-observer variability was measured with each technique

and averaged for all patients. In the subset of 20 patients in whom the 2DE results were least accurate compared with CMR, the RT3DE-derived biplane MOD measurements were compared with CMR using linear regression and Bland-Altman analysis, similar to the 2DE and RT3DE-derived values.

Results

Acquisition of RT3D datasets was feasible in all patients. Generating one LV volume value from RT3DE data required <2 min, including the manual initialization. Adjustment of the detected endocardial surface was necessary in 21 patients (42%), including four patients who had aneurysms. These adjustments increased the analysis time in these patients by up to five additional minutes per volume. RT3D measurements of LV volumes correlated highly with the CMR reference values (*r*: 0.96, 0.97, 0.93 for EDV, ESV, and EF, respectively). There were small negative biases (-14 mL, -6.5 mL, both $P < 0.05$, -1% , $P = 0.27$), reflecting the underestimation by the RT3D technique, and narrow limits of agreement (2SD: 34 mL, 32 mL, 12.8%) between the two methods. In comparison, volume determinations using the biplane MOD from 2DE images did not correlate as well with CMR values (*r*: 0.89, 0.92, 0.86 for EDV, ESV, and EF, respectively) and showed greater negative biases (-23 mL, -15 mL, both $P < 0.05$, 0.8%, $P = 0.57$) with wider limits of agreement (2SD: 58 mL, 48 mL, 19%) when compared with CMR (Figures 3 and 4). Of note, in the low EF range by MRI, the data is tightly clustered around the regression line (Figure 3, bottom right panel) and around the near-zero bias line (Figure 4, bottom right panel).

Table 1 shows the results for intra-observer, inter-observer, and inter-examination variability of the RT3DE-derived ESV, EDV, and EF measurements, revealing high reproducibility. Importantly, all variability values were significantly lower for the RT3DE-derived volumes compared with the corresponding 2DE values.

When the entire cohort was analysed by acquisition site, measurements performed in each group resulted in LV volumes that correlated equally well with CMR reference values ($r = 0.94$ for EDV and ESV in Chicago patients and $r = 0.98$ for EDV and ESV in Madrid patients). Bland-Altman analysis showed that the bias and limits of agreement were essentially the same in these subgroups and were not different from the cohort as a whole.

In the subgroup of 20 patients in whom the 2DE results were least accurate, the accuracy of the RT3DE biplane MOD measurements fell between those of traditional 2D biplane MOD and the RT3DE surface-derived values (Figure 5). Specifically, the 2D biplane MOD volume measurements had the greatest biases (-43 mL, -30 mL, 3.5% for EDV, ESV, and EF, respectively) and widest limits of agreement (2SD: 46 mL, 42 mL, 17.4%, respectively). The RT3DE biplane MOD measurements resulted in improved biases (-28 mL, -15 mL, -1.6% , respectively) but wider limits of agreement (2SD: 72 mL, 50 mL, 25.6%, respectively). The RT3D surface detection algorithm had the smallest biases (-19 mL, -9.9 mL, 0.4%, respectively) and the narrowest limits of agreement (2SD: 40 mL, 30 mL, 12.4%, respectively).

The comparisons with the volume values obtained using the TomTec analysis software resulted in high correlation coefficients (EDV: 0.96; ESV: 0.97), only small biases

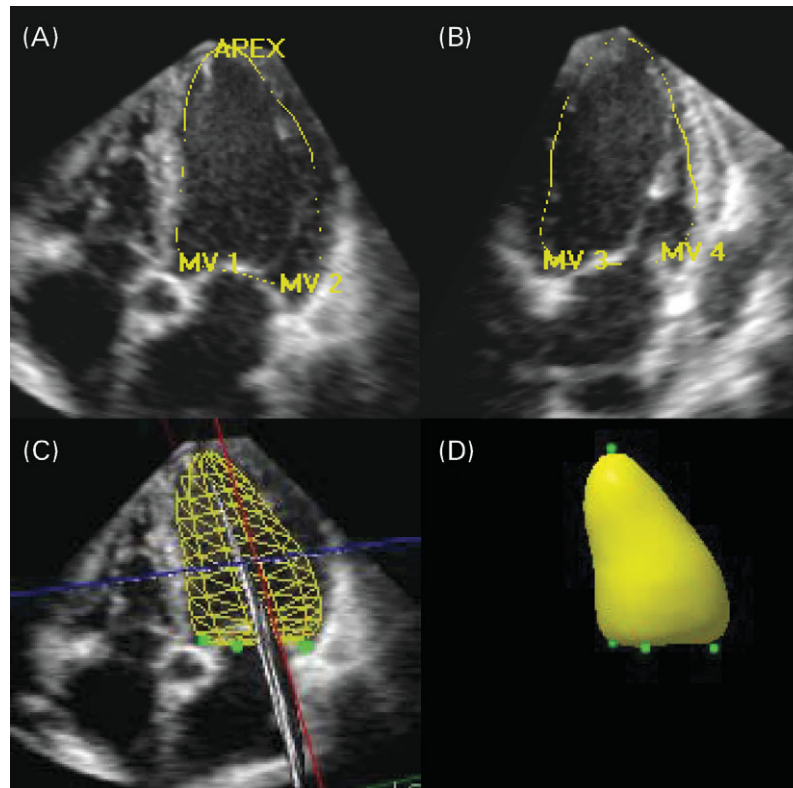


Figure 1 Method of LV volume analysis. Once the desired viewing planes were selected from the RT3DE datasets, five points were manually initialized. These included two points to identify the mitral annulus in each apical view (A and B), and a single point to identify the LV apex in either view (A). Then, the LV endocardial surface was automatically identified using a deformable shell model (C and D). Adjustments to the resultant surface could be made in cross-sectional planes (A and B) when necessary.

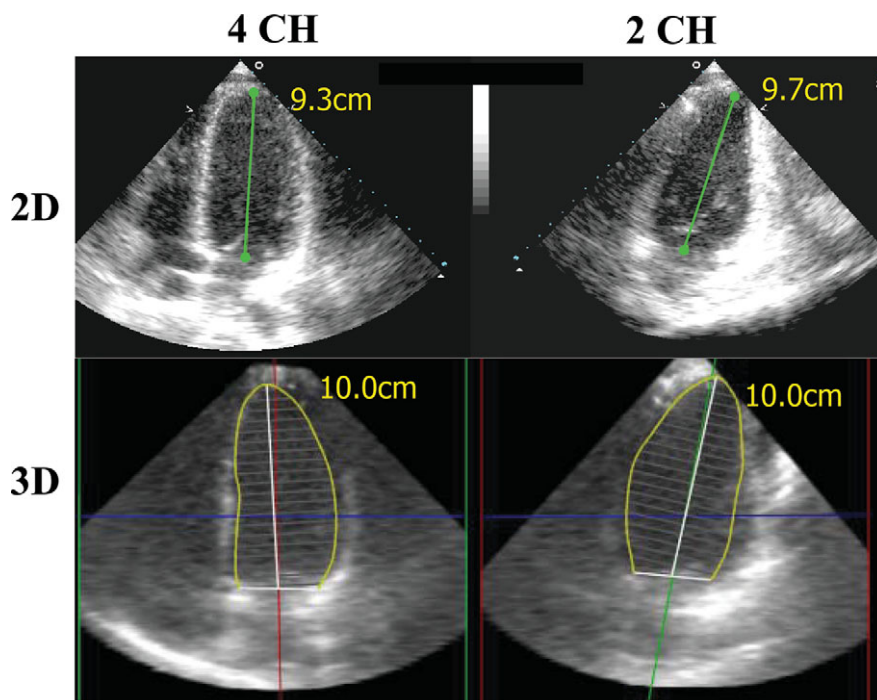


Figure 2 The effect of foreshortening on 2DE volume determinations and a method of using RT3DE data to reduce this source of error. The top panels represent 2DE apical 4-chamber (left) and 2-chamber (right) images with their respective long-axes indicated by the green lines. The bottom panels show the anatomically correct 4-chamber (left) and 2-chamber (right) images that have been extracted from the RT3DE dataset obtained in the same subject. When these non-foreshortened images are used to measure the long-axis of the ventricle, it is clear that the 2DE images are foreshortened, which explains the underestimation of the ventricular volume obtained by the biplane MOD. By performing a biplane MOD on the non-foreshortened images extracted from the RT3DE datasets, a more accurate result is obtained.

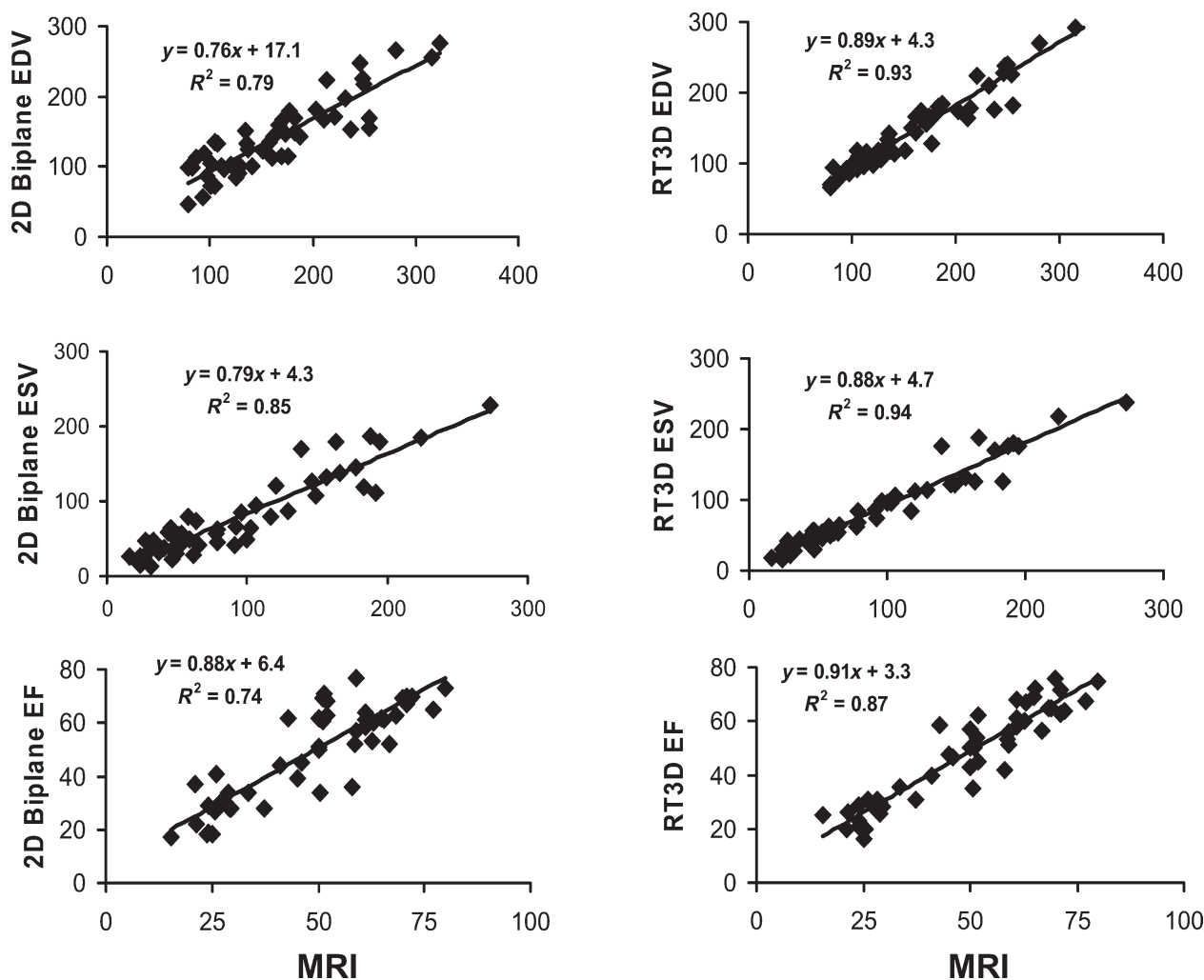


Figure 3 Linear regression analysis of the 2DE and RT3DE measurements of EDV, ESV, and EF against the CMR 'gold standard' in 50 subjects. 2DE EF values were calculated using Simpson's biplane MOD.

(EDV: 6 mL; ESV: -9 mL) and relatively narrow limits of agreement (EDV: 18 mL; ESV: 20 mL).

Discussion

The accurate and reliable determination of LV volumes and EF has important clinical implications for patients with cardiovascular disease, as they correlate well with prognosis and mortality across a wide range of cardiac diseases.^{1,2} EF is also a frequent criterion upon which the decision to employ or withhold certain therapies depends, including ICD implantation,¹⁵ valve replacement,¹⁶ and coronary artery bypass surgery.¹⁷ Despite the large volume of data published on the topic, there is currently no optimal method for the determination of LV volumes using echocardiography. The overall accuracy of the various available methods appears to relate directly to the frequency of data sampling and the ease with which the geometric model used adapts to irregularities in the true cavity shape. Methods with less sampling and more reliance upon geometric assumptions are inherently less accurate.

The shortcomings of standard methods currently in use are well illustrated by the 2D biplane MOD. First and foremost, this technique assumes that the ventricular cavity

has the idealized shape of a truncated ellipsoid. It then uses measurements performed in only two planes of the ventricle to estimate the volume of this three-dimensional structure. Unfortunately, even the healthiest hearts do not conform well to this geometric model. As the ventricle becomes diseased and asymmetric in its contraction because of the presence of regional wall motion abnormalities, the model usually becomes even less accurate. This creates a situation in which patients with cardiac disease, in whom the accurate measurement of ventricular function is of greatest significance, are the patients in whom current methods based on geometric models fail most profoundly.¹⁸ Yet, even if there were a geometric model that could translate 2D biplane measurements into volumes accurately, the results compared with 3D methods would still be disappointing. This is because foreshortening is difficult to avoid or even to recognize when acquiring apical 2D measurements of the left ventricle. Lastly, 2D imaging often has difficulty visualizing the apical lateral portion of the left ventricle, which makes accurate border tracing difficult in this region.

Although we are not the first to propose a 3D solution to overcome the limitations inherent to 2D estimations of ventricular volumes,¹⁹ most currently available 3D methods

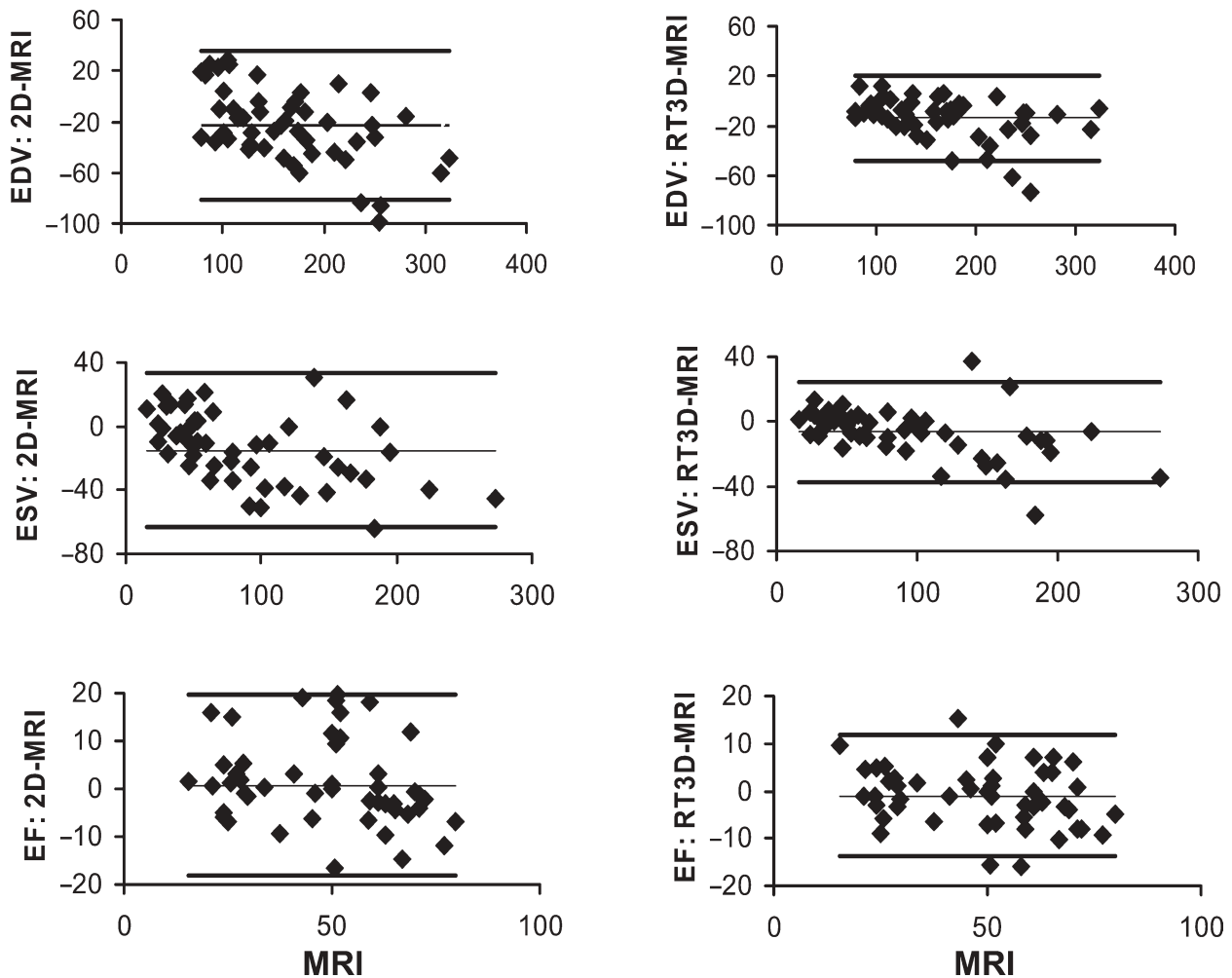


Figure 4 Bland-Altman plots comparing 2DE (left) and RT3DE (right) measurements with the CMR gold standard. The thin horizontal line in each plot represents the mean difference between the echo measurements and the CMR reference, which is the bias of the corresponding measurement. The thick horizontal lines represent the limits of agreement (2SD around the mean).

Table 1 Intra-observer, inter-observer, and inter-examination variability in EDV, ESV, and EF

| | EDV | | ESV | | EF | |
|--------------------------|---------|---------|---------|---------|---------|---------|
| | 2DE | RT3DE | 2DE | RT3DE | 2DE | RT3DE |
| Intra-observer | | | | | | |
| % Variability | 13 ± 21 | 10 ± 6 | 24 ± 24 | 11 ± 5 | 13 ± 11 | 10 ± 5 |
| Bias ± 2SD (mL) | 15 ± 46 | 13 ± 14 | 13 ± 24 | 6 ± 6 | 7 ± 12 | 6 ± 6 |
| Inter-observer | | | | | | |
| % Variability | 19 ± 20 | 10 ± 8 | 24 ± 21 | 11 ± 6 | 14 ± 17 | 5 ± 4 |
| Bias ± 2SD (mL) | 23 ± 42 | 14 ± 20 | 11 ± 20 | 7 ± 10 | 8 ± 18 | 3 ± 4 |
| Inter-examination | | | | | | |
| % Variability | 23 ± 21 | 12 ± 12 | 28 ± 31 | 17 ± 20 | 19 ± 24 | 16 ± 23 |
| Bias ± 2SD (%) | 13 ± 30 | 7 ± 16 | 8 ± 18 | 5 ± 16 | 6 ± 16 | 4 ± 12 |

The RT3DE measurements are compared with the 2DE measurements.

often require difficult or lengthy acquisition and offline reconstruction, which make them impractical for routine clinical use. Data analysis frequently involves tedious manual tracing of the endocardial border in multiple planes. In our previous studies as well as in those by other investigators who used RT3DE, endocardial surface detection was performed offline.^{11,12} In contrast, the technique

used in this study allows online analysis within the imaging system without the need to export data to an external computer for tracing and 3D reconstruction. Moreover, because this methodology has recently become widely available, it is imperative that it be rigorously validated prior to routine clinical use. This was the goal of our present study, and it was achieved by applying this new technique to

images obtained in a large group of patients at two different institutions and comparing the results to magnetic resonance measurements.

In our patients, the new technique resulted in a significant improvement over both traditional 2D estimations and currently available 3D measurement techniques. The underestimation of LV volumes by the standard 2DE biplane MOD technique compared with CMR was drastically reduced with the use of the RT3DE algorithm, as reflected by the 40% decrease in the negative bias for EDV and the 56% decrease for ESV. Furthermore, the RT3DE technique offers more reliable results, as shown by the significantly lower standard deviations and lower intra- and inter-observer variability compared with the 2D technique. An important implication of this result is that in future studies, a smaller sample of patient population of interest would be required for the RT3DE technique to conclusively demonstrate effects of treatment. It is not surprising that an echocardiographic method would tend to underestimate volumes compared with a CMR-based method. This may be because the endocardial border is automatically detected at the tips of the trabeculae, whereas in CMR images this border appears to be at their base, resulting in slight volume disparities.

The target number of patients was set to 50 to yield a sufficiently large subgroup of patients ($n = 20$), in whom the RT3DE-derived measurements disagreed with the CMR reference, to allow us investigate the relative contributions of the different sources of error. This ratio was determined on the basis of our preliminary results. Measurements performed in this subgroup illustrated the power of true 3D analysis to remove foreshortening errors by the comparison between standard 2D biplane determinations and RT3DE-derived biplane estimations that allowed anatomically correct measurement planes to be identified, so that they represented the accurate, non-foreshortened long-axis dimensions of the ventricle. In the subset of 20 patients in whom 2D calculations significantly underestimated the CMR results, foreshortening was shown to be the predominant cause for error. By reducing this source of error, the bias relative to CMR was reduced by 34% (-42.8 to -28.1 mL) for EDV and by 49% (-29.9 to -15.4 mL) for ESV. This strategy of using selected patients allowed us to determine the relative contributions of different sources of error in the standard 2D biplane LV volume measurements.

A shortcoming of the RT3DE technique lies in the fact that a significant minority of subjects required some degree of manual correction of the automated border detection, which increased the analysis time. This increase was particularly significant in patients with LV aneurysms, indicating that the performance of the deformable shell algorithm needs to be studied in a larger number of such patients. Despite the fact that this technique avoids some of the problems of the 2DE methods, it is still an echo-based technique and suffers from the limitations inherent to this imaging modality. Poor acoustic windows and imaging artefacts can significantly reduce the reliability of RT3DE measurements, just as with 2DE imaging. Finally, the use of short-axis CMR imaging as a reference could be viewed as a limitation of this study, because it also cannot provide perfectly accurate volume measurements, despite the superior endocardial definition. This is because these measurements are derived from manually traced, discrete slices of fixed thickness, thus ignoring

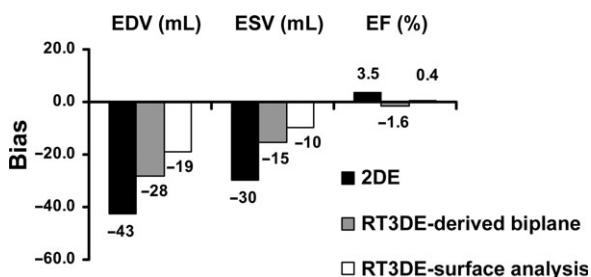


Figure 5 EDV, ESV, and EF biases obtained in a subgroup of 20 patients in whom the 2DE volume measurement most severely underestimated the CMR gold standard. The black bars represent the standard 2DE biplane measurements. The grey bars represent measurements obtained by extracting the non-foreshortened apical views from the RT3DE datasets and applying a biplane MOD. The white bars represent the results of the deformable shell model analysis.

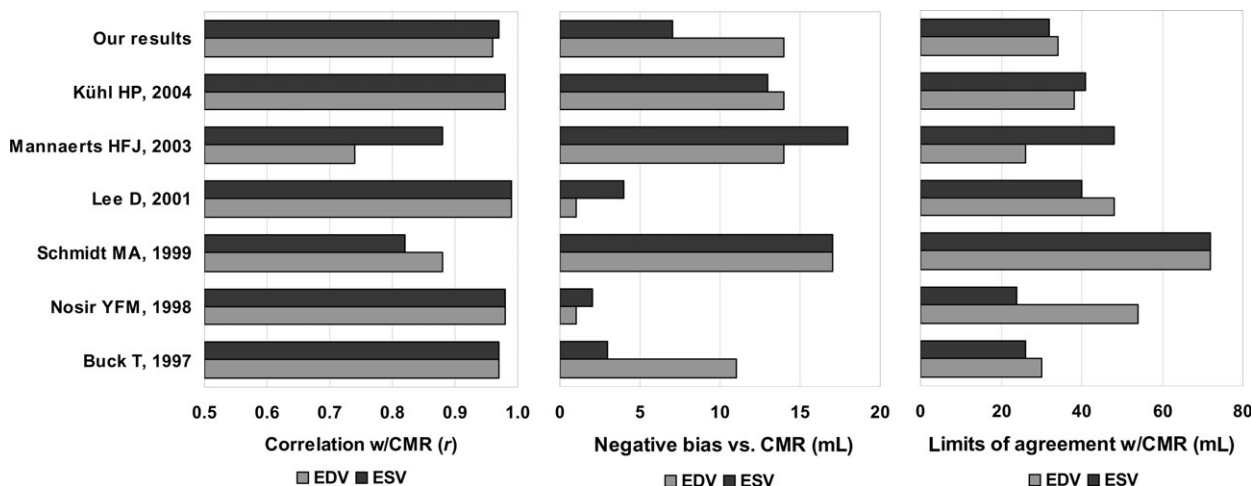


Figure 6 Correlation, bias, and limits of agreement between 3D echocardiographic measurements of LV volumes with CMR values: comparison of our results with previous studies.^{4,8,20-24}

longitudinal LV systolic shortening, as well as its other well known limitations such as poor endocardial definition near the apex because of partial-volume artefacts. Nevertheless, CMR imaging is widely used as the standard, although imperfect, for LV volume measurements.

Despite these limitations, we have shown that it is possible to obtain more accurate LV volume determinations from RT3DE data. This method showed excellent concordance with CMR, reflected by minimal bias and limits of agreement that were narrower than those of the 2DE-based measurements. It also provided highly reproducible results, with low intra-observer, inter-observer and inter-examination variability. These accurate and reproducible results were achieved rapidly, with data analysis being performed online. Importantly, the RT3DE algorithm led to highly accurate results in patients with both normal and significantly reduced EFs. These results need to be viewed in perspective to previous studies that compared 3D echocardiographic measurements of LV volumes with CMR.^{4,8,20-24} Comparisons with previous publications showed that our results are as accurate as those published by others (Figure 6). Moreover, the favourable comparisons with the TomTec technique previously validated by Kühl *et al.*⁸ further substantiated the applicability of the rapid online analysis tested in this study. Importantly, we see the greatest virtue of this new technique that is poised to become part of the routine clinical evaluation of LV function in its speed, ease of use and reproducibility. These are tremendous advantages even if some of the previous techniques had shown slightly better accuracy.

In summary, RT3DE imaging and volumetric analysis tested in this study has at least two advantages over traditional 2D methods which make it highly accurate. First, it eliminates foreshortening errors, which has long been the thorn in the side of echocardiographers attempting to obtain accurate volume estimations. Secondly, it dispenses with the need for geometric models and the errors that come with them. It also offers the promise of a technique that is reliable in both normal and abnormal hearts. Beyond this, it is rapid and user-friendly, and thus highly applicable not only to the research setting but also to the routine clinical examination.

Acknowledgement

This study was supported by a research grant from Philips Medical Systems.

Conflict of interest: I.S.S., O.G. and P.A. are full-time employees of Philips Medical Systems.

References

- White HD, Norris RM, Brown MA, Brandt PW, Whitlock RM, Wild CJ. Left ventricular end-systolic volume as the major determinant of survival after recovery from myocardial infarction. *Circulation* 1987; **76**:44-51.
- Wong M, Johnson G, Shabetai R, Hughes V, Bhat G, Lopez B, Cohn JN. Echocardiographic variables as prognostic indicators and therapeutic monitors in chronic congestive heart failure. Veterans Affairs cooperative studies V-HeFT I and II. V-HeFT VA Cooperative Studies Group. *Circulation* 1993; **87**:VI65-VI70.
- Chuang ML, Hibberd MG, Salton CJ, Beaudin RA, Riley MF, Parker RA, Douglas PS, Manning WJ. Importance of imaging method over imaging modality in noninvasive determination of left ventricular volumes and ejection fraction: assessment by two- and three-dimensional echocardiography and magnetic resonance imaging. *J Am Coll Cardiol* 2000; **35**:477-484.
- Gopal AS, Keller AM, Rigling R, King DL Jr, King DL. Left ventricular volume and endocardial surface area by three-dimensional echocardiography: comparison with two-dimensional echocardiography and nuclear magnetic resonance imaging in normal subjects. *J Am Coll Cardiol* 1993; **22**:258-270.
- Gopal AS, Shen Z, Sapin PM, Keller AM, Schnellbaecher MJ, Leibowitz DW, Akinboboye OO, Rodney RA, Blood DK, King DL. Assessment of cardiac function by three-dimensional echocardiography compared with conventional noninvasive methods. *Circulation* 1995; **92**:842-853.
- Hibberd MG, Chuang ML, Beaudin RA, Riley MF, Mooney MG, Fearnside JT, Manning WJ, Douglas PS. Accuracy of three-dimensional echocardiography with unrestricted selection of imaging planes for measurement of left ventricular volumes and ejection fraction. *Am Heart J* 2000; **140**:469-475.
- Sapin PM, Schroder KM, Gopal AS, Smith MD, DeMaria AN, King DL. Comparison of two- and three-dimensional echocardiography with cineventriculography for measurement of left ventricular volume in patients. *J Am Coll Cardiol* 1994; **24**:1054-1063.
- Kühl HP, Schreckenberger M, Rulands D, Katoh M, Schafer W, Schummers G, Bucker A, Hanrath P, Franke A. High-resolution transthoracic real-time three-dimensional echocardiography: quantitation of cardiac volumes and function using semi-automatic border detection and comparison with cardiac magnetic resonance imaging. *J Am Coll Cardiol* 2004; **43**:2083-2090.
- Mor-Avi V, Sugeng L, Weinert L, MacEneaney P, Caiani EG, Koch R, Salgo IS, Lang RM. Fast measurement of left ventricular mass with real-time three-dimensional echocardiography: comparison with magnetic resonance imaging. *Circulation* 2004; **110**:1814-1818.
- Ota T, Kisslo J, von Ramm OT, Yoshikawa J. Real-time, volumetric echocardiography: usefulness of volumetric scanning for the assessment of cardiac volume and function. *J Cardiol* 2001; **37**(Suppl. 1):93-101.
- Caiani EG, Corsi C, Zamorano J, Sugeng L, MacEneaney P, Weinert L, Battani R, Gutierrez JL, Koch R, Perez de Isla L, Furlong KT, Mor-Avi V, Lang RM. Improved semi-automated quantification of left ventricular volumes and ejection fraction using high-resolution real-time three-dimensional echocardiography: comparison with MRI. *J Am Soc Echocardiogr* 2005; **18**:779-788.
- Corsi C, Lang RM, Caiani EG, Weinert L, Sugeng L, Veronesi F, MacEneaney P, Lamberti C, Mor-Avi V. Volumetric quantification of global and regional left ventricular function from real-time three-dimensional echocardiographic images. *Circulation* 2005; **112**:1161-1170.
- Gerard O, Billon AC, Rouet JM, Jacob M, Fradkin M, Allouche C. Efficient model-based quantification of left ventricular function in 3-D echocardiography. *IEEE Trans Med Imaging* 2002; **21**:1059-1068.
- Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; **1**:307-310.
- Moss AJ, Zareba W, Hall WJ, Klein H, Wilber DJ, Cannom DS, Daubert JP, Higgins SL, Brown MW, Andrews ML. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *N Engl J Med* 2002; **346**:877-883.
- ACC/AHA guidelines for the management of patients with valvular heart disease. A report of the American College of Cardiology/American Heart Association. Task Force on Practice Guidelines (Committee on Management of Patients with Valvular Heart Disease). *J Am Coll Cardiol* 1998; **32**:1486-1588.
- Eagle KA, Guyton RA, Davidoff R, Edwards FH, Ewy GA, Gardner TJ, Hart JC, Herrmann HC, Hillis LD, Hutter AM Jr, Lytle BW, Marlow RA, Nugent WC, Orszulak TA, Antman EM, Smith SC Jr, Alpert JS, Anderson JL, Faxon DP, Fuster V, Gibbons RJ, Gregoratos G, Halperin JL, Hiratzka LF, Hunt SA, Jacobs AK, Ornato JP. ACC/AHA 2004 guideline update for coronary artery bypass graft surgery: summary article. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1999 Guidelines for Coronary Artery Bypass Graft Surgery). *J Am Coll Cardiol* 2004; **44**:1146-1310.
- Gutiérrez-Chico J, Zamorano JL, de Isla LP. Comparison of left ventricular volumes and ejection fractions measured by three-dimensional echocardiography versus by two-dimensional echocardiography and cardiac magnetic resonance in patients with various cardiomyopathies. *Am J Cardiol* 2005; **95**:809-813.
- Salgo IS. Three-dimensional echocardiography. *J Cardiothorac Vasc Anesth* 1997; **11**:506-516.

20. Buck T, Hunold P, Wentz KU, Tkalec W, Nesser HJ, Erbel R. Tomographic three-dimensional echocardiographic determination of chamber size and systolic function in patients with left ventricular aneurysm: comparison to magnetic resonance imaging, cineventriculography, and two-dimensional echocardiography. *Circulation* 1997;**96**: 4286–4297.
21. Lee D, Fuisz AR, Fan PH, Hsu TL, Liu CP, Chiang HT. Real-time 3-dimensional echocardiographic evaluation of left ventricular volume: correlation with magnetic resonance imaging—a validation study. *J Am Soc Echocardiogr* 2001;**14**:1001–1009.
22. Mannaerts HF, Van Der Heide JA, Kamp O, Papavassiliu T, Marcus JT, Beek A, Van Rossum AC, Twisk J, Visser CA. Quantification of left ventricular volumes and ejection fraction using freehand transthoracic three-dimensional echocardiography: comparison with magnetic resonance imaging. *J Am Soc Echocardiogr* 2003;**16**:101–109.
23. Nosir YF, Lequin MH, Kasprzak JD, van Domburg RT, Vletter WB, Yao J, Stoker J, Ten Cate FJ, Roelandt JR. Measurements and day-to-day variabilities of left ventricular volumes and ejection fraction by three-dimensional echocardiography and comparison with magnetic resonance imaging. *Am J Cardiol* 1998;**82**:209–214.
24. Schmidt MA, Ohazama CJ, Agyeman KO, Freidlin RZ, Jones M, Laurienzo JM, Brenneman CL, Arai AE, von Ramm OT, Panza JA. Real-time three-dimensional echocardiography for measurement of left ventricular volumes. *Am J Cardiol* 1999;**84**:1434–1439.

Clinical vignette

doi:10.1093/eurheartj/ehi523

Online publish-ahead-of-print 21 October 2005

Diagnosing acute myocarditis using cardiac MRI

Thomas N. Martin*, Bjoern A. Groenning, and Henry J. Dargie

Western Infirmary Glasgow, Glasgow G11 6NT, UK

* Corresponding author. E-mail address: t.martin@clinmed.gla.ac.uk

A 35-year-old man attended the Emergency Room with his first episode of central chest pain. The pain began 8 h prior to presentation and the 12-lead ECG showed ST-segment elevation of >1 mm in leads II, III, and aVF (Figure, lower panel). He was treated with thrombolysis and transferred to the Coronary Care Unit. Troponin I was 60.9 pg/mL (normal <0.2 pg/mL), and creatinine kinase and MB fraction were 2888 and 235 IU, respectively. No abnormality was demonstrated on transthoracic echocardiography. CMR examination was carried out the following day on a 1.5 T scanner (Siemens Sonata) with a phased-array chest coil, during breath hold and gated to the electrocardiogram. A steady-state free-precession (true FISP) sequence was used to acquire a short-axis cinematographic (CINE) stack of the left ventricle (field of view = 340 mm, slice thickness = 8 mm, interslice gap = 2 mm, TR = 47.4 ms, TE = 1.58 ms, flip-angle = 60°). Delayed contrast-enhanced cardiac magnetic resonance imaging was then performed using the standard turboFLASH inversion-recovery sequence. Briefly, gadolinium-DTPA (-Amersham Health), 0.2 mmol/kg, was administered intravenously and delayed enhancement short-axis images were recorded 10–20 min later [field of view = 340 mm, slice-thickness = 8 mm, interslice gap = 2 mm, TE = 4.3 ms, flip-angle = 30°, optimum inversion time adjusted to null normal myocardium (range 200–300 ms)].

An extensive area of hyper-enhancement that spares the subendocardium and does not match a coronary artery territory is demonstrated (Figure, upper left: four-chamber and upper right: mid-ventricular short axis). There is a preserved left ventricular function with no regional wall motion abnormality on the corresponding CINE images, and the patient has neither cardiovascular risk factors nor previous history of chest pain. Subsequent coronary angiography did not demonstrate a culprit lesion. Therefore, the myocardial damage should not be secondary to coronary artery disease (including emboli or spasm). A right ventricular endomyocardial biopsy was performed and was in keeping with an evolving cardiomyopathy. Correct diagnosis of myocardial infarction is always of clinical importance, and this case illustrates a novel use for CMR in the non-invasive determination of the aetiology of myocardial damage.

Delayed enhancement images on cardiac MRI shown in upper panels and admission 12-lead ECG in the lower panel. Upper left panel: four-chamber and upper right panel: mid-ventricular short-axis views.

