Quantitative Assessment of Left Ventricular Size and Function
Side-by-Side Comparison of Real-Time Three-Dimensional Echocardiography and Computed Tomography With Magnetic Resonance Reference

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Background—Cardiac CT (CCT) and real-time 3D echocardiography (RT3DE) are being used increasingly in clinical cardiology. CCT offers superb spatial and contrast resolution, resulting in excellent endocardial definition. RT3DE has the advantages of low cost, portability, and live 3D imaging without offline reconstruction. We sought to compare both CCT and RT3DE measurements of left ventricular size and function with the standard reference technique, cardiac MR (CMR).

Methods and Results—In 31 patients, RT3DE data sets (Philips 7500) and long-axis CMR (Siemens, 1.5 T) and CCT (Toshiba, 16-slice MDCT) images were obtained on the same day without β-blockers. All images were analyzed to obtain end-systolic and end-diastolic volumes and ejection fractions using the same rotational analysis to eliminate possible analysis-related differences. Intertechnique agreement was tested through linear regression and Bland-Altman analyses. Repeated measurements were performed to determine intraobserver and interobserver variability. Both CCT and RT3DE measurements resulted in high correlation ($r^2 > 0.85$) compared with CMR. However, CCT significantly overestimated end-diastolic and end-systolic volumes (26 and 19 mL; $P<0.05$), resulting in a small but significant bias in ejection fraction (~2.8%). RT3DE underestimated end-diastolic and end-systolic volumes only slightly (5 and 6 mL), with no significant bias in EF (0.3%; $P=0.68$). The limits of agreement with CMR were comparable for the 2 techniques. The variability in the CCT measurements was roughly half of that in either RT3DE or CMR values.

Conclusions—CCT provides highly reproducible measurements of left ventricular volumes, which are significantly larger than CMR values. RT3DE measurements compared more favorably with the CMR reference, albeit with higher variability. (Circulation. 2006;114:654-661.)

Key Words: imaging ■ echocardiography ■ magnetic resonance imaging ■ tomography

The evaluation of left ventricular (LV) function is an indispensable component of routine clinical cardiology practice. For decades, 2D echocardiography has been the main noninvasive imaging modality used to evaluate LV function. However, the relatively low reproducibility and inaccuracy of this methodology have been attributed to the inadvertent use of foreshortened views of the left ventricle and the reliance on geometric modeling. In an attempt to overcome these limitations, alternative techniques based on 3D reconstruction from multiple planes1–4 have been developed and tested. This methodology, albeit time-consuming and prone to artifacts, has shown promise for more accurate assessment of LV function.3,5–8 More recently, real-time 3D echocardiographic (RT3DE) technology, which allows fast acquisition of dynamic pyramidal data sets that encompass the entire left ventricle, has become widely available. Several studies have demonstrated the improved accuracy of RT3DE measurements of LV volume,9–14 despite the continued reliance on endocardial tracing in selected planes and geometric modeling.12,15 To circumvent these limitations, a novel approach based on the detection of dynamic endocardial surface in 3D space was recently developed and tested.16,17 We showed that by fully exploiting the volumetric information contained in RT3DE data sets without the need for either plane selection or geometric modeling, this technique provides accurate objective evaluation of LV function.18 A similar approach was recently implemented in commercial software that is currently available to RT3DE users.19,20
At the same time, MRI technology has gone through technological leaps that brought it to speeds that allow dynamic imaging of the beating heart. Combined with excellent spatial and contrast resolution and the built-in multislice imaging ability, cardiac MR (CMR) has quickly gained popularity and is currently considered the reference technique for LV size and function measurements. Nevertheless, the current standard for CMR assessment of LV function is based on analysis of stacks of short-axis slices of the ventricle. This methodology is increasingly recognized as less than ideal because of (1) the need to select slices to be included in the analysis, which is difficult near the LV base and apex; (2) poor endocardial definition near the apex as a result of partial-volume artifacts, the main source of intermeasurement variability; and (3) the use of spatially fixed slices that disregards LV systolic shortening. Therefore, better reference techniques are needed that would become the future gold standard of LV function. A recent study suggested that analysis of radial long-axis CMR images could potentially minimize these limiting factors and thus provide a better reference.21

CT also has recently undergone major technological developments that currently allow quantification of LV function. The unprecedented quality of cardiac CT (CCT) images, which offer superb endocardial definition optimal for boundary detection, suggests that this modality could potentially constitute a more reproducible reference technique. However, the few studies aimed at validating these measurements against a CMR reference22–26 or other techniques26–28 have not unequivocally established their accuracy. Several studies found that LV volumes were overestimated and ejection fraction (EF) was underestimated by CCT and suggested the intermodality differences in acquisition and analysis strategies as the main source of this discrepancy.22,25,26

Accordingly, to allow intermodality comparisons while eliminating such differences as a potential source of error, we implemented volumetric quantification of LV function in prototype software that allows analysis of radial long-axis CMR and CCT images and RT3DE data sets. The aim of this study was to compare side-by-side indices of LV function derived through analysis of these 3 types of images by using this rotational approach. To achieve this goal, we studied the agreement between CCT- and RT3DE-derived LV function indices against the CMR reference and the reproducibility of these indices for each of the 3 modalities.

Methods

Population

Thirty-one patients (17 men, 14 women; age, 60±15 years) were studied. These patients were selected from 33 consecutive patients referred for clinically indicated CT angiography who were scanned for transthoracic 2D acoustic windows that allowed adequate endocardial visualization. Patients with atrial fibrillation or other cardiac arrhythmias or dyspnea precluding a 10- to 15-second breathhold and patients with implanted pacemakers or defibrillators or with claustrophobia were excluded. Also, patients were excluded if they could not undergo CCT imaging because of renal dysfunction (creatinine >1.3 mg/dL) or known allergy to iodine. Of these 31 patients, 9 had normal hearts, 14 had coronary artery disease, 7 had dilated ventricles, and 1 had apical hypertrophic cardiomyopathy. CMR, CCT, and RT3DE images were performed in each patient on the same day. Heart rate was monitored continuously throughout image acquisition by all 3 modalities. No β-blockers were used to lower the heart rate before CCT imaging. Written informed consent was obtained from all patients.

CMR Imaging

CMR images were obtained with a 1.5-T Sonata scanner (Siemens, Forchheim, Germany) with a phased-array cardiac coil. ECG-gated localizing spin-echo sequences were used to identify the long axis of the left ventricle and to allow imaging in 6 planes rotated around the long axis at 30° steps. Steady-state free precession dynamic gradient-echo mode was then used to acquire dynamic cine loops (20 frames per cardiac cycle) of radial long-axis views of the ventricle (10-mm slice thickness; 1.4- to 1.8-mm in-slice resolution) and stacks of short-axis images from the AV ring to the apex (10-mm slice thickness, no gaps). All images were acquired during 10- to 15-second breathholds and stored digitally for offline analysis of LV function.

CCT Imaging

CCT images were obtained with a Toshiba 16-slice multidetector scanner (Toshiba, Otawara, Japan). Nonionic iodinated contrast agent (Iomeron) was injected into the antecubital vein (140 mL at 3.5 mL/s) and was followed by a 50-mL saline chaser bolus. Image acquisition was triggered by the appearance of contrast in the aortic root and was performed during a single breathhold at end-inspiration preceded by mild hyperventilation. Imaging parameters included 250-ms gantry rotation time with 5 mm per rotation and tube voltage of 120 kV with currents of 300 mA. Scan data were then reconstructed at 0.5-mm slice thickness and 0.5-mm in-slice resolution with retrospective ECG gating and a smooth-tissue filter kernel from early systole (0% of the RR interval) to late diastole (90% of the RR interval) at 10% steps, resulting in 10 phases of the cardiac cycle. For each phase, the reconstructed data were stored digitally. Then, for each phase, 6 planes rotated around the long axis of the left ventricle at 30° steps were selected and used for analysis of LV function.

RT3DE Imaging

RT3DE imaging was performed from the apical window with the patient in the left lateral decubitus position with a SONOS 7500 scanner (Philips, Andover, Mass) equipped with a fully sampled matrix array transducer (X4) in the harmonic mode. To include the entire LV cavity within the pyramidal scan volume, data sets were acquired using the wide-angled mode, wherein 4 wedge-shaped subvolumes (93×21) were acquired during a single breathhold. Acquisition of each subvolume was performed by the ECG R wave of every other heartbeat (total of 8 heartbeats) to allow sufficient time for each subvolume to be stored.31 Six automatically selected long-axis planes rotated around the long axis of the left ventricle at 30° steps were subsequently used to analyze LV function.

Image Analysis

RT3DE data sets were analyzed with 4D-LV Analysis software (TomTec Imaging Systems, Unterschleisheim, Germany). Radial long-axis images obtained from CMR and CCT data were analyzed with prototype software (TomTec) based on the same principle of rotational analysis. In every slice, LV endocardial contours were traced semiautomatically frame by frame, with the papillary muscles and trabeculae included in the LV cavity. These contours were corrected manually when necessary and then used to reconstruct for each phase of the cardiac cycle the endocardial surface in the 3D space. These reconstructed surfaces were used to calculate LV volume over time throughout the cardiac cycle. Each volume curve was analyzed to obtain end-diastolic (EDV) and end-systolic (ESV) volumes that were identified as the maximum and minimum values, and EF was computed as follows: (EDV – ESV)/EDV. Endocardial tracing and volume measurements were performed in a random order by an investigator experienced in the interpretation of cardiac images who was blinded to the results of all prior measurements. In 10 randomly selected patients, image analysis was repeated a month...
later by the same primary reader and by an additional investigator to
determine the reproducibility of LV volume and EF measurements
for each imaging modality. In addition, commercial software was
used to analyze the short-axis CMR images using standard semiau-
tomated endocardial boundary detection and calculation of EDV,
ESV, and EF by the method of disks (Argus, Siemens, Forchheim,
Germany).

Statistical Analysis
All LV volume and EF values were expressed as mean±SD. The
relationship between each technique, CCT and RT3DE, and CMR
was evaluated with linear regression analysis with Pearson's corre-
lation coefficient. The agreement between CCT and RT3DE mea-
surements and CMR reference values was evaluated through the use
of Bland-Altman analysis29 by calculating the bias (mean difference)
and the 95% limits of agreement (2 SD around the mean difference).
The difference between values yielded by each modality and the
CMR reference values was plotted against their mean to avoid
artificial trends.30 The significance of the biases was tested through
the use of paired t tests with a 2-sided alternative. Similarly, CMR
measurements obtained from radial acquisitions were compared with
those derived from short-axis CMR images. Values of P<0.05 were
considered significant.

The reproducibility of the CMR-, CCT-, and RT3DE-derived
measurements of EDV and ESV and EF was evaluated by calculating
the intraobserver and interobserver variability of each technique,
which was defined as the absolute difference between the corre-
sponding repeated measurements expressed in percent of their mean.
Variability values obtained for each index in each patient for each
imaging modality were then averaged over the entire group of
patients and presented as mean±SD.

The authors had full access to the data and take responsibility for
their integrity. All authors have read and agree to the manuscript as
written.

Results
No significant changes were noted in heart rate during image
acquisition by either modality. The time required for image
analysis of each data set (including data retrieval) was ~20 to
40 minutes on a Pentium 4 personal computer. Manual
adjustments were necessary to optimize the position of the
endocardial boundaries in all patients for all 3 imaging
modalities, but the required corrections were more extensive
for RT3DE than for CCT and CMR.

Figure 1 (left) shows an example of radial long-axis images
obtained at end diastole in a patient with normal wall motion from
the 3 imaging modalities: CMR (top), CCT (center), and
RT3DE (bottom), with the corresponding reconstructed LV
endocardial surfaces (middle column) and volume-over-time curves (right column).

Figure 1. Example of radial long-axis images of
the left ventricle obtained at end diastole in a
patient with normal wall motion from CMR images
(top), CCT images (center), and RT3DE images
(bottom), with the corresponding reconstructed LV
endocardial surfaces (middle column) and volume-
over-time curves (right column).
of Bland-Altman analysis for CCT (top) and RT3DE (bottom) measurements of LV volumes and EF versus the CMR reference values. CCT measurements resulted in significantly overestimated values of both EDV and ESV, as reflected by biases of 26 and 19 mL, respectively. EF was slightly but nevertheless significantly underestimated as reflected by a bias of −2.8%. In contrast, RT3DE measurements resulted in slightly underestimated values of both EDV and ESV, as reflected by nonsignificant biases of −5 and −6 mL, respectively, and virtually no bias (0.3%). The 95% limits of agreement with CMR were tighter for CCT than RT3DE for both EDV (42 versus 52 mL) and ESV (50 versus 52 mL) but not for EF (13% versus 8%).

The Table shows the interobserver and intraobserver variability in EDV, ESV, and EF measurements for all 3 imaging modalities. CCT seemed to be the most reproducible technique, as reflected by the interobserver and intraobserver variability values that were lower than those of CMR for all measured indices. RT3DE seemed to be the least reproducible of the 3 techniques as reflected by the highest variability.
values with the exception of intraobserver variability of ESV and consequently EF, which were similar for both the RT3DE and CMR techniques.

Figure 5 shows the results of the comparisons between CMR measurements of LV volumes and EF derived from the radial acquisition versus the traditional short-axis stacks. All 3 variables showed high correlations (r² = 0.95 to 0.98). Bland-Altman analysis resulted in small negative biases in EDV (-4 mL), ESV (-1 mL), and EF (-1.8%). The 95% limits of agreement were 38 mL for EDV, 30 mL for ESV, and 10% for EF.

Interobserver and Intraobserver Variability of LV EDV and ESV and EF Obtained From Repeated Measurements by CMR, CCT, and RT3DE Images

<table>
<thead>
<tr>
<th>Variable</th>
<th>Interobserver Variability, %</th>
<th>Intraobserver Variability, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDV</td>
<td>CCT 2.6±2.0, CMR 6.3±5.7, RT3DE 11.2±8.6</td>
<td>CCT 2.0±1.3, CMR 2.4±2.3, RT3DE 3.9±2.0</td>
</tr>
<tr>
<td>ESV</td>
<td>CCT 5.7±5.2, CMR 7.7±6.6, RT3DE 14.2±11.8</td>
<td>CCT 2.2±3.1, CMR 6.3±4.6, RT3DE 5.6±3.9</td>
</tr>
<tr>
<td>EF</td>
<td>CCT 6.5±4.9, CMR 8.5±9.7, RT3DE 10.5±8.3</td>
<td>CCT 2.1±3.4, CMR 6.2±6.2, RT3DE 5.6±3.4</td>
</tr>
</tbody>
</table>

Data are shown as mean±SD.

Discussion

In routine clinical cardiology practice, critical decision making such as defibrillator implantation, biventricular pacing, treatment of congestive heart failure is based heavily on EF. Accordingly, it is extremely important that this index be measured accurately and reproducibly. For decades, the 2D nature of ultrasound imaging has affected the quantification of LV size and function by errors that stemmed mainly from foreshortened views and inaccurate geometric modeling. The inadequacy of this methodology has been demonstrated by several investigators who compared 2D echocardiographic measures against multislice CMR reference.15,18,20,31 The recent development of live volumetric ultrasound imaging promises to provide a quick, inexpensive, portable, and accurate alternative for LV size and function analysis. In view of the rapidly growing popularity of noninvasive coronary angiography with multidetector “spiral” CT scanners, which are capable of continuous volumetric imaging of the beating heart with unparalleled endocardial definition allowing for highly reproducible quantification of ventricular size and function, this modality has been increasingly referred to as a potential tool for the combined assessment of coronary anatomy, myocardial perfusion, and LV function. It is imperative, however, that the ability of both volumetric imaging techniques to provide accurate indices of LV size and function be tested thoroughly before widespread clinical use. This study is the first to validate side-by-side RT3DE- and CCT-derived indices of LV size and function with reference values obtained from radial long-axis CMR images that offer significant advantages over the conventional short-axis images, including no need to exclude slices that contain LV outflow tract, more uniform endocardial definition from base to apex, and optimal visualization of LV systolic shortening.
within the imaging plane. Furthermore, the use of the same rotational approach to analyze images obtained with all 3 modalities allowed us to minimize possible analysis-related differences as a source of error.

Our results confirmed the linear relationship between both volumetric imaging techniques and the CMR reference, as reflected by the high correlation coefficients obtained for all measured indices (Figure 3). CCT measurements were found to be highly reproducible, as reflected by minimal interobserver and intraobserver variability in all measured indices (see the Table). However, CCT significantly overestimated LV volumes compared with the CMR values, resulting in a small but significant negative bias in the calculated EF (Figure 4). Although several previous studies have demonstrated good agreement between CCT and CMR evaluation of LV function,23–25 others reported findings similar to ours.22,26 Grude and coworkers22 reported positive biases of 10% and 38% in EDV and ESV, respectively, resulting in a negative bias in EF that was 3 times larger than measured in our study (-8.5%). Salm et al.26 found a smaller negative bias in EF (-1.5%) but did not report results for LV volumes. Both groups made positive conclusions with regard to the agreement between the 2 techniques by interpreting the statistically significant small biases in the measured EF as clinically insignificant.26 However, the differences in LV volumes noted in our study are large enough to warrant future studies aimed at obtaining normal LV volume values specifically for CCT.

The relatively low temporal resolution of the reformatted CCT data, which is typically reconstructed at 20 phases of the cardiac cycle, has previously been suggested as a possible explanation for overestimated LV volumes.26 Although such undersampling could theoretically explain overestimated ESV by missing the fast transition from ventricular contraction to filling, it is not likely to result in overestimated EDV because there is very little change in LV volume over a relatively long time in late diastole. To test this hypothesis, in this study, we reconstructed CCT data at even lower temporal resolution (10 phases of the cardiac cycle) and found that both EDV and ESV were overestimated to a similar degree, as reflected by respective biases of 26 and 19 mL. It also is possible that rapid injection of a large volume of iodine contrast solution could have resulted in transient changes in preload and negative inotropic effects. In addition, acute changes in blood pressure in response to the power injection of contrast could not be ruled out because arterial blood pressure was not monitored continuously. Alternative explanations for this finding could be the intermodality differences in the ability to visualize endocardial boundary details and to include or exclude trabeculae from the LV cavity. One might also suggest that β-blockers, which are used routinely with CCT imaging, could result in increased LV volumes and thus could impede direct comparisons between CCT and other imaging modalities that do not use β-blockers. However, to avoid this issue, β-blockers were not used in this study.

As expected, because of the relatively low spatial resolution of ultrasound imaging limiting endocardial visualization, RT3DE-derived LV volume values are subject to wider intermeasurement variability compared with CCT and CMR. Interestingly, however, despite this variability, RT3DE volume estimates were in agreement with the CMR reference, unlike the previous reports of significant biases in RT3DE-based LV indices compared with CMR.13,18 However, in that study, the CMR reference values were obtained from stacks of short-axis slices with their known limitations, thus rendering analysis-related differences impossible to rule out. By
applying the same rotational approach, we eliminated this bias and revealed good agreement with CMR reference values and decreased underestimation of RT3DE-derived volume data.

In addition, one might view the use of the unconventional radial CMR acquisitions as somewhat problematic because most clinical laboratories and published articles routinely calculate LV volumes by applying the method of disks to stacks of short-axis images. Although our choice of reference technique was part of the study design in an attempt to apply uniform analysis techniques to images from 3 modalities and overcome the known limitations of the traditional CMR methodology, we acquired CMR images using both approaches and compared the results in every patient. These comparisons showed close agreement between the 2 CMR techniques, which justified the deviation from the accepted standard.

In addition to the relatively low temporal resolution of the volumetric techniques we tested in this study, the small number of imaging planes could be viewed as an additional limitation, which might have limited the accuracy of endocardial surface reconstruction. However, in a previous study, planes were found to be sufficient to adequately assess global LV function. The known factors that limit the use of RT3DE imaging in daily practice include the relatively low spatial resolution, limited sector size, and large transducer footprint. Further miniaturization, advances in ultrasound technology, and increasing sector size may overcome these limitations. The addition of contrast and triggered RT3DE acquisition also may improve border definition and thus the accuracy of LV volume measurements.

In summary, the results of this study confirmed that analysis of dynamic volumetric data, either CCT or RT3DE, allows meaningful measurements of LV size and function. With the rapid technological developments and the growing availability of fast volumetric imaging and analysis software, these measurements are likely to become part of routine clinical cardiology practice soon.

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Disclosures
None.

References
Cardiac computed tomography (CCT) and real-time 3D echocardiography (RT3DE) are being used increasingly in clinical cardiology. CCT offers superb spatial and contrast resolution, resulting in excellent endocardial definition. RT3DE has the advantages of low cost, portability, and live 3D imaging without offline reconstruction. We sought to compare both CCT and RT3DE measurements of left ventricular size and function to the standard reference technique, cardiac MR (CMR). RT3DE data sets and CCT and CMR images were obtained in 31 patients on the same day without β-blockers. All images were analyzed to obtain end-systolic and end-diastolic volumes. Intertechnique agreement was tested and repeated measurements were performed to determine intraobserver and interobserver variability. Both CCT and RT3DE measurements resulted in high correlation with CMR (r^2>0.85). CCT provided highly reproducible measurements of left ventricular volumes, which were however significantly larger than CMR values. RT3DE measurements compared more favorably with the CMR reference, albeit with 2-fold-wider variability. With the rapid technological developments and the growing availability of fast volumetric imaging and analysis software, CCT and RT3DE measurements of LV size and function are likely to soon become part of routine clinical cardiology practice. These measurements must be interpreted with care in view of the results of this study, which underscored important intermodality differences.
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