Advanced computed tomography for cardiac applications : from cardiovascular diagnosis to clinical management

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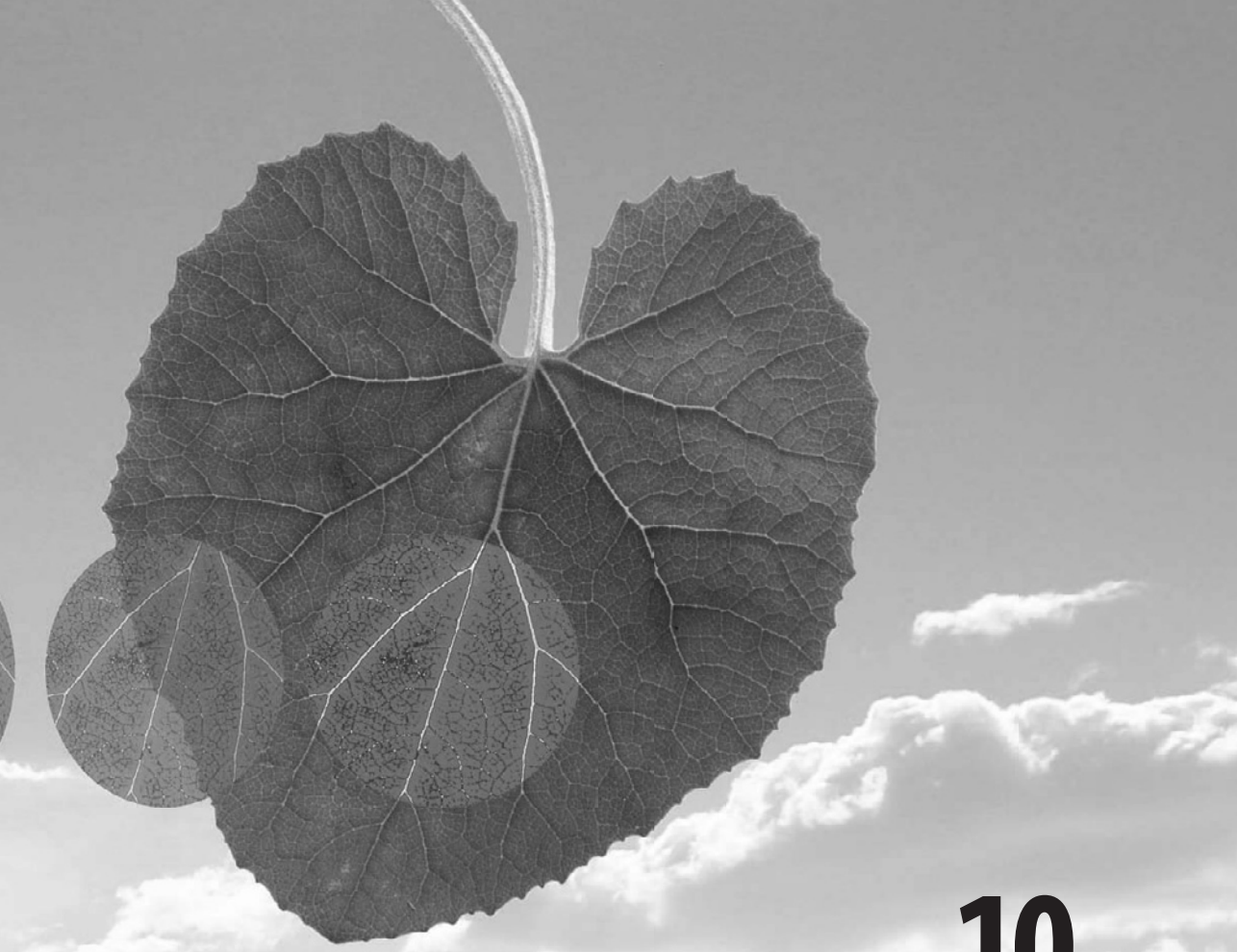

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Assessment of Global Left Ventricular Function and Volumes with 320-row Multi-Detector Computed Tomography: A Comparison with 2D-Echocardiography

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ABSTRACT

Multi-detector computed tomography (MDCT) has been demonstrated as a feasible imaging modality for non-invasive assessment of coronary artery disease and left ventricular (LV) function. Recently, 320-row systems have become available with 16 cm anatomical coverage allowing image acquisition of the entire heart within a single heartbeat. The purpose of the present study was to evaluate the accuracy of 320-row MDCT in the assessment of global left ventricular (LV) function compared to 2-dimensional (2D) echocardiography as the standard of reference. A head-to-head comparison between 320-row MDCT and 2D-echocardiography was performed in 114 patients (68 male; mean age 62 ± 13 years) who were clinically referred for MDCT coronary angiography. The entire heart was imaged in a single heart beat, using prospective dose modulation. LV end-diastolic volumes (LVEDV) and LV end-systolic volumes (LVESV) were determined and the LV ejection fraction (LVEF) was derived. Average LVEF was 60 ± 10% (range 26 - 78%) as determined on MDCT, compared with 59 ± 10% (range 25 - 77%) on 2D-echocardiography. Evaluation of LVEF by linear regression analysis showed a good correlation between MDCT and 2D-echocardiography (r^2 = 0.87; $p < 0.001$). Good correlations between MDCT and 2D-echocardiography were demonstrated for the assessment of LVEDV (r^2 = 0.91; $p < 0.001$) and LVESV (r^2 = 0.94; $p < 0.001$). At Bland-Altman analysis, mean differences (± SD) of 7.3 ± 12.1 ml ($p < 0.05$) and 1.8 ± 7.4 ml ($p < 0.05$) were observed between MDCT and 2D-echocardiography for LVEDV and LVESV, respectively. LVEF was slightly overestimated with MDCT (0.9 ± 3.6%; $p < 0.05$). Accurate assessment of LV function and volumes is feasible with single heart beat 320-row MDCT in patients referred for MDCT coronary angiography.

INTRODUCTION

The assessment of global left ventricular (LV) function and volumes is important in patients with coronary artery disease (CAD) and serves as a valuable diagnostic and prognostic marker.[1 2] There are several noninvasive imaging modalities to analyze cardiac function, which include 2-dimensional (2D)-echocardiography,[3] single photon emission computed tomography (SPECT)[4] and cardiac magnetic resonance imaging (MRI).[5] In recent years, multi-detector computed tomography (MDCT) has emerged as a rapidly advancing imaging modality for the non-invasive assessment of CAD. Since the introduction of MDCT in the early 1990's, acquisition times, spatial and temporal resolution have continuously improved resulting in excellent image quality and diagnostic accuracy in the detection of CAD.[6] Furthermore, various studies have shown that accurate simultaneous assessment of CAD and LV function is feasible.[7-13] Accurate evaluation of cardiac function and volumes with MDCT, in addition to noninvasive assessment of the coronary arteries is likely to optimize the clinical evaluation of patients with CAD.[14]

Previous 4-, 16- and 64-row MDCT systems used a helical scanning technique with retrospective ECG gating. These systems covered entire heart in multiple heart beats, which involved a considerable risk of motion artifacts due to arrhythmias and breathing. With the recent introduction of 320-row MDCT, a cylindrical volumetric data set covering the entire heart is acquired within a single rotation or heart beat. This technology, in combination with prospective ECG gating, markedly reduces scan time and contrast administration, while at the same time reducing motion artifacts. In addition, 320-row MDCT has a reduced gantry rotation time with improved temporal resolution. The accuracy of 320-row MDCT for the evaluation of LV function and volumes has not been reported. The purpose of the present study therefore was to evaluate the accuracy of 320-row MDCT in the assessment of global LV function compared to 2D-echocardiography as the standard of reference.

MATERIALS AND METHODS

Patients and Study Protocol

The study group consisted of 114 patients who were clinically referred for MDCT coronary angiography to evaluate the presence and extent of CAD. All patients were consecutively enrolled and prospectively included in the study. All patients underwent 320-row cardiac MDCT. Exclusion criteria were: 1) (supra)ventricular arrhythmias, 2) renal insufficiency (glomerular filtration rate < 30 ml/min), 3) known allergy to iodine contrast material, 4) severe claustrophobia and 5) pregnancy. The study population

Table 1. Clinical characteristics of the study population

Number of patients	114
Age (yrs)	62 ± 13
Men / women	68 / 46
Body mass index (kg/m^2)	27 ± 4
Family history of coronary artery disease	40 (35%)
Diabetes	28 (25%)
Hypertension	78 (68%)
Hypercholesterolemia	54 (47%)
Current smoker	17 (15%)
Previous myocardial infarction	9 (8%)
Location	
Anterior	2 (2%)
Inferior	7 (6%)
Previous percutaneous coronary intervention	16 (14%)
Previous coronary artery bypass grafting	9 (8%)
Pacemaker or implantable cardioverter defibrillator	6 (5%)

consisted of 68 men and 46 women, with a mean age of 62 ± 13 years. The main clinical characteristics of the study population are listed in Table 1. LV volumes and LV ejection fraction (LVEF) were assessed and compared with 2D-echocardiography. MDCT and 2D-echocardiography were performed within 3 months of each other. In 21 patients, both examinations were performed on the same day. No cardiac events occurred between examinations.

MDCT

Data acquisition

MDCT studies were performed using a 320-row MDCT scanner (Toshiba Multi-row Aquilion ONE system, Toshiba Medical Systems, Otawara, Japan) with 320 detector rows (each 0.5 mm wide) and a rotation time of 350 ms (with a temporal resolution of 175 ms for half reconstruction). Unless contraindicated, beta-blocker was administered orally (50-100 mg metoprolol depending on heart rate) 1 hour before data acquisition to patients with a heart rate exceeding 65 beats per minute (bpm) to reduce cardiac motion artifacts. During the MDCT examination, the average heart rate ± standard deviation (SD) was 57 ± 9 bpm. The entire heart was imaged in a single heart beat, using prospective dose modulation attaining maximal tube current during 65-85% of R-R interval (in patients with a heart rate ≥ 60 bpm), or during 75% of R-R interval (in patients with stable heart rate < 60 bpm). Outside the pre-defined interval, tube current was 25% of the maximal tube current. In addition, at the start of the R-R interval image acquisition was performed

at maximal tube current. Six patients had a heart rate > 65 bpm and in these patients images were acquired during multiple heart beats (typically two). Tube voltage and tube current were adapted to body weight and thoracic anatomy. Tube voltage was 100 kV (n=4), 120 kV (n=109) or 135 kV (n=1). Tube voltage was adapted to 135 kV in patients with a body mass index > 30 kg/m^2. Maximal tube current was 400 mA (n=5), 450 mA (n=7), 480 mA (n=2), 500 mA (n=61), 550 mA (n=3) or 580 mA (n=36). A tri-phasic injection of intra-venous contrast was used and the total amount of non-ionic contrast media (Iomeron 400; Bracco, Milan, Italy) injected into the antecubital vein was 60-70 ml (depending on body weight). First, 50-60 ml of contrast media was administered at a flow rate of 5.0 or 6.0 ml/s, followed by 20 ml of 50% contrast/saline. Subsequently a saline flush of 25 ml was administered at a flow rate of 3.0 ml/s. In order to synchronize the arrival of the contrast media and the scan, bolus arrival was detected using automated peak enhancement detection in the LV. After the preset contrast enhancement threshold of baseline Hounsfield units (HU) + 100 HU was reached, the MDCT examination was automatically initiated. After a 2 second delay, images were acquired during an inspiratory breath hold of approximately 5 seconds. During the scan, the ECG was registered simultaneously for prospective gating of the data. Average estimated radiation exposure (± SD) during a single examination was 11.5 ± 2.1 mSv. Radiation dose was quantified with a dose-length product conversion factor of 0.014 mSv/(mGy×cm) as described.[15] MDCT was performed successfully in all patients without complications. The average investigation time for the MDCT acquisitions was approximately 20 minutes.

Data analysis

To assess LV function and LV volumes, 10 series of 2.0-mm slices were reconstructed in the short-axis orientation at every 10% throughout the cardiac cycle, starting at early systole (0% of cardiac cycle) to end-diastole (90% of cardiac cycle). Subsequently, images were transferred to a remote workstation with dedicated cardiac function analysis software (Vitrea FX 1.0, Vital Images, Minnetonka, MN, USA). To acquire the appropriate phases for LV end-systolic volume (LVESV) and LV end-diastolic volume (LVEDV), the smallest and largest cross-sectional LV cavity areas were selected respectively. Upper limit of the LV was determined at the basal level of the mitral valve and the start of the LV outflow tract. Endocardial borders were manually outlined from the base to the apex on the short-axis cine images by an independent observer. Papillary muscles were excluded from the ventricular cavity. The LVEDV and LVESV volumes were calculated and the LVEF was derived by subtracting the LVESV from the LVEDV and dividing the result by the LVEDV. Time to reconstruct the required image sets and calculate LV volumes and LVEF was approximately 10 minutes. Inter-observer agreement of LV volume and function analyses was analyzed with repeated measurements of a second experienced independent observer in 13 randomly selected patients.

2D-echocardiography

For comparison of LVEF and LV volumes, 2D-echocardiography was performed to serve as the standard of reference. All patients were imaged in left lateral decubital position with a commercially available system (Vivid 7 Dimension, GE Healthcare, Horten, Norway) equipped with a 3.5-MHz transducer. Images were obtained in the standard 4- and 2-chamber apical views and were saved in cine-loop format. Analyses were subsequently performed offline using EchoPAC version 7.0.0 (GE Healthcare, Horten, Norway) by a cardiologist, with 10 years of experience, blinded to MDCT data. LVEDV and LVESV volumes were measured according to the Simpson's biplane method[16] and LVEF was derived.

Statistical Analysis

Continuous data were expressed as mean ± SD and compared using the paired 2-tailed Student's t test. Agreement for the LV volumes and function by MDCT and echocardiography was determined by Pearson's correlation coefficient for linear regression and Bland-Altman analysis. The 95% limits of agreement were defined as the range of values ± 2 SDs from the mean value of the differences. A p value <0.05 was considered statistically significant. To determine inter-observer agreement, intra-class correlation coefficients were used as indicators of reproducibility. Good agreement was defined as intra-class correlation coefficients > 0.80.

RESULTS

LVEDV

Average LVEDV was 146 ± 40 ml (range 78 – 278 ml) on MDCT, as compared with 139 ± 40 ml (range 72 – 269 ml) on 2D-echocardiography. Linear regression analysis showed a good correlation between MDCT and 2D-echocardiography for the assessment of LVEDV ($r^2 = 0.91$; $p < 0.001$) (Figure 1A). At Bland-Altman analysis, mean differences (± SD) of 7.3 ± 12.1 ml ($p < 0.05$) were observed between MDCT and 2D-echocardiography, with 95% limits of agreement ranging from -16.5 to 31.1 (Figure 1B).

LVESV

On MDCT, average LVESV was 61 ± 30 ml (range 17 – 195 ml), as compared with 59 ± 29 ml (range 18 – 183 ml) on 2D-echocardiography. The correlation coefficient between the two modalities for the assessment of LVESV was good ($r^2 = 0.94$; $p < 0.001$) (Figure 2A). Bland-Altman analysis showed a mean value of difference (± SD) of 1.8 ± 7.4 ml ($p < 0.05$) between MDCT and 2D-echocardiography. The 95% limits of agreement ranged from -12.7 to 16.2 (Figure 2B).

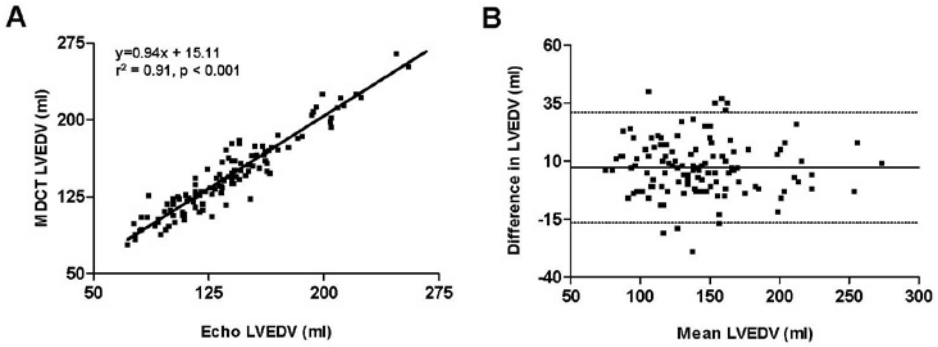

Figure 1. Comparison of MDCT and 2D-echocardiography in the assessment of LVEDV. Linear regression plot shows the correlation between LVEDV as measured by MDCT and 2D-echocardiography (A). Bland-Altman plot of LVEDV shows the difference between each pair plotted against the average value of the same pair (solid line, mean value of difference; dotted line, mean value of differences ± 2 SDs) (B).

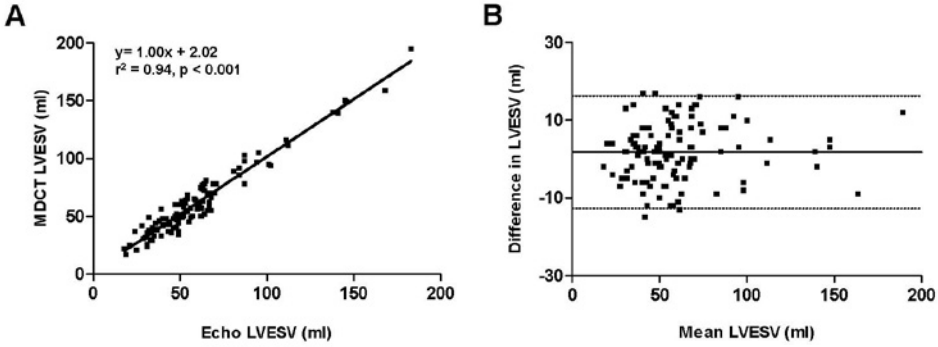

Figure 2. Comparison of MDCT and 2D-echocardiography in the assessment of LVESV. Linear regression plot shows the correlation between LVESV as measured by MDCT and 2D-echocardiography (A). In a Bland-Altman plot of LVESV the difference between each pair plotted against the average value of the same pair is shown (solid line, mean value of difference; dotted line, mean value of differences ± 2 SDs) (B).

LVEF

Average LVEF was 60 ± 10% (range 26 - 78%) as determined on MDCT, compared with 59 ± 10% (range 25% - 77%) on 2D-echocardiography. Evaluation of LVEF by linear regression analysis demonstrated a good correlation between MDCT and 2D-echocardiography (r^2 = 0.87; $p < 0.001$) (Figure 3A). At Bland-Altman analysis LVEF was slightly overestimated with MDCT (0.9 ± 3.6%; $p < 0.05$) (Figure 3B). The inter-observer agreement for LVEDV, LVESV and LVEF, measured by intra-class correlation, were 0.98, 0.97 and 0.92 respectively.

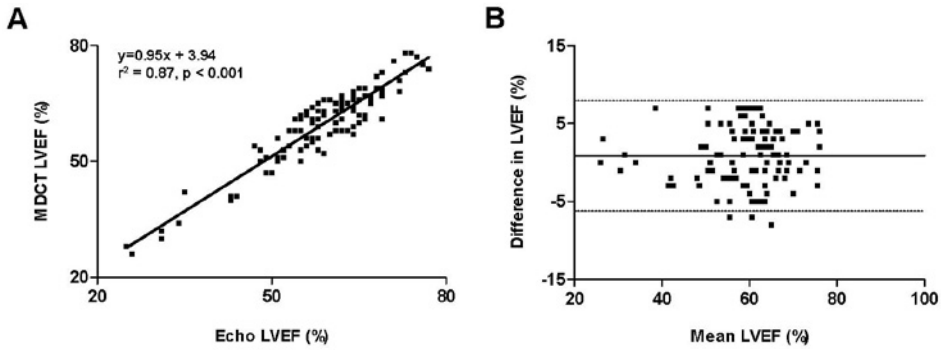

Figure 3. Comparison of MDCT and 2D-echocardiography in the assessment of LVEF. Linear regression plot comparing MDCT and 2D-echocardiography in the assessment of LVEF (A). Bland-Altman plot of LVEF shows the difference between each pair plotted against the average value of the same pair (solid line, mean value of difference; dotted line, mean value of differences ± 2 SDs) (B).

DISCUSSION

In the current study, the accuracy of single heart beat 320-row MDCT in the assessment of global cardiac function was evaluated in patients clinically referred for MDCT coronary angiography. 2D-echocardiography served as the standard of reference. The present study demonstrates that evaluation of LV volumes and global LV function is feasible with single heart beat 320-row MDCT in patients clinically referred for MDCT coronary angiography. Excellent correlations were observed between MDCT and 2D-echocardiography for LVEDV ($r^2 = 0.91$; $p < 0.001$) and LVESV ($r^2 = 0.94$; $p < 0.001$). Minor overestimations for LVESV and LVEDV of 1.8 ml and 7.3 ml respectively were observed on MDCT. Consequently, LVEF measured by MDCT yielded a slight overestimation of 0.9% compared with 2D-echocardiography.

Comparison with previous studies

The results of the present study are in line with results of previous MDCT studies.[7-13] In a prior study conducted by Kim et al[9] a good agreement was demonstrated for LVEF, as determined by 16-row MDCT and 2D-echocardiography ($r = 0.86$; $p < 0.001$). Similar to our study, a slight overestimation of 2.9% using MDCT was shown. More recently, global LV function was investigated by Wu et al[13] using 64-row MDCT and 2D-echocardiography. The investigators showed a good correlation between the two imaging modalities for the assessment of LVEF ($r = 0.87$, $p < 0.001$). However, also with 64-row MDCT, systematic overestimation of LVEF has been reported.[12] Accordingly, the results of the current study using 320-row MDCT technology appear to be in agreement with prior results using 16- and 64-row MDCT. Possibly, assessment with 320-row MDCT may even be more closely

related to 2D-echocardiography as compared to older MDCT generations due to the fact that data are acquired in a single heart beat rather than during multiple heart beats.

Overestimation LV volumes by MDCT

In the present study, a slight overestimation of LV volumes by MDCT was observed as compared with 2D-echocardiography. A factor that might contribute to the overestimation in LV volumes by 320-row MDCT is the use of dose modulation. While this feature has become available as a means to reduce radiation exposure to the patient as compared to full-dose scanning, it is associated with a slight decrease in image quality in images acquired during decreased tube current (Figures 4). However, it is unlikely that this minor decrease in image quality would have affected global LV volume measurements. Second, discrepancies may be explained by differences in the definition of the upper limits of the ventricle, which can be set at different levels depending on the technique used. Currently, there are no clear guidelines on the systematic analysis of MDCT data for the purpose of cardiac function assessment. Finally, the minor overestimation of LV volumes by MDCT as compared to 2D-echocardiography may be explained by the different approach of LV volume calculation between the two techniques. While 2D-echocardiography is most routinely used to measure cardiac function in daily clinical practice, its main limitation remains that measurements are based on a geometric assumption of two-dimensional images. As a result, inaccuracies in volumetric calculations may occur. In contrast, MDCT allows endocardial border definition with high-resolution using true three-dimensional reconstructions. Yamamuro et al recently showed that measurements between MDCT

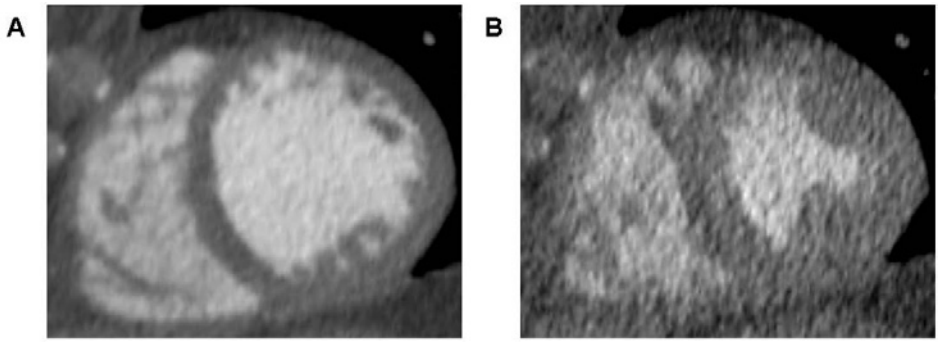

Figure 4. Example of 320-row MDCT image acquisition using dose modulation. Short-axis view of the left ventricle during end-diastolic phase (A) and end-systolic phase (B), acquired with 320-row MDCT using dose modulation. To reduce radiation dose, image acquisition was performed using dose modulation, attaining maximal tube current at 75% of the R-R interval. Of note, at the start of the R-R interval image acquisition was still performed at maximal tube current. Outside the pre-defined interval and the first portion of the R-R interval, tube current was 25% of the maximal tube current. As a result, the end-diastolic phase (typically 0%) still has good image quality whereas an increase in image noise in the end-systolic phase was observed. Additional scan parameters were: 120 kV and 580 mA at maximal tube current.

and MRI, the current gold standard for LV function assessment, were more closely related as compared to measurements between 2D-echocardiography and MRI.[17] MDCT may therefore be a more accurate tool for LV function analysis than 2D-echocardiography and this may explain the small differences in LV volumes between the two techniques.

Study Limitations

Although assessment of cardiac function is feasible with 320-row MDCT, several limitations should be addressed. First, the main limitation of the current study is the lack of a true gold standard such as cardiac MRI. Cardiac MRI has long been regarded as the gold standard in noninvasive analysis of LV function.[18] Importantly, many studies have previously shown excellent correlations between MDCT and MRI in the assessment of LVEF and LV volumes.[17 19 20] Accordingly, in order to further validate the performance of 320-row MDCT for the assessment of LV volumes and function, a direct comparison between 320-row MDCT and MRI is desirable. Second, in patients with a heart rate > 65 bpm additional beta-blocking medication was administered prior to MDCT investigation, but not before 2D-echocardiography. A potential bias may have been introduced by the administration of beta-blockade immediately prior to MDCT examination, [21] as well as the use of contrast agents at the time of MDCT, as these pharmacological interventions may have affected LV volumes and LVEF. Third, a disadvantage of MDCT in general is the radiation exposure to the patient. Previously, information for LV function analysis could be derived retrospectively from the data set acquired for the noninvasive evaluation of the coronary arteries.[12] Recently prospective ECG gating has become possible, allowing data-acquisition for MDCT coronary angiography during only a small proportion of the cardiac cycle. Since assessment of LV function requires data-acquisition during an entire cardiac cycle, in systems employing prospective ECG gating, including 320-row MDCT, functional analysis extends total exposure time. Consequently, the assessment of LV function by MDCT increases the radiation dose when compared to MDCT analysis for the purpose of coronary angiography alone. The necessity for LV function analysis should therefore be carefully considered for each individual patient. Importantly, lower mean radiation doses may be achieved with more optimal heart rate reduction, e.g. by using intra-venous beta-blockade, which allows scanning at 75% of R-R interval in a larger proportion of patients. Furthermore, although the current population was scanned at 16 cm cranio-caudal scan-range, 320-row MDCT allows scanning of smaller ranges, which also decreases radiation exposure. In addition, only few patients with an LVEF lower than 50% were included. As a result, the study is limited by the inclusion of a relatively homogeneous population with predominantly normal LV function. Further research is warranted to determine the accuracy of this technique in patients with low LVEF. Additionally, the time difference between 2D-echocardiography and MDCT may limit accurate comparison. Last, as almost all patients were scanned during a single

heart beat, the current results predominantly reflect the evaluation of LV function using half-scan reconstructions.

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