Assessment of left ventricular parameters in orthotopic heart transplant recipients using dual-source CT and contrast-enhanced echocardiography: comparison with MRI

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Purpose

To establish the accuracy and reliability of cardiac dual-source CT (DSCT) and two-dimensional contrast-enhanced echocardiography (CE-Echo) in estimating left ventricular (LV) parameters with respect to cardiac magnetic resonance imaging (CMR) as the reference standard.
Methods and Materials

For the purpose of the study 25 consecutive orthotopic heart transplant recipients who underwent coronary DSCT angiography, CE-Echo and CMR to exclude cardiac allograft vasculopathy were prospectively recruited. All individuals were in stable clinical condition and in sinus rhythm at the time of examinations, which were conducted in a time interval of < 1 day. Exclusion criteria included previous allergic reaction to iodinated contrast media, pregnancy, chronic renal failure (serum creatinine <1.4 mg/dl), and arrhythmia. Subjects with classical contraindications for CMR, such as claustrophobia, pacemaker or automated implantable cardioverter-defibrillator (AICD) implantation or MR unsafe objects were also excluded. No patient was given beta-blockers prior to DSCT examination. The study was approved by the ethics committee of our center. Written informed consent was obtained from all participants.

Cardiac CT acquisition and reconstruction protocol

Retrospectively ECG-gated coronary CT angiograms were carried out using a DSCT system (Somaton Definition, Siemens Healthcare, Forchheim, Germany) with the patient in supine position, at end-inspiration, and in cranio-caudal direction. Data were acquired with tube voltage of 120 kV. Tube current-time product was applied depending on patient-specific parameters (Caredose 4D) with reference tube current-time product set at 350-410 mAs per rotation. Detector collimation was 2x32x0.6 mm, slice acquisition 64 x 0.6 mm by means of a z-flying focal spot, gantry rotation time 330 ms, and temporal resolution 83 ms. The pitch was variable depending on the heart rate (0.2-0.45). Automated tube current modulation (ECG pulsing) was used with full tube current administration between 30 and 80% of the cardiac cycle. The studies were acquired after injecting 70 ml of iodinated contrast (Iomeron 400, Iomeprol, Bracco s.p.a, Milan, Italy) followed by a bolus of 50 ml of saline through an antecubital vein at a constant flow rate of 5 ml/s with a dual-syringe injector (CT Stellant, Medrad Inc. Indianola, USA). The bolus tracking technique with the region of interest placed in the ascending aorta and a trigger threshold of 100 Hounsfield units (HU) was employed for timing. The average acquisition time of the studies was 8 s. From the DSCT raw data, 8-millimetre section thickness double oblique short-axis images were retrospectively reconstructed in 5% steps (20 phases) throughout the entire cardiac cycle (0-95% of the R-R interval), with a medium smooth convolution kernel (B26f), and 512 x 512 pixel image matrix. No manual ECG-editing was performed.

Contrast-enhanced transthoracic echocardiography protocol
Contrast-enhanced echocardiographic studies (iE33 ultrasound system and S5 transducer (Philips Healthcare, Andover, MA, USA,) were performed with the patient in left lateral decubitus position. In baseline, two- and four- chamber apical views and standard parasternal long- and short-axis views were obtained. Lower power continuous imaging was used after contrast administration. The contrast medium (SonoVue, Bracco, Milan, Italy) was administered intravenously by a trained nurse at 1ml/min infusion rate for LV opacification. Cine-loops of three cardiac cycles per view were digitally stored in raw-data format.

**Cardiac MRI acquisition protocol**

CMR studies were performed on a 1.5 Tesla system (MAGNETOM Symphony TIM, version syngo MR 2002B, Siemens Healthcare, Erlangen, Germany) equipped with Quantum gradients (maximum gradient amplitude of 52 mT/m). A four-element phased array surface coil and retrospective ECG synchronization was employed. Contiguous 8-12 steady-state free precession (SSFP) short axis orientation cine images were acquired including the base and left ventricular apex with the following parameters: TR: 2.89 ms, TE: 1.3 ms, flip angle 80°, field of view: 260-280 x 325-375 mm, matrix 156 x 192, slice thickness 8 mm, no interslice gap, in-plane resolution 1.7 x 1.7 mm, 15 segments, 25 phases per cardiac cycle, temporal resolution 25-50 ms. The acquisition time per slice was variable (7-10 s).

**DSCT, echocardiography and CMR image analysis**

Two observers analyzed independently DSCT, CE-Echo and CMR images blindly and at random order, unaware of the results of the other imaging modalities. For DSCT and CMR exams, readers defined the basal slice of the left ventricle as the slice in which at least half of the circumference of the ventricular cavity was surrounded by myocardium in all phases of the cardiac cycle, and the apical slice as the last slice with visible ventricular cavity. Observers visually arranged the images for end-diastole and end-systole as those presenting the largest and the smallest luminal cavity areas at mid-ventricular level, respectively, and manually drew left ventricular endocardial and epicardial contours using commercially available software (Argus, Siemens Healthcare). Trabeculations and papillary muscles were included in the volumetric analysis. Left ventricular ejection fraction (EF), end-diastolic volume (EDV), end-systolic volume (ESV), and stroke volume (SV) were calculated using Simpson's rule. For CE-Echo images were analyzed by an experienced cardiologist using the modified biplane Simpson's rule after manual tracing of the inner contour of the left ventricular cavity (Philips Q lab 8.1, Andover, MA, USA). End-diastole was defined as the frame closest to the R-wave, whereas end-systole was assigned as the minimal cavity area just before mitral valve opening. Papillary muscles and trabeculations were left within the ventricular cavity (13). The EDV and ESV were averaged from three cardiac cycles **Fig. 1 on page 6.**
Statistical analysis

Data are presented as mean ± standard deviation. Normal data distribution was determined with the Kolmogorov-Smirnov test. Differences in left ventricular volumes and ejection fraction obtained with DSCT, CE-Echo and CMR were compared with Student t test for paired samples. The Pearson correlation coefficient (r) was determined for linear correlation analysis. Bland and Altman plots (14) and Lin’s concordance-correlation coefficients (CCC) (15) were calculated to establish the degree of concordance and agreement between the results of imaging modalities for each pair of left ventricular values. Interobserver agreement for each technique was determined with CCC. Statistical analysis was performed with SPSS for Windows (version 15.0/SPSS Inc., Chicago, IL) and MedCalc (version 9.3.0.0. MedCalc Software, Mariakerke, Belgium). A p-value #0.05 was considered for statistical significance.

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Results

All 25 orthotopic heart transplant recipients underwent coronary DSCT angiography, CE-Echo, and CMR without complications. No patient had to be excluded from the analysis. The mean age of individuals (20 male and 5 female) included in the study was 62.7±10.4 years (range 37-78 years). Their mean body mass index (BMI) was 26.5±3.6 kg/m² (range 21.8-37 kg/m²). Mean time from heart transplantation to cardiac imaging examinations was 8.1±5.9 years (range 2-19.3 years). The average heart rate during DSCT (89.2±14.2 beats per minute [bpm], range 70-114 bpm), CMR (88.9±13.2 bpm, range 71-113 bpm), and CE-Echo (89.3±13.9 beats per minute [bpm], range 70-116 bpm) was similar (p=0.90). Patient characteristics are summarized in Fig. 2 on page 9. There was no clinical evidence of allograft rejection at the time of cardiac DSCT, CE-Echo and CMR examinations. The average radiation dose delivered to patients in DSCT studies was 13.7 ± 2.8 mSv (dose length product, DLP: 808.1±165.7 mGy-cm).

Quantification of left ventricular parameters

There was not statistical difference between left ventricular parameters determined by DSCT and CMR. The mean EF (63.5±10.8%), EDV (102.7±23 ml), ESV (37.9±19 ml), and SV (64.7±15.9 ml) estimated from DSCT examinations was similar to the mean EF (65.1±10.7%), EDV (103.8±25.5 ml), ESV (36.7±18.5 ml), and SV (67.1±18.8 ml) assessed on CMR examinations (p>0.05). Good correlation was found between DSCT and CMR for left ventricular measurements (r #0.77). Data are summarized in table 2. Left ventricular measurements statistically differed when CE-Echo was compared with the cross-sectional imaging modalities. CE-Echo showed lower mean EDV (86.7±24.2 ml), ESV (29.4±18.7 ml), SV (57.5±14.1 ml) and higher mean EF (67.3±10.4%) than DSCT and CMR (p<0.05). Pearson correlation coefficient was r #0.61 for left ventricular measurements quantified with DSCT and echocardiography and r #0.60 for data derived from CMR and echocardiography. Comparative results with respect to DSCT and CMR are shown in tables 3 and 4, respectively.

Agreement between imaging modalities

The Bland-Altman analysis (Fig. 3 on page 10, Fig. 4 on page 20, Fig. 5 on page 19, Fig. 6 on page 18) showed minimal underestimation of left ventricular EF (mean difference of 1.64±4 %), EDV (mean difference of 1.21±7.74 ml) and SV (mean difference of 2.38±12.07 ml), and slight overestimation of ESV (mean difference of 1.21±7.74 ml) by DSCT compared to CMR. Concordance correlation coefficients for left ventricular parameters quantified using DSCT and CMR were 0.92 (0.83-0.96) for
EF, 0.86 (0.71-0.93) for EDV, 0.97 (0.93-0.99) for ESV, and 0.75 (0.53-0.88) for SV (Fig. 7 on page 9).

Overall, CE-Echo resulted in significant underestimation of left ventricular volumes and overestimation of ejection fraction compared with the cross-sectional imaging modalities. Comparison of CE-Echo with respect to CMR demonstrated mean differences of 2.14±8.35% for EF, 17.1±17.06 ml for EDV, 7.32±9.14 ml for ESV, and 9.62±15.36 ml for SV (Fig. 8 on page 17, Fig. 9 on page 16, Fig. 10 on page 15, Fig. 11 on page 14). The correlation coefficients for left ventricular values were 0.67 (0.39-0.84), 0.61 (0.37-0.78), 0.81 (0.64-0.91), and 0.49 (0.19-0.70) for EF, EDV, ESV, and SV, respectively (Fig. 12 on page ). As showed by the Bland-Altman analysis, mean differences were 3.78±8.47% for EF, 15.94±14.19 ml for EDV, 8.5±9.3 ml for ESV, and 7.24±13.41 ml for SV when CE-Echo and DSCT were compared (Fig. 13 on page 13, Fig. 14 on page 12, Fig. 15 on page 11, Fig. 16 on page 21). Concordance correlation coefficients for left ventricular parameters quantified using these two imaging modalities were 0.64 (0.36-0.81), 0.66 (0.45-0.81), 0.81 (0.64-0.90), and 0.54 (0.24-0.75) for EF, EDV, ESV, and SV, respectively (Fig. 17 on page ).

Interobserver agreement

The interobserver agreement for the quantification of left ventricular parameters with DSCT was 0.72 (0.46-0.86) for EF, 0.94 (0.87-0.97) for EDV, 0.95 (0.90-0.98) for ESV, and 0.83 (0.67-0.92) for SV. The interobserver agreement for the quantification of left ventricular parameters using CE-Echo was 0.64 (0.40-0.80) for EF, 0.41 (0.13-0.63) for EDV, 0.58 (0.31-0.77) for ESV, and 0.46 (0.17-0.67) for SV. The interobserver agreement was 0.88 (0.70-0.95) for EF, 0.88 (0.71-0.95) for EDV, 0.89 (0.73-0.96) for ESV, and 0.87 (0.68-0.95) for left ventricular SV determined by CMR.
Table 1. Patient characteristics.

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
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<tbody>
<tr>
<td>Number of patients</td>
<td>25</td>
</tr>
<tr>
<td>Male/Female</td>
<td>20 / 5</td>
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<tr>
<td>Age (years)</td>
<td>62.7±10.4</td>
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<tr>
<td>Body mass index (kg/m²)</td>
<td>26.5±3.6</td>
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<tr>
<td>Body surface area (m²)</td>
<td>1.8±0.1</td>
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<tr>
<td>Surgical technique (standard/bicaval)</td>
<td>10 / 15</td>
</tr>
<tr>
<td>Time from transplantation (years)</td>
<td>8.1±5.9</td>
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Fig. 2: Table 1. Patient characteristics.

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Table 2. Comparison of left ventricular volumes and function as determined by DSCT and MRI.

<table>
<thead>
<tr>
<th></th>
<th>DSCT</th>
<th>MRI</th>
<th>P value</th>
<th>r value</th>
<th>Bland - Altman</th>
<th>CCC</th>
<th>Bias correction factor (accuracy)</th>
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</thead>
<tbody>
<tr>
<td>EF (%)</td>
<td>63.5±10.8</td>
<td>65.1±10.7</td>
<td>0.051</td>
<td>0.93*</td>
<td>1.64±4</td>
<td>0.92 (0.83-0.96)</td>
<td>0.99</td>
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<tr>
<td>EDV (ml)</td>
<td>102.7±23</td>
<td>103.8±25.5</td>
<td>0.656</td>
<td>0.86*</td>
<td>1.16±26.39</td>
<td>0.86 (0.71-0.93)</td>
<td>0.99</td>
</tr>
<tr>
<td>ESV (ml)</td>
<td>37.9±19</td>
<td>36.7±18.5</td>
<td>0.196</td>
<td>0.97*</td>
<td>1.21±7.74</td>
<td>0.97 (0.93-0.99)</td>
<td>0.99</td>
</tr>
<tr>
<td>SV (ml)</td>
<td>64.7±15.9</td>
<td>67.1±18.8</td>
<td>0.334</td>
<td>0.77*</td>
<td>2.38±12.07</td>
<td>0.75 (0.53-0.88)</td>
<td>0.98</td>
</tr>
</tbody>
</table>

Note. Data are presented as mean ± SD. EF: ejection fraction; EDV: end-diastolic volume; ESV: end-systolic volume; SV: stroke volume. CCC: concordance correlation coefficient.

* p < 0.001.

Fig. 7: Table 2. Comparison of left ventricular volumes and function as determined by DSCT and MRI.

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**Fig. 3:** Bland-Altman plots representing the agreement between left ventricular ejection fraction (EF) (A), end-diastolic volume (EDV) (B), end-systolic volume (ESV) (C), and stroke volume (SV) (D) estimated with DSCT and CMR.

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Fig. 15: Bland-Altman plots representing the agreement between left ventricular ejection fraction (EF) (A), end-diastolic volume (EDV) (B), end-systolic volume (ESV) (C), and stroke volume (SV) (D) estimated with CE-Echo and DSCT.

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Fig. 14: Bland-Altman plots representing the agreement between left ventricular ejection fraction (EF) (A), end-diastolic volume (EDV) (B), end-systolic volume (ESV) (C), and stroke volume (SV) (D) estimated with CE-Echo and DSCT.

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Fig. 13: Bland-Altman plots representing the agreement between left ventricular ejection fraction (EF) (A), end-diastolic volume (EDV) (B), end-systolic volume (ESV) (C), and stroke volume (SV) (D) estimated with CE-Echo and DSCT.
Fig. 11: Bland-Altman plots representing the agreement between left ventricular ejection fraction (EF) (A), end-diastolic volume (EDV) (B), end-systolic volume (ESV) (C), and stroke volume (SV) (D) estimated with CE-Echo and CMR.

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Fig. 10: Bland-Altman plots representing the agreement between left ventricular ejection fraction (EF) (A), end-diastolic volume (EDV) (B), end-systolic volume (ESV) (C), and stroke volume (SV) (D) estimated with CE-Echo and CMR.

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**Fig. 9:** Bland-Altman plots representing the agreement between left ventricular ejection fraction (EF) (A), end-diastolic volume (EDV) (B), end-systolic volume (ESV) (C), and stroke volume (SV) (D) estimated with CE-Echo and CMR.

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Fig. 8: Bland-Altman plots representing the agreement between left ventricular ejection fraction (EF) (A), end-diastolic volume (EDV) (B), end-systolic volume (ESV) (C), and stroke volume (SV) (D) estimated with CE-Echo and CMR.

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Fig. 6: Bland-Altman plots representing the agreement between left ventricular ejection fraction (EF) (A), end-diastolic volume (EDV) (B), end-systolic volume (ESV) (C), and stroke volume (SV) (D) estimated with DSCT and CMR.

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Fig. 5: Bland-Altman plots representing the agreement between left ventricular ejection fraction (EF) (A), end-diastolic volume (EDV) (B), end-systolic volume (ESV) (C), and stroke volume (SV) (D) estimated with DSCT and CMR.

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Fig. 4: Bland-Altman plots representing the agreement between left ventricular ejection fraction (EF) (A), end-diastolic volume (EDV) (B), end-systolic volume (ESV) (C), and stroke volume (SV) (D) estimated with DSCT and CMR.

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Fig. 16: Bland-Altman plots representing the agreement between left ventricular ejection fraction (EF) (A), end-diastolic volume (EDV) (B), end-systolic volume (ESV) (C), and stroke volume (SV) (D) estimated with CE-Echo and DSCT.

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Conclusion

In orthotopic heart transplant recipients DSCT enables accurate estimation of left ventricular parameters compared with CMR, whereas two-dimensional CE-Echo seems to be insufficient to obtain precise measurements. Cardiac DSCT may allow comprehensive assessment of the heart in transplant recipients undergoing coronary DSCT imaging by allowing to rule out cardiac allograft vasculopathy and quantify left ventricular functional parameters without additional contrast administration or radiation exposure.
References

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