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Extracellular volume quantitation using dual-energy CT in patients with heart failure: Comparison with 3T cardiac MR

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ABSTRACT

Backgrounds: Cardiac magnetic resonance (CMR) T1 mapping and the extracellular volume (ECV) have been developed to quantitative analysis of diffusely abnormal myocardial fibrosis (MF). However, dual-energy CT (DECT) has a potential for calculation of ECV. The aim of this study is to evaluate the feasibility and accuracy of DECT technique in determining the ECV in patients with heart failure, with 3T CMR as the reference.
Methods: Thirty-five patients with various reasons of heart failure were enrolled in this study. Both DECT and CMR exams were completed within 24 h. ECVs were calculated, and the relationship between DECT-ECV, CMR-ECV, and other heart function parameters, including left ventricular end systolic and diastolic volume, cardiac output and ejection fraction (LVESV, LVEDV, CO, LVEF), Brain natriuretic peptide (BNP) was determined. All participants gave informed consent, and the study was approved by the institutional review board.
Results: The median ECVs on DECT and CMR were 33% (95%CI: 32%–36%) and 30% (95%CI: 30% - 32%), respectively. A good correlation between myocardial ECV at DECT and that at CMR ($r = 0.945$, $P < 0.001$) was observed. Bland-Altman analysis between DECT and CMR showed a small bias (2.6%), with 95% limits of agreement of −0.4% and 5.6%. Interobserver agreement for ECV at DECT was excellent (ICC = 0.907). Both ECVs, for DECT and CMR, were inversely associated with LVEF and CO.
Conclusion: DECT-based ECV could be an alternative non-invasive imaging tool for myocardial tissue characterization. However, overestimation of the extent of diffuse MF is observed with use of DECT.

1. Introduction

Myocardial fibrosis (MF) occurs in a wide variety of heart conditions including heart failure with reduced or preserved ejection fraction (EF), diabetic and hypertensive heart disease, and non-ischemia cardiomyopathies. MF may represent a principal phenotype of cardiac vulnerability that improves risk stratification. Moreover, MF quantification is associated with cardiac outcomes [1,2]. Endomyocardial biopsy is widely recognized as the "gold standard" for diagnosis of MF. However, its application is limited in the routine clinical practice given its intrinsic issues, such as invasive and serious complications. Recently, T1 mapping using cardiac magnetic resonance (CMR) imaging has been established as a reliable technique to quantify diffuse MF [2,3]. CMR-derived extracellular volume fraction (ECV) calculated from native and contrast T1 maps, enables assessment of the extent of diffuse myocardial fibrosis [2]. CMR-derived ECV using T1 mapping has been validated in animal and human studies [4–6], including in patients with heart failure secondary to non-ischemic and ischemic cardiomyopathies, valve disease, cardiac amyloidosis and hypertrophic cardiomyopathy. However, CMR exam is not widely available and has some known contraindications. A recent published study showed that 5775 (16.7%) out of 34,587 patients had failed MR exams because of unanticipated issue [7]. Moreover, the calculated ECV value is influenced by MR field strength, which is well documented that ECV value calculated from 3 T MR are substantially different from that of 1.5 T MR [8].

Cardiac computed tomography (CCT) has been widely used in the clinical work-up of cardiac patients and can accurately measure myocardial perfusion [9,10] and focal myocardial scarring [11]. In recent human studies [12,13], CCT-derived ECV has demonstrated the ability to detect diffuse MF, with higher inter- and intra-observer reproducibility

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[14]. Although CCT has higher temporal and spatial resolution than CMR, it is less sensitive than CMR in terms of contrast resolution. Advanced dual source dual-energy CT (DECT) offers the possibility of tissue characterization using 2 different kV levels. DECT has been shown the potential for measuring ECV in both animal and humans studies [15,16]. However, it is unclear that whether DECT could measure diffuse MF in heart failure patients. Therefore, the aim of this study is to evaluate the feasibility and accuracy of DECT derived -ECV for the assessment of diffuse MF in heart failure patients, compared with 3T CMR derived ECV, which is regarded as the reference method.

2. Methods

2.1. Study population

This was a single-center study approved by the local institutional review board. All participants gave written informed consent and completed both the DECT and CMR examinations within 24-h. From December 2016 to October 2017, 35 patients with clinically diagnosed HF were prospectively enrolled in this study. The included heart failure patients were those with New York Heart Association (NYHA) grade II or higher, in addition to left ventricular ejection fraction (LVEF) <35% or HF with persistent LVEF >50%. Hematocrit and blood BNP measurements were performed within a 24-h interval of the DECT and CMR exams. Exclusive criteria included: allergy to iodine; renal failure (glomerular filtration rate, GFR < 60 ml/min); pregnancy; patients with stent or CABG (coronary artery bypass graft).

2.2. DECT scan protocol and DECT-ECV analysis

All patients were examined with a second generation dual-source CT (Somatom Definition Flash, Siemens Healthcare, Forchheim, Germany). The CCT exam protocol included a prospective ECG-gated calcium score acquisition, a prospective ECG-gated coronary CT angiography (CCTA), and a delay DECT scan. The DECT scan was run after a 7-min delay. For the prospective ECG-gated CCTA, the tube potential was selected based on the patient's body mass index (BMI) and the tube current was modulated by automatic exposure control. The setting for patients with a BMI < 24 kg/m^2 were 100 kV, and the setting for patients with a BMI ≥ 24 kg/m^2 were 120 kV. Bolus-tracking was performed with a region of interest (ROI) placed in the root of the aorta, and image acquisition was automatically started 6 s after a predefined threshold of 100 HU was reached. The scanning range was set from the tracheal bifurcation to the diaphragm. Delayed post-contrast DECT was obtained with the following scan parameters: 185 effective mA at 100 kV, and 157 effective mA at 140 kV with a Sn filter, 64 × 0.6 mm collimation, 0.32 pitch factor, and 0.28 s rotation time. The effective radiation dose of CT was calculated by multiplying the dose-length product by a conversion factor of 0.014 [17].

The contrast agent was injected with a dual-head power injector (Stellant D, Medrad, Indianola, PA, USA) through an 18 G intravenous needle placed in the right antecubital vein. Depending on the scan time, 60–90 ml of contrast agent (Ultravist, 370 mg iodine/ml, Bayer, Wayne, NJ, USA) was injected, followed by 30 ml of saline as a bolus chaser. The injection rate was 4.5–5 ml/s for all phases.

2.3. Dual-energy CT data post processing

DECT post-processing was performed on a commercially available workstation (Syngo MMWP; Siemens Medical Solutions, Forchheim, Germany) using dedicated "Heart PBV (perfused blood volume)" software. First, DECT data was loaded into the Heart PBV. The software constructs iodine maps based on the material decomposition method, showing the distribution of iodine in the entire left ventricle myocardium. All iodine maps were reconstructed in short axis view from base to apex of heart with 8 mm slice thickness without any gap.

2.4. Dual-energy CT ECV measurement

Two observers selected iodine map images that matched the CMR T1 mapping images and measured independently. Overlay attenuation values of the myocardium and blood pool were obtained from the iodine maps. Depending on the 16-segment of LV myocardium (excluding 17th apex segment), ROIs were drawn manually in each segment in a conservative manner to avoid the periphery of the myocardium. At the same slice, a manual ROI with a minimum size of 100 mm^2 was drawn in the LV blood pool and papillary muscles were avoided (Fig. 1). The DECT-ECV was calculated as follows: $ECV_{DECT} = (HU_m/HU_b) * (1\text{-hematocrit level}) * 100\%$, where HU_m is the attenuation value (Overlay value) of the myocardium (in Hounsfield units) and HU_b is the attenuation value (Overlay value) of blood (in Hounsfield units) [15,16].

2.5. Cardiac MR protocol and CMR-ECV analysis

All CMR exams were performed on a 3T MR scanner (Verio; Siemens, Erlangen, Germany) with a 32-channel cardiovascular array coil (Vivo, Orlando, Fla). An 11-heart-beat modified Look Locker sequence with inversion recovery (MOLLI) was used for cardiac MR imaging T1 measurement, as described previously [2,3]. Scanning parameters were as follows: repetition time msec/echo time msec/minimum inversion time msec, 1.9/1.0/110.0; inversion time increment, 80.0 msec; field of view, 290–360 mm2; pixel size, 1.7 × 1.4 mm2; readout resolution, 192; phase resolution, 75%–85%; section thickness, 8 mm; 35° flip angle; and generalized auto calibrating partially parallel acquisition factor, 2. Short-axis images were acquired at the basal, mid-ventricle, and apical level of the LV.

Images for T1 measurements were obtained pre- and post- intravenous infusion of GA-DTPA (0.2 mmol/Kg, Magnevist; Bayer Healthcare Pharmaceuticals, Wayne, NJ) injected as a bolus at a rate of 0.15–0.2 ml/s/kg and followed by a 20-ml saline flush. Post-contrast examinations were performed at the same positions as pre-contrast examinations 15–20 min after the injection of contrast agent. Steady state free precession cine MR short-axis images were acquired for assessment of left ventricular function parameters (LVESV, LVEDV, and LVEF). Late gadolinium enhanced (LGE) MR imaging was performed 10 min after injection to detect local MF.

All CMR images were transferred to a dedicated workstation for image analysis (Siemens). The ROIs were placed comparable with the DECT images on both pre-contrast and post-contrast T1-mapping images at each segment of LV. The T1 LV blood pool value was measured a circular ROI (100 mm2), excluding the papillary muscles (Fig. 1). The ECV fraction was calculated as follows: $ECV_{CMR} = \Delta T1M/\Delta T1B * (1\text{-HcT}) * 100\%$ [2,3], ΔT1M = T1 post-contrast Myocardium-T1-pre-contrast Myocardium, ΔT1B = T1 post-contrast Blood-T1-pre-contrast Blood.

2.6. Statistical analysis

All statistical analyses were performed using statistical software (Medcalc 15.8). Continuous variables are described as median (95% CI for median) because of no normal distribution. Comparison of ECV between CMR and DECT was assessed using the Wilcoxon test. The correlation and the agreements between DECT-ECV and CMR-ECV were described with the Pearson test and the Bland-Altman plots, respectively. The correlation between DECT-ECV and left ventricular function parameters using CMR and BNP was assessed using linear correlation. Interobserver agreement was tested by calculating the intraclass correlation coefficient (ICC). $P < 0.05$ is recognized as statistical difference.

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