Assessment of left ventricular ejection fraction using low radiation dose computed tomography

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Background. **Cardiac CT is a non-invasive modality with the ability to estimate LVEF. However, given its limited temporal resolution and radiation, there has been initial resistance to use CT to measure LVEF. Developing an accurate, fast, low radiation dose protocol is desirable.**

Objective. **The objective of this study is to demonstrate that a 'low radiation dose' 64 slice cardiac computed tomography (CT) protocol is feasible and can accurately measure left ventricular ejection fraction (LVEF) while delivering a radiation dose lower than radionuclide angiography (RNA).**

Methods. **Patients undergoing RNA were prospectively screened and enrolled to undergo a 'low-dose' 64 slice CT LVEF protocol. LVEF measures, duration of each study and radiation dose between CT and RNA were compared.**

Results. **A total of 77 patients (mean age = 61.8 ± 12.2 years and 58 men) were analyzed. The mean LVEF measured by CT and RNA were 41.9 ± 15.2% and 39.4 ± 13.9%, respectively, ($P = 0.154$) with a good correlation ($r = 0.863$). Bland-Altman plot revealed a good agreement between the CT and RNA LVEF (mean difference of −2.4). There was good agreement between CT LVEF and RNA for identifying patients with LVEF ≤30% (kappa = 0.693) and LVEF ≥50% (kappa = 0.749). The mean dose estimated effective dose for CT and RNA were 4.7 ± 1.6 and 9.5 ± 1.0 mSv, respectively. The mean CT LVEF imaging duration (4:32 ± 3:05 minutes) was significantly shorter than the RNA image acquisition time (9:05 ± 2:36 minutes; $p < 0.001$).**

Conclusion. **The results of our study suggest that low-dose CT LVEF protocol is feasible, accurate, and fast while delivering a lower radiation dose than traditional RNA. (J Nucl Cardiol 2016;23:414–21.)**

Key Words: Computed tomography • ejection fraction • radionuclide angiography

See related editorial, pp. 423–424

INTRODUCTION

Left ventricular ejection fraction (LVEF) has been demonstrated to have prognostic value in numerous cardiac conditions and is often used to guide medical and device therapy.[1-9] Recent guidelines have identified patients with LVEF ≤30% who may benefit from primary prevention using devices such as implantable cardioverter defibrillators (ICD) and cardiac resynchronization therapy (CRT).[10] Thus the accurate measure of LVEF is extremely desirable. Cardiac CT is a non-invasive modality with the ability to

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estimate LVEF with prognostic value incremental to coronary artery disease (CAD) severity.[11] Studies have demonstrated good correlation between CT and echocardiography,[12-16] biplane cine-ventriculography,[13] gated myocardial perfusion imaging,[17,18] and radionuclide LV angiography (RNA).[19] However, given its limited temporal resolution and radiation, there has been initial resistance to use CT to measure LVEF.

The objective of this study is to demonstrate that a relatively 'low radiation dose' 64 slice cardiac CT protocol is feasible and can accurately measure LVEF while delivering a radiation dose lower than RNA.

METHODS

Between June 2012 and August 2013, patients undergoing radionuclide angiography (RNA) for assessment of LVEF were prospectively screened and enrolled. On the same day as their RNA, eligible candidates underwent a 'low-dose' CT LVEF protocol. Patients with renal dysfunction (GFR <45 mL/minutes), atrial arrhythmias, and allergy to iodinated contrast agents were excluded. The study was approved by the Institutional Human Research Ethics Board and all patients provided written informed consent.

CT LVEF Protocol

Image acquisition was performed without metoprolol, diltiazem, or nitroglycerin to ensure that the test was feasible and was not limited by heart rate. A bi-phasic timing bolus was used to measure transit time[11,20] and CT LVEF image acquisition was performed using a tri-phasic intravenous contrast administration protocol. The volume and rate of contrast were individualized according to scan time and patient body habitus.[11,20] Retrospective ECG-gated data sets were acquired with the GE Volume CT (GE, Milwaukee, Wisconsin) with 64 × 0.625 mm slice collimation and a gantry rotation of 350 ms (mA = 200-300, kV = 80-100) without ECG-gated X-ray tube modulation. Pitch (0.16-0.24) was individualized according to heart rate. Data sets were reconstructed using 10 phases (5-95%) with 1.25 mm slice collimation and an increment of 1.25 mm.

CTA Image Analysis

ECG-gated CT images were post-processed, using the GE Advantage Volume Share Workstation (GE, Milwaukee, Wisconsin) and the Aquarius iNtuition (TeraRecon San Mateo, California), by expert observers blinded to all clinical data and RNA results. Using a semi-automated volumetric algorithm (Advantage Workstation, Ejection Fraction), LV volumes were measured at end-diastole and end-systole, and LVEF was calculated.[11,21,22]

Radionuclide Angiography

RNA was performed using the local clinical protocol using the 'modified in-vivo method'.[23] In brief, equilibrium planar RNA with Tc-99m-labeled red blood cells was performed with a small field-of-view Siemens ZLC gamma camera and a low-energy all-purpose collimator.[24] Gated acquisition was performed for 24 frames per cardiac cycle with a beat rejection window of 10%. Scans were acquired in the best septal left anterior oblique view and a minimum of six million counts were acquired. Calculations of LVEF and LV volumes were performed twice using FUGA software (version 4.7, HERMES Medical Solutions, Stockholm, Sweden) and the mean LVEF and LV volumes were used for analysis.[24-26]

Statistical Analysis

Statistical analyses were performed using SAS (version 9.2, SAS Institute Inc., Cary, NC), and statistical significance was defined as $P < 0.05$. Continuous variables are presented as means with standard deviations and median with interquartile range (IQR), and categorical variables are presented as frequencies with percentages. To compare patient characteristics, Wilcoxon rank-sum test was used to compare continuous variables and Fisher's exact test was used for categorical variables. Kappa analysis was used to assess the agreement of LVEF categories. The inter-observer reliability for measures of LVEF and volumes were assessed using intra-class correlation coefficients (ICC) and the Bland-Altman plot was also used to assess agreement and potential biases.

RESULTS

A total of 78 patients presenting for RNA imaging to assess LVEF were recruited for same day CT LVEF imaging. 77 (99%) patients had CT LVEF imaging the same day as the RNA, but 1 patient, due to time restraints, elected to return 4 days later for CT LVEF imaging. One patient was excluded from analysis for missing CT image data, therefore, the final analysis comprised 77 patients (mean age = 61.8 ± 12.2 years and 58 men) (Table 1).

Measured Left Ventricular Ejection Fraction

The mean LVEF measured by CT and RNA were 41.9 ± 15.2% and 39.4 ± 13.9%, respectively ($P = 0.154$) with a good correlation ($r = 0.863$) (Fig. 1). Bland-Altman plot revealed a good agreement between the CT and RNA LVEF (mean difference of −2.4; Fig. 2). The kappa agreement between CT and RNA for patients with LVEF ≤30%, 30-49%, and ≥50% was good (kappa = 0.658), and the kappa agreement for patients with LVEF ≤30% and LVEF ≥50% were 0.693 and 0.749, respectively (Table 2). 44 (57%) patients had CT and RNA LVEF measurements within 5% of each other and 64 (83%) patients were within 10%.

Acknowledging the temporal resolution of CT, a subanalysis was performed in the 30 patients with HR >60 bpm. The mean LVEF measured by CT and RNA were

Table 1. Baseline characteristics

	N = 77
Age (years)	61.8 ± 12.2
Men (%)	58 (75.3)
Body mass index (kg/m^2)	29.4 ± 6.4
Medical history	
Diabetes (%)	20 (26.0)
Hypertension (%)	45 (58.4)
Smoker/ex-smoker (%)	41 (53.2)
Dyslipidemia (%)	43 (58.8)
Family history of coronary artery disease (%)	37 (48.1)
Congestive heart failure	30 (39.0)
Prior myocardial infarction (%)	22 (28.6)
Prior PTCA (%)	17 (22.1)
Previous CABG (%)	12 (15.6)
Medications	
Anti-platelets (%)	57 (74.0)
Beta-blocker (%)	58 (75.3)
Calcium channel blocker (%)	9 (11.7)
ACE-inhibitor (%)	46 (59.7)
Statin (%)	49 (63.6)
Indications for radionuclide angiography	
History of heart failure or LV dysfunction (%)	51 (66.2)
Coronary artery disease (%)	14 (18.2)
Valve disease (%)	4 (5.2)
Arrhythmia (%)	3 (3.9)
Other (%)	5 (6.5)

PCI, percutaneous coronary intervention; *CABG*, coronary artery bypass graft surgery

40.4 ± 18.2% and 38.1 ± 15.3%, respectively ($P = 0.301$) (Table 3) with a good correlation ($r = 0.844$) (Fig. 3).

Radiation Exposure

The mean mA and kVp used for CT LVEF were 295.4 ± 14.5 and 87.5 ± 9.8, respectively (Table 4). The mean dose length product of CT LVEF was 335.7 ± 114.3 mGy*cm with an estimated effective dose of 4.7 ± 1.6 mSv. With RNA, the mean administered pertechnetate dose was 1358.7 ± 148.8 MBq with an estimated effective dose of 9.5 ± 1.0 mSv (Table 4).

Image Acquisition

The mean heart rate at the time of CT LVEF imaging was 60.2 ± 14.7 bpm and the mean contrast volume used for CT LVEF was 94.1 ± 5.5 mL (Table 4).

Imaging duration was measured using both imaging modalities (Table 4). The mean CT LVEF imaging time (duration between initial scout to final retrospective ECG-gated image acquisition) (4:32 ± 3:05 minutes) was significantly shorter than both the RNA image acquisition time (9:05 ± 2:36 minutes; $P < 0.001$) and the total duration of the RNA study (stannous injection to completion of image acquisition) (85:39 ± 23:44 minutes; $P < 0.001$).

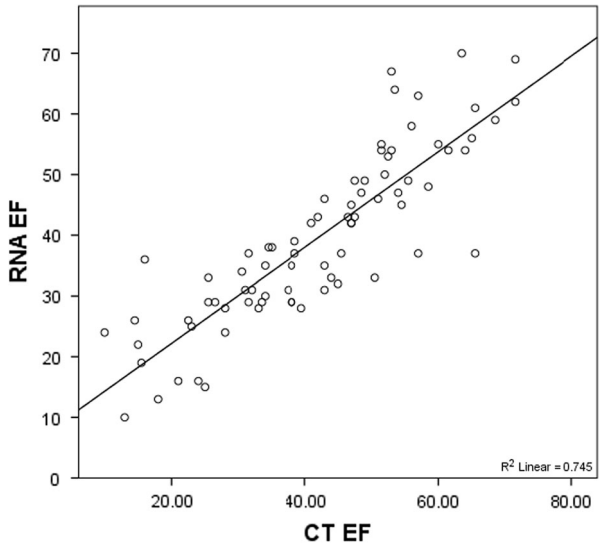

Fig. 1. Correlation between LVEF measured by RNA and CT.

Variability in LVEF Measures

The inter-observer variability of CT LVEF was 0.94 (0.91-0.96). RNA LVEF was measured twice using automated and semi-automated method and the variability between the two measures was 0.99 (0.98-0.99).

DISCUSSION

Our study explores a protocol, using existing 64-slice single-source CT, which minimizes radiation while maintaining diagnostic accuracy. The results of our study suggest that low-dose CT LVEF protocol is feasible, accurate, and fast while delivering a lower radiation dose than traditional RNA.

Left ventricular ejection fraction (LVEF) is important in determining the prognosis of many cardiac conditions and its measurement is often used as a guide for medical and device therapy.[1-9] Decisions to initiate specific cardiac medications in patients with congestive heart failure (CHF) are based upon LVEF and symptoms. The continuation of chemotherapy, in cancer patients, is often determined by stability in LVEF. LVEF measures are important to the decision-making for CABG and cardiac valve surgery. Recent guidelines

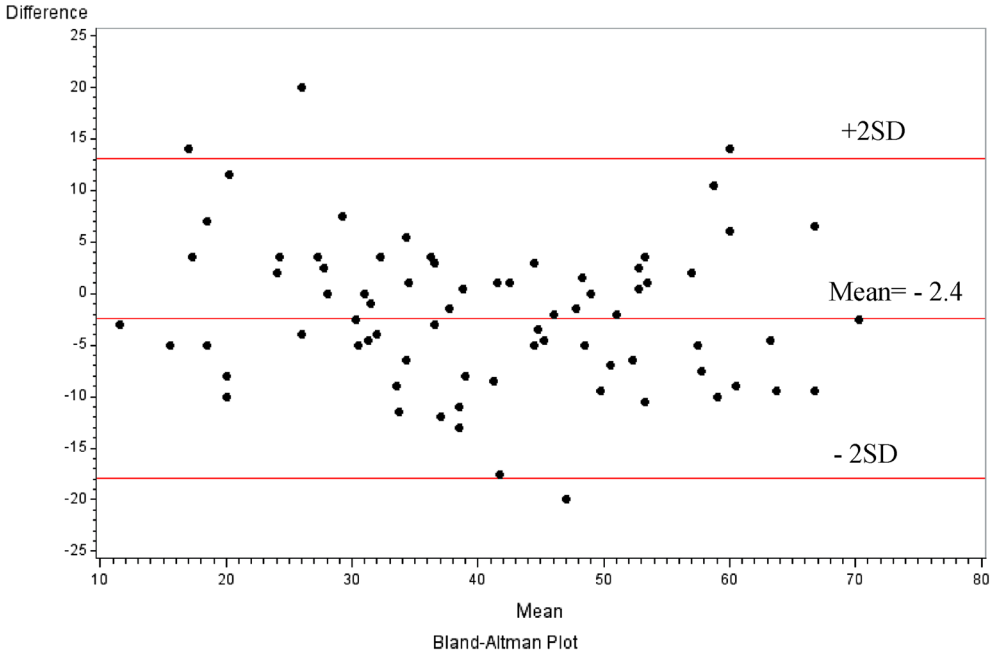

Fig. 2. Bland-Altman plot of the difference in mean LVEF percent between RNA and CT methods.

Table 2. Kappa agreement between CT and RNA

	CT (*n* = 77)		
RNA	**≤30%**	**30–49%**	**≥50%**
≤30%	15	7	0
30–49%	2	27	8
≥50%	0	0	18

Patients with LVEF ≤30%, 30–49%, and ≥50%: Kappa = 0.658 (0.515–0.802)
Patients with LVEF ≤30%: Kappa = 0.693 (0.504–0.881)
Patients with LVEF ≥50%: Kappa = 0.749 (0.584–0.914)
LVEF, left ventricular ejection fraction; *CT*, computed tomography; *RNA*, radionuclide angiography

have identified patients with LVEF ≤30% and 35% benefit from primary prevention using devices such as implantable cardioverter defibrillators (ICD) and cardiac resynchronization therapy (CRT).[10] Thus the accurate assessment of LVEF is extremely important to patient care. Due to the increasing demand to assess LVEF for clinical decision-making, safe, accurate, and accessible non-invasive methods are being sought.

We observed that our CT volumes were smaller than those obtained with RNA. This is likely explained by overlapping vascular structures. Since RNA images were obtained in the left anterior oblique position, counts from the vascular structures such as the left atrium and aorta would have been included, thereby increasing end-systolic and end-diastolic volumes (Fig. 4).

Table 3. Subgroup analysis with CT imaging heart rate >60 (*n* = 30)

	CTA	**MUGA**	***P* value****
LVEF	40.4 ± 18.2	38.1 ± 15.3	0.301
LVEDV	195.6 ± 72.3	244.2 ± 100.3	0.018
LVESV	187.5 ± 90.8	163.6 ± 88.8	0.029
Effective dose (mSv)	4.5 ± 1.6	9.6 ± 1.2	<0.001
Imaging time (minutes:seconds)	4:18 ± 2:17	9:30 ± 2:57	<0.001
Total time (minutes:seconds)	4:18 ± 2:17	91:18 ± 28:22	<0.001

LVEF, left ventricular ejection fraction; *LVEDV*, left ventricular end-diastolic volume; *LVESV*, left ventricular end-systolic volume
** *P* values were calculated using *t* test

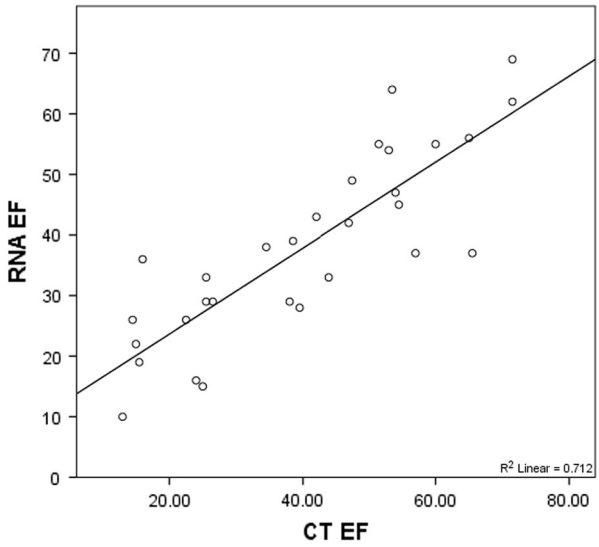

Fig. 3. Correlation between LVEF measured by RNA and CT in subjects with CT heart rates >60 (r = 0.844).

Methods for Assessing Left Ventricular Ejection Fraction

Currently, cardiac magnetic resonance imaging (CMR) and radionuclide angiography (RNA) are considered the most accurate measures of LVEF. However, access to CMR can be limited and potentially costly. Though RNA is more available, it requires the administration of a radiotracer that exposes patients to 8-10 mSv of ionizing radiation. This becomes a concern when patients require repeat studies for monitoring or changes in clinical status.

Echocardiography is equally accessible as RNA, however, studies have demonstrated inaccuracies in echocardiographic LVEF measurements, which may be related to extrapolation of volumes using 2-dimensional measures, poor acoustic windows, and local expertise.

The radiation exposure of CT using a retrospective ECG-gated image acquisition protocol (10-15 mSv) has limited its widespread acceptance. If a new CT protocol could be developed to minimize radiation exposure, lower than that of RNA, then CT may be a viable modality for measuring LVEF when echocardiography or CMR are not immediately available. However, efforts made to reduce patient radiation exposure will result in the inability to assess the coronary arteries. Future advances in both hardware and software may facilitate low radiation dose studies while maintaining sufficient CT image quality to evaluate for LVEF and CAD. Although we would not advocate that this new technique be used routinely, we demonstrate that it is a viable option for measuring LVEF especially when other modalities are unavailable, not feasible or inconclusive.

Limitations

This is a single centre study using a single-source 64-slice CT. Although our results require confirmation using newer technologies, one would anticipate similar or better results. The need for contrast is another potential limitation of this technique; our results cannot be extrapolated to

Table 4. CT and RNA results

	CTA	MUGA	*P* value**
CT imaging parameters			
Imaging heart rate (bpm)	60.2 ± 14.7		
Contrast infusion rate (cc/seconds)	4.5 ± 0.5*		
Timing bolus contrast (cc)	25.0 ± 0.0		
Total contrast volume (cc)	94.1 ± 5.5		
LVEF	41.9 ± 15.2	39.4 ± 13.9	0.154
LVEDV	209.5 ± 70.2	249.4 ± 80.6	<0.001
LVESV	127.4 ± 68.2	158.3 ± 73.2	0.004
DLP (mGy*cm)	335.7 ± 114.3		
Pertechnetate (mBq)		1358.7 ± 148.8	
Effective dose (mSv)	4.7 ± 1.6	9.5 ± 1.0	<0.001
Imaging time (minutes:seconds)	4:32 ± 3:05	9:05 ± 2:36	<0.001
Total procedural time (minutes:seconds)	4:32 ± 3:05	85:39 ± 23:44	<0.001

bpm, beats per minute; *LVEF*, left ventricular ejection fraction; *LVEDV*, left ventricular end-diastolic volume; *LVESV*, left ventricular end-systolic volume
* Six patients with missing data
** *P* values were calculated using *t* test

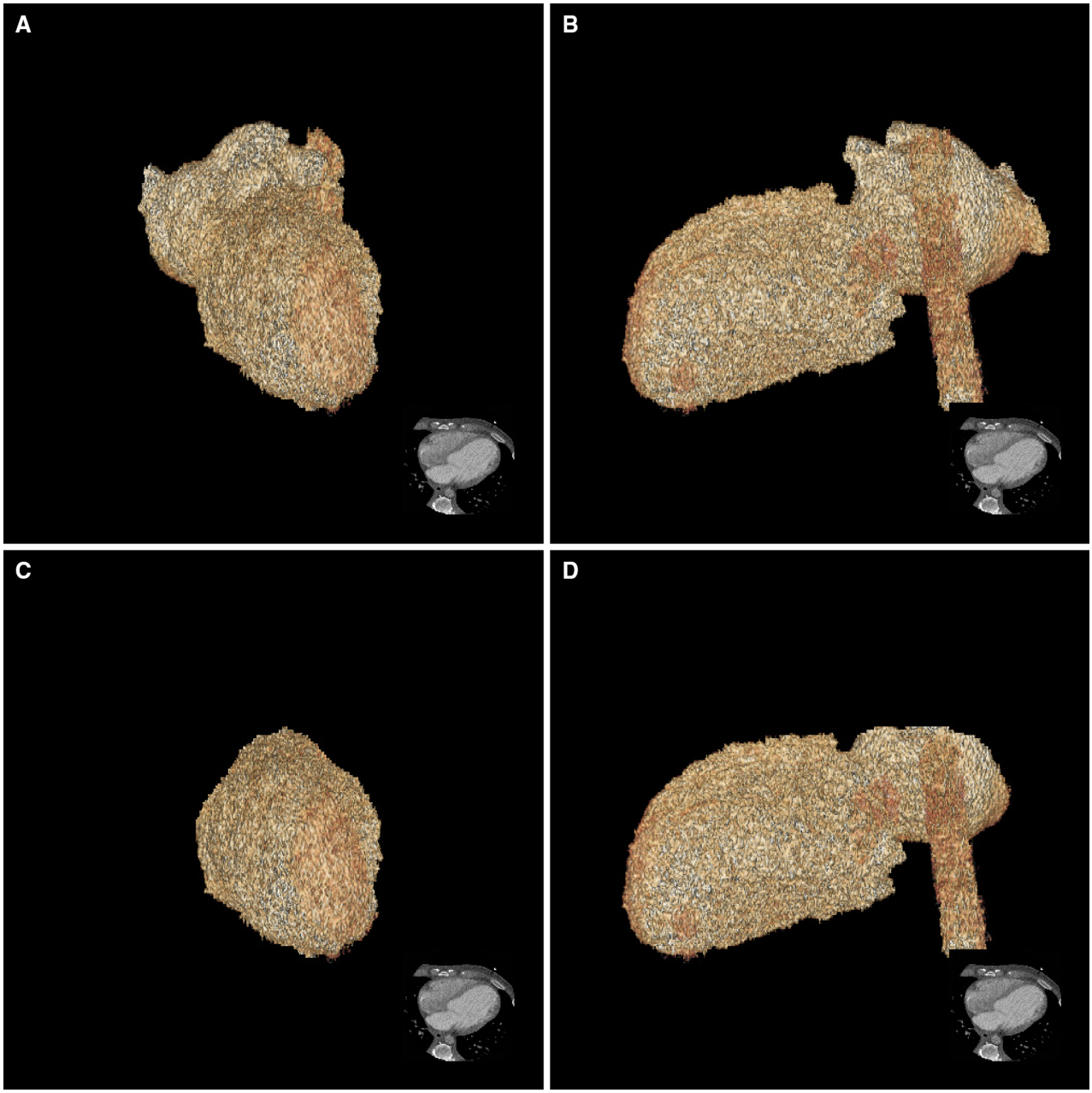

Fig. 4. 3D-volume rendered image of the left ventricle, left atrium, and aorta in LAO 45° and left lateral positions (**A**, **B**). Left lateral view demonstrating vascular structures (left atrium and aorta) that would contribute to the RNA counts using a region of interest in the LAO 45° position (**C**, **D**).

all patient populations. Due to the risk of acute contrast-induced kidney injury, patients with low GFR were excluded from the study. Such patients may be best studied using modalities which would minimize this renal risk. However, some studies have demonstrated that the risks of contrast may be small.[27] Similarly, patients with atrial fibrillation may not be routine CT LVEF candidates but would be dependent upon available CT technology. Although the temporal resolution of CT is limited, our study purposely did not use acute b-blocker for heart rate control. The subanalysis of patients with HR >60 demonstrated that the agreement between RNA and CT LVEF was still very good. In addition, this study assesses accuracy and not test-retest repeatability. Future studies are still needed to demonstrate the reproducibility of CT LVEF measures.

NEW KNOWLEDGE GAINED

This study demonstrates that a new ''low radiation dose'' 64-slice CT protocol can accurately measure LVEF while delivering less radiation than RNA. Thus, it is a potential option for assessing heart function when other traditional modalities may not be available or feasible.

CONCLUSIONS

The results of our study suggest that a low-dose CT LVEF protocol is feasible, fast, yields similar results as RNA and can be performed with a lower radiation dose than traditional RNA.

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Disclosures

No other authors have conflicts of interest to disclose.

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