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Reference absolute and indexed values for left and right ventricular volume, function and mass from cardiac computed tomography

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Abstract

Introduction: Left ventricular (LV) and right ventricular (RV) volumetric and functional parameters are important biomarkers for morbidity and mortality in patients with heart failure.

Purpose: To retrospectively determine reference mean values of LV and RV volume, function and mass normalised by age, gender and body surface area (BSA) from retrospectively electrocardiographically gated 64-slice cardiac computed tomography (CCT) by using automated analysis software in healthy adults.

Materials and Methods: The study was approved by the institutional review board with a waiver of informed consent. Seventy-four healthy subjects (49% female, mean age 49.6 ± 11) free of hypertension and hypercholesterolaemia with a normal CCT formed the study population. Analyses of LV and RV volume (end-diastolic, end-systolic and stroke volumes), function (ejection fraction), LV mass and inter-rater reproducibility were performed with commercially available analysis software capable of automated contour detection. General linear model analysis was performed to assess statistical significance by age group after adjustment for gender and BSA. Bland–Altman analysis assessed the inter-rater agreement.

Results: The reference range for LV and RV volume, function, and LV mass was normalised to age, gender and BSA. Statistically significant differences were noted between genders in both LV mass and RV volume (*P*-value < 0.0001). Age, in concert with gender, was associated with significant differences in RV end-diastolic volume and LV ejection fraction (*P*-values 0.027 and 0.03). Bland–Altman analysis showed acceptable limits of agreement (±1.5% for ejection fraction) without systematic error.

Conclusion: LV and RV volume, function and mass normalised to age, gender and BSA can be reported from CCT datasets, providing additional information important for patient management.

Key words: cardiac CT; function; left ventricle; mass; right ventricle; volume.

Introduction

Left ventricular (LV) and right ventricular (RV) volumetric and functional parameters are important biomarkers for morbidity and mortality in patients with heart failure (HF). Knowledge of these parameters relative to mean reference values and accurate and reliable determination of these values are crucial for prognosis and treatment in patients with HF.[1–3]

The assessment of LV and RV volumes, function and mass can be performed non-invasively using echocardiography, electrocardiographic (ECG)-gated multidetector cardiac computed tomography (CCT) or cardiac magnetic resonance (CMR) imaging, or invasively with cardiac catheterisation. Two-dimensional (2D) echocardiography (ECHO)-derived volumes may not represent true chamber volumes when compared to CCT or CMR, both of which demonstrate cardiac chamber anatomy

in an omnidimensional fashion[4] due to the complex geometry of cardiac chambers and the presence of trabeculations, which pose significant challenges. Three-dimensional ECHO should be more comparable to the reference standard of CMR than 2D ECHO,[5] but CMR is considered to be the current non-invasive reference standard for evaluation of cardiac anatomy, volume and function.[6] However, CMR may not be feasible for reasons such as claustrophobia, unavailability and presence of pacemakers/defibrillators, which are relative contraindications for MR imaging. In this group of patients, CCT may be a valid option.

CCT has good spatial and temporal resolution, and when performed using retrospective ECG gating, with data acquisition throughout the entire cardiac cycle, it can optimally anatomically orient the heart for the assessment of the cardiac chamber anatomy, volume, ejection fraction and cardiac mass, with no additional contrast administration.[7] CCT has excellent correlation with CMR, generally regarded as a current standard of reference for analysis of left ventricular function.

LV and RV volumes vary by patient age, gender and body surface area (BSA).[8,9] Significant differences in the cardiac chamber reference values may exist when using different sequences with MRI and even when using different software analysis packages.[10,11] Therefore, modality and software analysis require specific mean reference values for LV and RV function, volume and mass. The purpose of this study is to establish the CCT-based reference mean values (absolute and indexed) for LV and RV volumes, function and mass, normalised by age, gender and BSA, in healthy adults free of hypertension and hypercholesterolaemia by means of automated analysis software with minimal manual correction by the user.

Materials and methods

Study design

A retrospective cohort study of ECG-gated multidetector cardiac CT scans performed at our institution was used to establish mean reference values of LV and RV volume and function indexed to age, gender and BSA using automated analysis software package in healthy adults free of hypertension and hypercholesterolaemia by means of descriptive statistics and general linear model analysis.

Study population

The medical records and CCT reports of 675 adult subjects with atypical chest pain presenting either in the emergency department (ED) or in an outpatient clinic who underwent CCT from 2006 to 2011 were retrospectively reviewed (Fig. 1). Seventy-four subjects (36 females and 38 males, mean age 49.6 ± 11 years, age range 31–72 years) who fulfilled the inclusion criteria of normal cardiovascular function with no evidence of coronary artery disease (normal ECG and normal retrospectively gated CCT angiogram (CCTA) of the coronary arteries) and had no risk factors for coronary artery disease such as hypertension, hypercholesterolaemia, diabetes or structural heart disease (normal history, physical examination and normal echocardiography were available and confirmed in 47 patients). No major adverse cardiac events were noted at subsequent 6-month chart review in any patient. All subjects had a low pretest probability for coronary artery disease based on Framingham criteria.[12] ED patients were discharged with a diagnosis of non-cardiac chest pain, such as pain

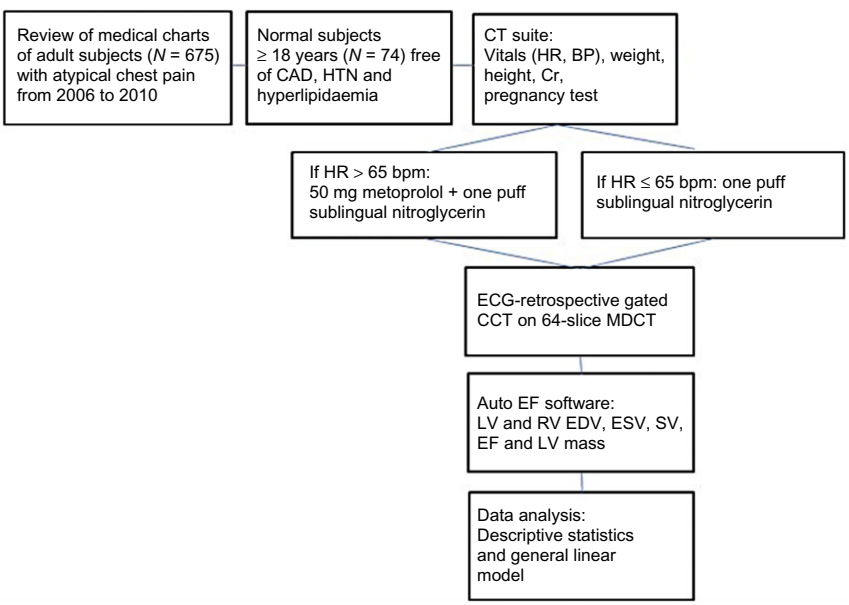

Fig. 1. Study design flow. CAD, coronary artery disease; CCT, cardiac computed tomography; Cr, creatinine; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; HR, heart rate; HTN, hypertension; LV, left ventricle; MDCT, multidetector computed tomography; RV, right ventricle; SV, stroke volume.

of musculoskeletal or gastrointestinal origin or panic attack. Height, weight, blood pressure and heart rate during the CCTA examination were recorded for all subjects. BSA was calculated using the Mosteller formula.[13] Four age groups by decade were established: group 1 = ages 30–39, group 2 = ages 40–49, group 3 = ages 50–59 and group 4 = ages 60–70. The study was approved by the institutional review board with a waiver of informed consent.

ECG-gated CCT technique

All subjects underwent assessment of vital signs (blood pressure and heart rate) at least an hour before CCTA. Only subjects with heart rate higher than 65 beats per minute (bpm) underwent oral premedication with 50 mg of metoprolol at least 45 min before the scanning. A heart rate of ≤ 60 bpm was achieved in all patients during the scan. All subjects underwent premedication with one puff of sublingual nitroglycerin 1–5 min before CT scanning.

All scans were acquired in the supine position with the patient's arms elevated above and behind the head on a 64-row multidetector CT (MDCT; Lightspeed VCT, GE Healthcare, Milwaukee, WI, USA). After the localising scan was obtained, image acquisition was performed in the craniocaudal direction at end-inspiration within a single breath hold, while the patient's ECG trace was recorded simultaneously. Scan *z*-axis coverage ranged from 2 cm above the most cephalad coronary artery to 2 cm below the cardiac apex. Scan parameters were the following: slice thickness, 0.625 mm; tube voltage, 100–120 kVp; mA, adjusted for patient size based on a body mass index (BMI) look-up table; and tube rotation, 0.35 s.

Iso-osmolar contrast material (Visipaque 370, GE Healthcare) was administered through an 18-gauge intravenous canula placed in the right antecubital fossa. A test bolus of 15 mL of contrast material was injected at 5 mL/sec with the region of interest in the aortic root at the level of the left main coronary artery. For each patient a Hounsfield unit time graph was obtained from which the scan delay was calculated as peak enhancement plus 6 s. The dedicated CCTA acquisition was then acquired using a triphasic contrast bolus with a total of 80 mL of contrast material – first 50 mL of contrast material, followed by 30 mL contrast material diluted with 30 mL normal saline, followed by 50 mL of normal saline – all at 5 mL/s. All examinations were performed using retrospective gating with tube current modulation (100% peak tube current during the mid-end-diastole and up to 80% reduction at end systole) to reduce radiation exposure.

CT image reconstruction and postprocessing

ECG-gated images were retrospectively reconstructed at 1.25-mm slice thickness at 1.25-mm intervals at 5% increments from 0–95% of the R–R interval of the ECG, for a total of 20 phases at the CT scanner console (Cardiac Volume Navigator, GE Healthcare). All reconstructed images were sent to and postprocessed on a GE workstation (Advantage Windows Workstation version 4.5, GE Healthcare) using the Automated Ejection Fraction protocol in the CardIQ function software (GE Healthcare, Wisconsin). After launching the Auto Ejection Fraction protocol, the LV/RV volumes and ejection fractions are automatically calculated and displayed for all selected phases loaded. The edit valve button is only available for the LV, which allows repositioning relative to the mitral valve plane (Fig. 2), which recalculates cavity segmentation. The short-axis and horizontal and vertical long-axis views were obtained with autosegmentation of both the right and left ventricles (Figs 3,4). The automatically obtained endocardial contours were visually reviewed in all planes (short axis, horizontal and vertical long axes) for correctness to ensure inclusion of ventricular outflow tracts (just distal to the aortic and pulmonary valves) and cardiac apex throughout each of the 20 cardiac phases reconstructed (Figs. 1–3) and, if necessary, manually edited/adjusted in a meticulous fashion using valve edit, add and remove structure tools. Papillary muscles and left ventricular outflow tracts were included in the LV cavity. Trabeculations and right ventricular outflow tracts were included in the RV cavity. The analysis software provided calculation of (i) LV and RV volume including end-diastolic volume (EDV) and end-systolic volume (ESV); (ii) LV and RV stroke volume (SV); (iii) LV and RV ejection function (EF); and (iv) left ventricular myocardial mass. The following measurement definitions were used:

- EDV: maximal ventricular volume when the cavity is largest
- ESV: minimal ventricular volume when the ventricular cavity is smallest
- SV: the difference between EDV and ESV
- EF: the fraction of EDV ejected with each heart beat (SV/EDV times 100).
- Indexed values: normalised to BSA

Volumetric and functional analysis was performed independently on all examinations by a fellowship-trained cardiothoracic radiologist with 4 years of experience and a cardiovascular imaging fellowship-trained cardiologist with 2 years of experience, each blinded to patient information.

The LV and RV volume and function analysis using the automated software takes approximately 5 min if the optimal threshold of the luminal blood pool is obtained and approximately 10 min if no optimal threshold of the luminal blood pool (usually the RV) is obtained, in which case more extensive user interaction is required.

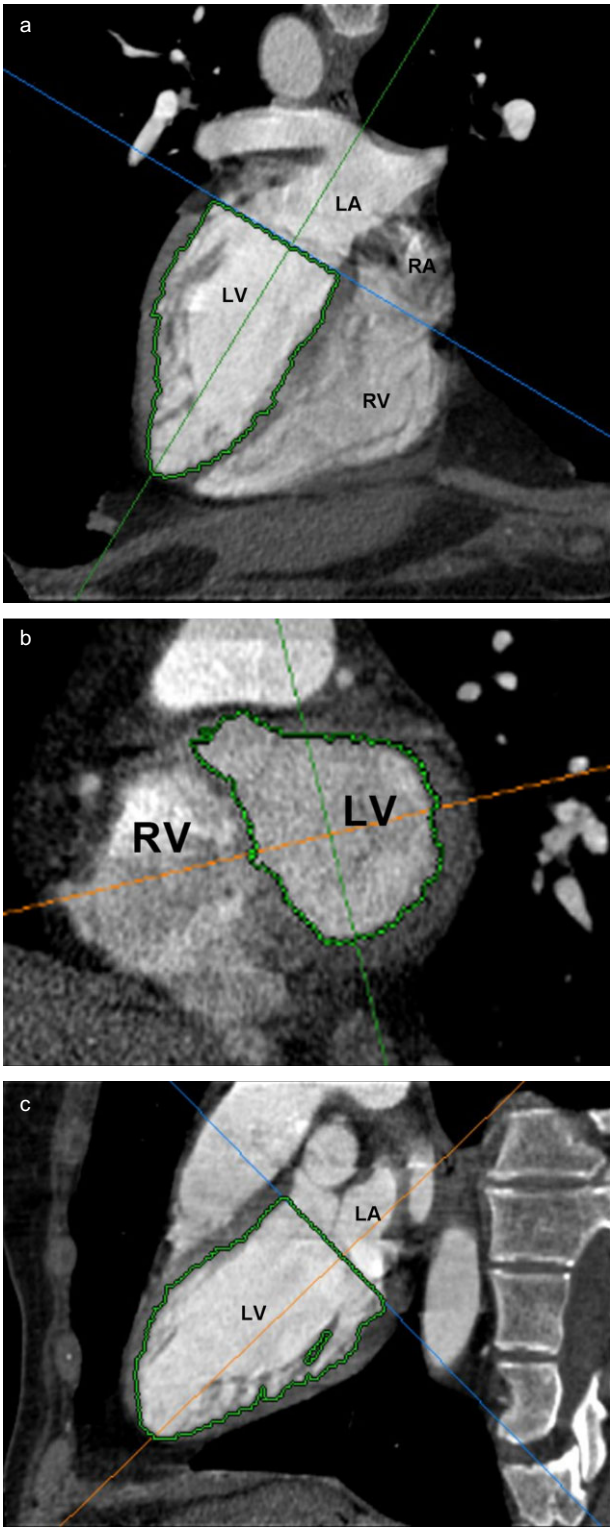

Fig. 2. Views of the left and right ventricles demonstrating adjustment of long and short planes using valve edit tool. (a) Horizontal long-axis view. (b) Short-axis view. (c) Vertical long-axis view. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

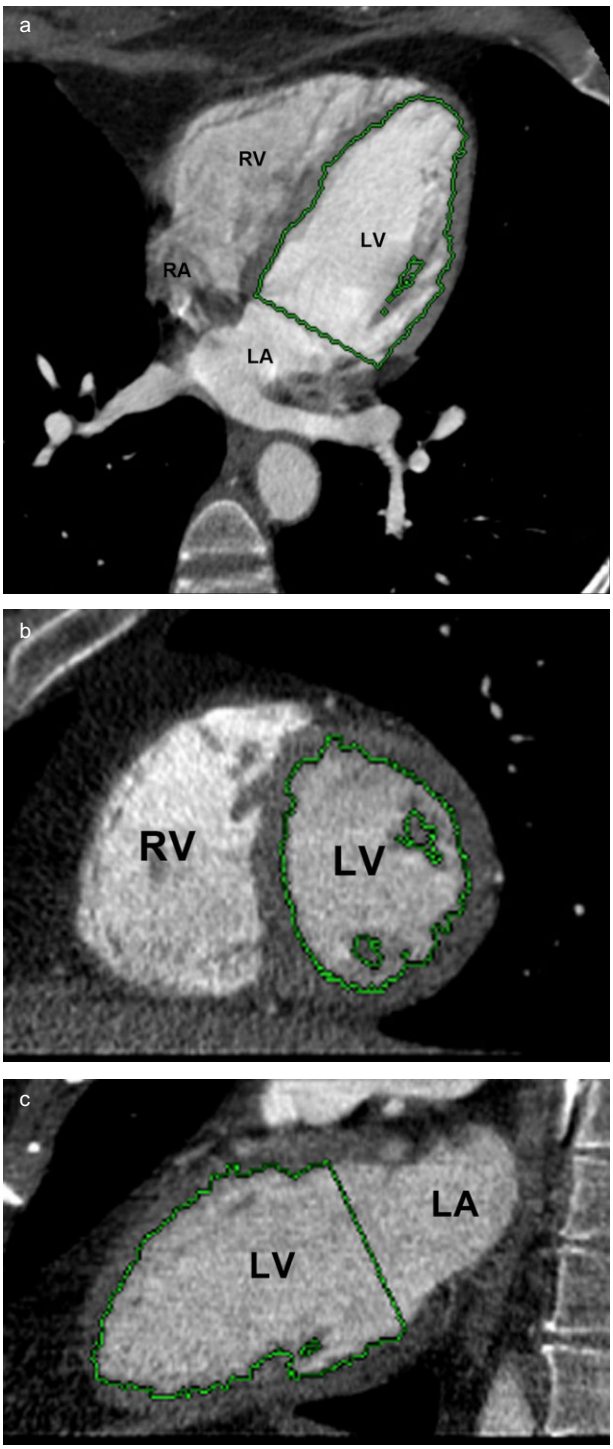

Fig. 3. Endocardial tracings of the left ventricle. (a) Horizontal long-axis view. (b) Short-axis view, involving left ventricular outflow tract; papillary muscles were also included in LV mass analysis. (c) Vertical long-axis view. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

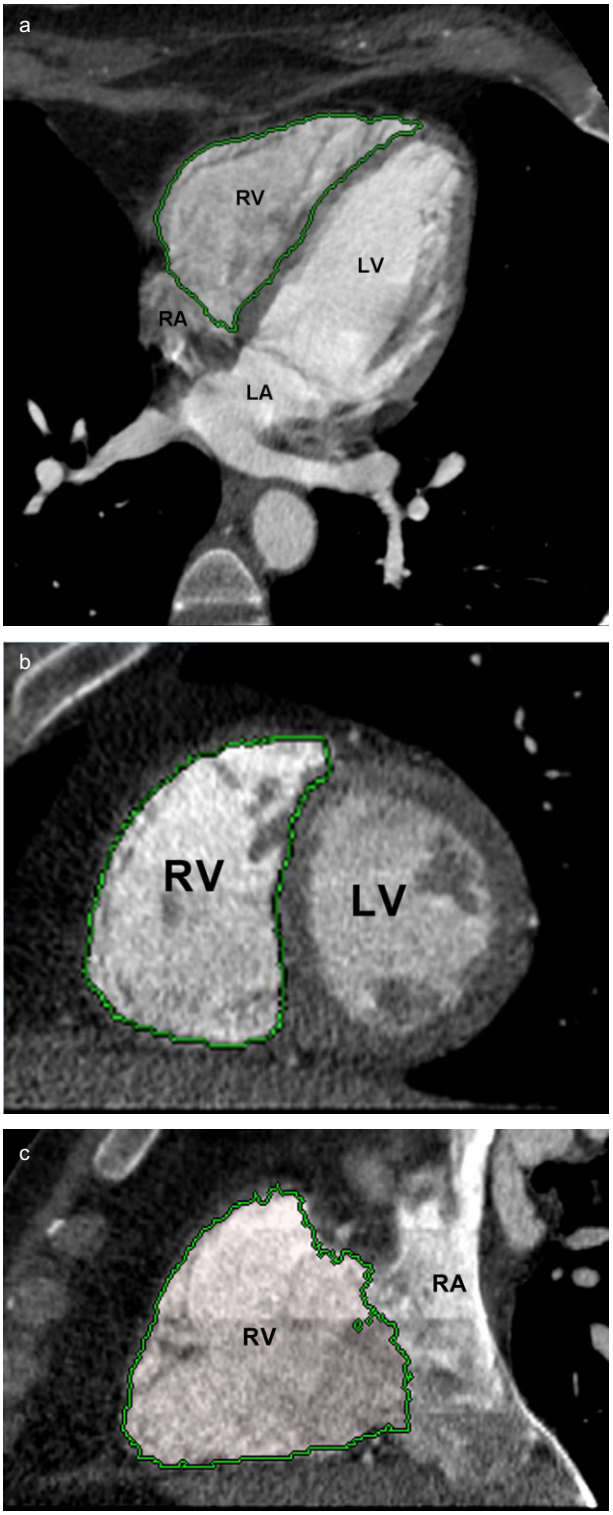

Fig. 4. Endocardial tracings of the right ventricle. (a) Horizontal long-axis view. (b) Short-axis view. (c) Vertical long-axis view. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

Hounsfield unit measurements

The Automated Ejection Fraction protocol is a threshold-based region-growing segmentation approach that usually requires minimal to almost no user interaction if the optimal threshold is reached. For adequate segmentation of the left and right ventricles, a minimum of 150 Hounsfield units (HU) of contrast enhancement of the ventricular cavity is needed. To test for optimal contrast opacification and automatic segmentation, mean HU measurements were obtained in 72 subjects using the region of interest tool of the LV and RV blood pool.

Reproducibility

To test for inter-reader variability of contouring, the data from 69 randomly selected subjects were independently analysed by a second reader 1 year later, using the same methodology and blinded to patient information and previous calculations.

Definitions

BMI was defined as the individual's body mass (kg) divided by the square of his/her height (m^2), with a normal BMI range of 18.5–25 kg/m^2. Individuals with BMI less than 18.5 are defined as underweight, individuals with BMI between 25–30 kg/m2 as overweight and individuals with BMI above 30 kg/m2 as obese.

Statistical analysis

Continuous data are presented as mean ± standard deviation or median (interquartile range) where appropriate. Categorical data are presented as numbers and percentages. The univariate association between the tested variables was calculated with Student's *t*-test for continuous variables with normal distribution, Mann–Whitney *U*-test for ordinal variables or continuous variables without normal distribution, and χ^2 or Fisher's exact test for categorical variables as appropriate. The data were summarised using descriptive statistics. To test the independent univariate and multivariate associations and statistical significance of LV and RV volume and function values between the age groups after adjusting for gender, BSA and age as a continuous variable, a general linear model analysis was performed. A method comparison test or difference of means test as described by Bland and Altman[14] was used to assess inter-reader agreement. A *P*-value of <0.05 was considered statistically significant. All computations were performed with SAS/STAT (Version 9.2, SAS Institute Inc, Cary, NC, USA).

Results

Baseline characteristics

The study population of 74 patients (38/74, 51% men and 36/74, 49% female) consisted of 60/74 (81%)

Caucasians, 10/74 (14%) African Americans, 3/74 (4%) Asians and one (1%) Hispanic. The patients ranged in age from 30 to 70 years (mean age 49.9 ± 11.1 years) (Table 1). The subjects were stratified into four age groups based on age in decades. The mean heart rate was 73 ± 12 bpm before the scan and was 56.9 ± 0.2 bpm during the scan. The ventricular functional parameters for males and females stratified by age groups for each ventricle are presented in Tables 2–5, and ventricular functional parameters for all subjects and stratified by gender for each ventricle are presented in Tables 6 and 7.

Influence of BMI

Our study population contained 22/73 (30%) normal, 29/73 (40%) overweight and 22/73 (30%) obese subjects. There was a statistically significant difference in the BMI distribution according to BMI group (*P*-value of <0.0001). There was no statistically significant difference in the BMI distribution according to gender (*P*-value of 0.6, Table 1). A statistically significant difference in the

Table 1. Baseline characteristics of normal subjects

Age (years)	30–39	40–49	50–59	60–70
Females				
N	8	10	9	9
Weight (kg)	87 ± 22	74 ± 14	75 ± 9	68 ± 10
Height (cm)	165 ± 10	165 ± 13	163 ± 5	64 ± 5
BMI (kg/m^2)	32 ± 6	33 ± 7	37 ± 9	42 ± 9
BSA (m^2)	2 ± 0.3	1.8 ± 0.2	1.8 ± 0.1	1.7 ± 0.1
SBP (mmHg)	122 ± 8	123 ± 10	126 ± 9	120 ± 9
DBP (mmHg)	74 ± 7	77 ± 12	77 ± 8	65 ± 8
Males				
N	10	10	10	8
Weight (kg)	90 ± 13	86 ± 15	91 ± 22	90 ± 15
Height (cm)	180 ± 5	175 ± 10	183 ± 8	180 ± 5
BMI (kg/m^2)	28 ± 3	43 ± 15	41 ± 11	41 ± 14
BSA (m^2)	2 ± 0.2	2 ± 0.2	2.1 ± 0.3	2.1 ± 0.2
SBP (mmHg)	120 ± 7	123 ± 12	123 ± 11	124 ± 11
DBP (mmHg)	70 ± 7	77 ± 8	74 ± 11	76 ± 8

All data are given as mean ± SD unless otherwise indicated. BMI, body mass index; BSA, body surface area; DBP, Diastolic blood pressure; SBP, systolic blood pressure.

Table 2. Female left ventricular function and volume by age

Age (years)	30–39	40–49	50–59	60–70
Absolute values				
EDV (mL)	146 (121–171)	142 (127–157)	143 (131–154)	150 (118–182)
ESV (mL)	40 (30–50)	43 (36–50)	49 (34–64)	42 (36–48)
SV (mL)	106 (88–123)	99 (88–110)	94 (86–102)	109 (80–137)
EF (%)	73 (69–77)	70 (67–73)	67 (59–75)	72 (68–76)
Mass (g)	76 (57–95)	76 (64–90)	77 (66–88)	73 (67–79)
Indexed values				
EDV/BSA (mL/m^2)	75 (62–88)	77 (70–84)	78 (69–86)	87 (63–111)
ESV/BSA (mL/m^2)	21 (15–27)	23 (20–26)	27 (18–35)	24 (20–28)
SV/BSA (mL/m^2)	54 (46–61)	54 (48–60)	51 (46–56)	63 (42–84)
Mass (g/m^2)	38 (30–46)	42 (37–47)	42 (35–49)	42 (37–46)

All values given as mean (95% confidence interval). BSA, body surface area; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; SV, stroke volume.

Table 3. Male left ventricular function and volume by age

Age (years)	30–39	40–49	50–59	60–70
Absolute values				
EDV (mL)	165 (159–171)	157 (137–177)	152 (139–165)	151 (129–172)
ESV (mL)	55 (48–62)	46 (35–57)	43 (35–51)	45 (28–62)
SV (mL)	110 (106–114)	111 (94–127)	109 (98–120)	106 (93–119)
EF (%)	67 (63–70)	65 (49–81)	72 (68–76)	71 (62–79)
Mass (g)	110 (104–116)	109 (92–126)	118 (101–135)	113 (101–125)
Indexed values				
EDV/BSA (mL/m^2)	78 (74–81)	77 (66–88)	73 (66–80)	73 (63–73)
ESV/BSA (mL/m$_2$)	26 (23–29)	23 (18–28)	21 (17–25)	22 (13–30)
SV/BSA (mL/m^2)	52 (48–55)	55 (46–64)	52 (48–56)	51 (46–56)
Mass (g/m^2)	52 (47–57)	53 (45–61)	55 (50–60)	55 (47–63)

All values given as mean (95% confidence interval). BSA, body surface area; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; SV, stroke volume.

Table 4. Female right ventricular function and volume by age

Age (years)	30–39	40–49	50–59	60–70
Absolute values				
EDV (mL)	173 (146–200)	157 (138–176)	169 (150–187)	155 (133–177)
ESV (mL)	74 (56–92)	56 (32–80)	78 (57–99)	57 (36–78)
SV (mL)	99 (83–115)	101 (87–115)	91 (80–102)	97 (82–112)
EF (%)	58 (51–65)	66 (53–79)	54 (46–62)	64 (52–76)
Indexed values				
EDV/BSA (mL/m^2)	88 (75–100)	85 (78–92)	92 (85–99)	88 (78–97)
ESV/BSA (mL/m^2)	38 (28–48)	30 (18–42)	42 (33–51)	32 (20–44)
SV/BSA (mL/m^2)	50 (45–55)	55 (47–63)	50 (44–56)	56 (47–64)

All values given as mean (95% confidence interval). BSA, body surface area; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; SV, stroke volume.

Table 5. Male right ventricular function and volume by age

Age (years)	30–39	40–49	50–59	60–70
Absolute values				
EDV (mL)	214 (197–230)	197 (169–225)	182 (160–204)	203 (74–131)
ESV (mL)	100 (71–128)	84 (52–115)	71 (47–95)	91 (58–124)
SV (mL)	113 (96–130)	113 (91–135)	111 (98–124)	112 (97–126)
EF (%)	54 (42–66)	59 (45–72)	62 (51–73)	57 (45–67)
Indexed values				
EDV/BSA (mL/m^2)	101 (94–107)	96 (84–107)	86 (77–95)	99 (84–114)
ESV/BSA (mL/m^2)	47 (34–60)	41 (26–56)	34 (22–45)	45 (27–63)
SV/BSA (mL/m^2)	54 (43–65)	56 (44–67)	52 (45–58)	54 (47–61)

All values given as mean (95% confidence interval). BSA, body surface area; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; SV, stroke volume.

distribution of normal and overweight subjects was seen only for RV EF with mean of 67 ± 20 and 56 ± 10 (*P*-value of 0.005), absolute RV EDV with mean of 167 ± 35 and 189 ± 34 (*P*-value of 0.001) and absolute RV ESV with mean of 59 ± 44 and 85 ± 28 (*P*-value of 0.003). After adjustment for age groups and gender, the only statistically significant differences of BMI were in RV EF (*P*-value of 0.01) and absolute RV ESV (*P*-value of 0.03).

Influence of gender

Mean ± SD with 95% confidence intervals for men and women are presented in Table 3. Men had statistically

Table 6. Left ventricular volume and function for all ages

	All subjects (*n* = 74)	Females (*n* = 36)	Males (*n* = 38)
Absolute values			
EDV (mL)	151 ± 25 (145–157)	145 ± 28 (136–154)	157 ± 22 (150–164)
ESV (mL)	45 ± 14 (42–48)	43 ± 13 (39–47)	47 ± 15 (42–52)
SV (mL)	106 ± 20 (101–110)	102 ± 23 (94–109)	109 ± 16 (104–114)
EF (%)	69 ± 10 (67–71)	70 ± 7 (68–72)	69 ± 13 (65–73)
Mass (g)	94 ± 25 (88–100)	76 ± 16 (71–81)	112 ± 19 (106–118)
Indexed values			
EDV/BSA (mL/m^2)	77 ± 15 (74–80)	79 ± 18 (73–85)	76 ± 11 (72–79)
ESV/BSA (mL/m^2)	23 ± 7 (21–25)	24 ± 7 (22–26)	23 ± 7 (21–25)
SV/BSA (mL/m^2)	54 ± 12 (51–57)	56 ± 15 (51–61)	53 ± 8 (50–55)
Mass/BSA (g/m^2)	47 ± 10 (45–49)	41 ± 8 (38–44)	54 ± 9 (51–57)

All data given as mean ± SD (95% confidence interval. BSA, body surface area; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; SV, stroke volume.

Table 7. Right ventricular volume and function for all ages

	All subjects (n = 74)	Females (n = 36)	Males (n = 38)
Absolute values			
EDV (mL)	181 ± 36 (174–188)	163 ± 28 (155–171)	199 ± 34 (190–208)
ESV (mL)	76 ± 36 (69–83)	66 ± 28 (58–74)	86 ± 40 (75–97)
SV (mL)	105 ± 22 (101–109)	97 ± 18 (92–102)	112 ± 23 (106–118)
EF (%)	59 ± 15 (56–62)	61 ± 14 (51–65)	58 ± 16 (54–62)
Indexed values			
EDV/BSA (mL/m^2)	92 ± 14 (89–95)	88 ± 12 (85–91)	96 ± 15 (92–100)
ESV/BSA (mL/m^2)	39 ± 17 (56–42)	36 ± 15 (32–40)	42 ± 19 (37–47)
SV/BSA (mL/m^2)	53 ± 11 (51–55)	53 ± 10 (50–56)	54 ± 13 (50–57)

All data given as mean ± SD (95% confidence interval. BSA, body surface area; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; SV, stroke volume.

significantly higher absolute and indexed RV EDV (P-value of <0.0001 for absolute and P-value of 0.006 for indexed values), absolute RV ESV (P-value of 0.008) and absolute RV SV (P-value of 0.001) as well as higher absolute LV EDV (P-value of 0.04). Men also had statistically significantly higher absolute and indexed LV mass values (P-values of <0.0001). A significant independent influence of gender on absolute RV EDV, RV ESV and LV mass (absolute and indexed), even after adjusting for age and BSA, was demonstrated. Otherwise, the genders had no significant differences, particularly in ejection fraction (P-value of 0.4 for LVEF and RVEF respectively).

Influence of age

The only statistically significant difference observed in LV and RV volume and function value distribution according to age group was found in women aged 50–59 years. Women aged 50–59 had a 7% lower LVEF than women aged 30–39 (P = 0.03), with an expected mean LVEF for females of 67% versus 74%, respectively. Similarly, men aged 50–59 had 31 mL lower absolute and 15 mL lower indexed RV EDV than men aged 30–39 (P = 0.027).

Influence of BSA

On multivariable analysis, BSA was found to have significant independent influence on absolute LV mass (P = 0.01), RV EDV (P = 0.03) and RV SV (P = 0.04) values.

Hounsfield unit measurements

The mean HU measurements of LV and RV blood pools were 346 ± 74 and 270 ± 106 respectively. Only four of 72 subjects (0.05%) had RV blood pool mean HU of less than 150, a lower-bound threshold for optimal autosegmentation of the ventricular cavity. In these cases, the endocardial RV contours had to be corrected manually. No statistically significant difference was obtained between the LV and RV blood pool mean HU measurements.

Inter-reader agreement

There was no statistically significant difference in ventricular volume and functional parameters between readers by either Pearson's correlation coefficient or Bland–Altman analysis (Tables 8,9; Figs 5,6).

Table 8. Inter-rater variability between two raters for left ventricular volume, function and mass

	Pearson correlation of the means of two raters (n = 69)				Method comparison test using Bland–Altman procedure (n = 69)			
	Mean, rater 1/ rater 2	SD, rater 1/ rater 2	Pearson's r	P-value	Mean difference of two raters	SD of the mean difference of two raters	Pearson's r	P-value
EDV (mL)	151/146	25/25	0.65	<0.001	2.57	10.74	0.04	0.71
ESV (mL)	45/41	14/13	0.77	<0.001	1.99	4.64	0.05	0.65
SV (mL)	106/105	20/20	0.63	<0.001	0.38	8.68	0.00	0.99
EF (%)	70/72	7/8	0.74	<0.001	–0.90	2.62	–0.11	0.37
Mass (g)	95/89	25/25	0.93	<0.001	2.41	4.69	–0.06	0.63

All data given as mean ± SD (95% confidence interval. EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; SV, stroke volume.

Table 9 Inter-rater variability between two raters for right ventricular volume and function

	Pearson correlation of the means of two raters (n = 69)				Method comparison test using Bland–Altman procedure (n = 69)			
	Mean, rater 1/ rater 2	SD, rater 1/ rater 2	Pearson's r	P-value	Mean difference of two raters	SD of the mean difference of two raters	Pearson's r	P-value
EDV (mL)	182/177	35/33	0.91	<0.001	3.12	7.1	0.11	0.36
ESV (mL)	77/75	35/33	0.92	<0.001	1.68	6.8	0.06	0.63
SV (mL)	105/102	22/24	0.92	<0.001	1.17	4.5	–0.02	0.053
EF (%)	59/58	14/14	0.93	<0.001	–0.01	2.6	–0.03	0.78

All data given as mean ± SD (95% confidence interval. EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; SV, stroke volume.

Discussion

We established mean values and 95% confidence interval for LV and RV volumes, function and LV mass by MDCT in healthy patients without hypertension and hypercholesterolaemia, stratified by age, gender and BSA. Our results demonstrate significant gender differences for LV mass and ventricular volumes.

We believe that these data have significant impact for current and future clinical practice and research. Previously published MDCT data have compared favorably with CMR,[15] which is considered the current gold standard for LV and RV volume and function.

Of note, significant differences can exist among measurements obtained with different software tools (semi-automated versus automated) from the same dataset.[15] Many previously published studies used semi-automated methods with Simpson's method to assess LV and RV volume and function without inclusion of the outflow tracts in analysis.[8,9] Our absolute volumetric values were slightly higher, especially in women, when compared with the values reported by Maceira *et al.* using CMR; however, the volumetric values indexed to BSA are similar.[8,9] These authors had not included the outflow tracts in their chamber analysis, which likely accounts for the difference. Furthermore, our absolute volumetric measurements are slightly higher, but our indexed values are similar to prior observations with MDCT using 3D measures using the Hounsfield unit-based endocardial border detection technique with manual correction, which is an older version (4.3) of our currently used software (4.5).[16]

Influence of age and gender on LV and RV volume, function and mass

Age alone may not have a significant impact on ventricular function and mass,[17,18] but age in concert with gender demonstrated a significant difference in volume in men and function in women. These observations parallel autopsy findings with progressive myocyte loss that occurs with increasing age in men and values remaining constant in women.[19] Such age-related gender differences may result from a reduction of physical activity with age and also from reduced testosterone level with age in men, which may explain the reduced ventricular mass.[18] Also, we observed that myocardial hypertrophy does not develop with age in either women or men, consistent with previously published autopsy findings.[19] Similar to prior reports, gender independently had a significant influence on LV mass and ventricular volumes.[8,9,17,18]

Effect of BSA on LV and RV volume, function and mass

As expected, BSA also had a significant impact on LV mass and RV volumes. This indicates the need for and the appropriateness of indexing LV/RV volume and LV mass to BSA when reporting these parameters.

To our knowledge, our study is the first to report age-, gender- and BSA-specific reference ranges of LV and RV volume, function and mass with MDCT using threshold-based function analysis software.

Reproducibility

We demonstrated excellent reproducibility of LV functional parameters and RV functional parameters. We could have expected differences in RV volume and function, mainly explained by the difficulty in defining the most basal slice. especially in the cases where the endocardial RV contours had to be corrected manually secondary to lower-bound threshold for optimal autosegmentation of the RV. Prior studies demonstrated higher variability of RV measurements than for the LV, further illustrating the complexity of RV measurements.[18]

Clinical application

The increasing availability and use of contrast-enhanced retrospectively ECG-gated CT in the care of cardiac patients allows volumetric and functional analysis of cardiac chambers. Impairment of LV and RV function is extremely important in patients with cardiomyopathy

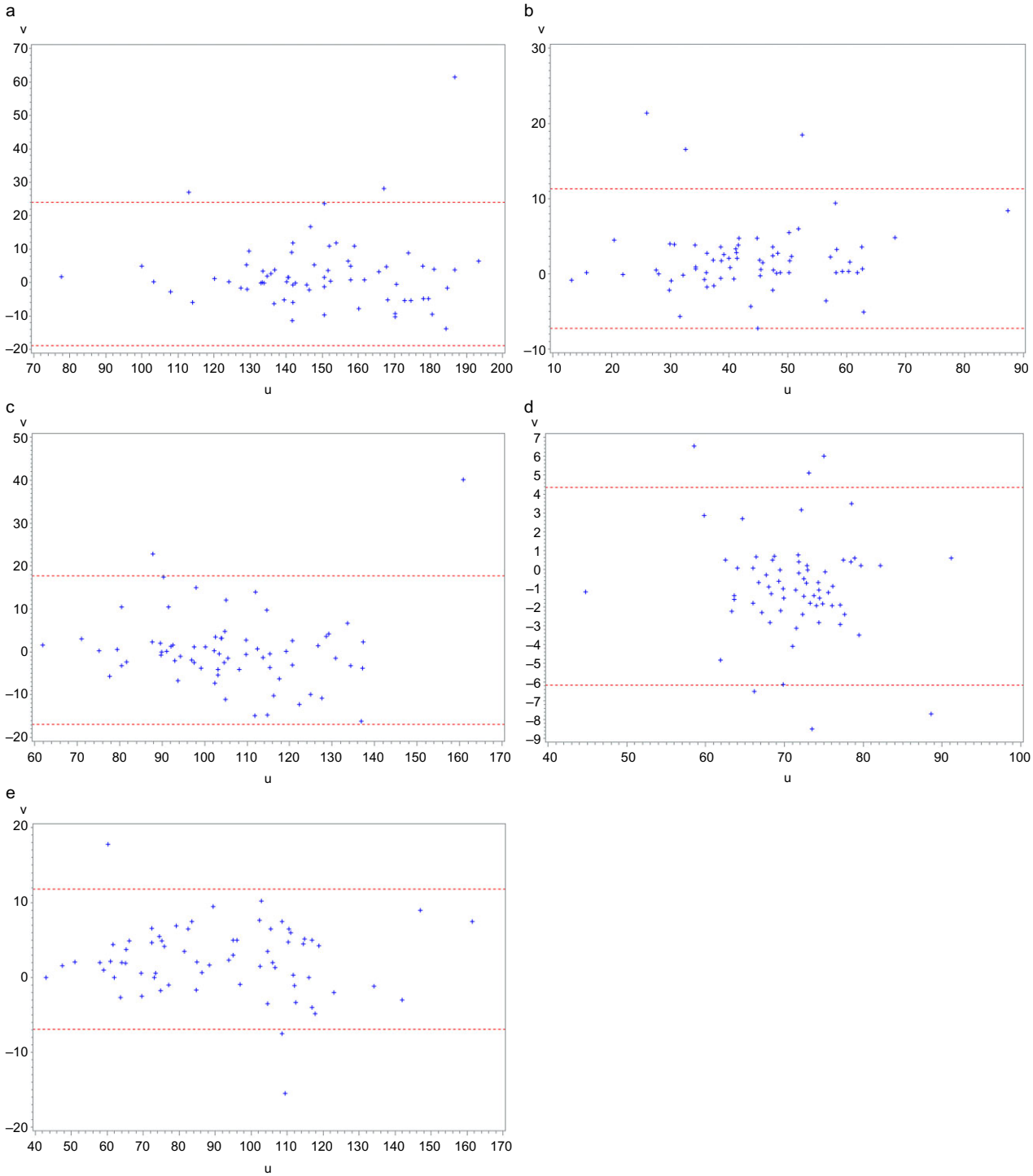

Fig. 5. Inter-reader agreement (Bland–Altman plots of mean differences and 95% confidence intervals for two readers) for left ventricular volume and function for 69 subjects. (a) End-diastolic volume. (b) End-systolic volume. (c) Stroke volume. (d) Ejection fraction. (e) Mass.

because of increased risk of sudden cardiac death.[20] Even though MRI is an established gold standard for evaluation of ventricular function and volume, there is a relative contraindication of its use in patients with implantable cardioverter–defibrillator/pacemaker. Therefore, use of contrast-enhanced retrospectively ECG-gated CT as an alternative problem-solving tool in the care of cardiac patients and establishing reference

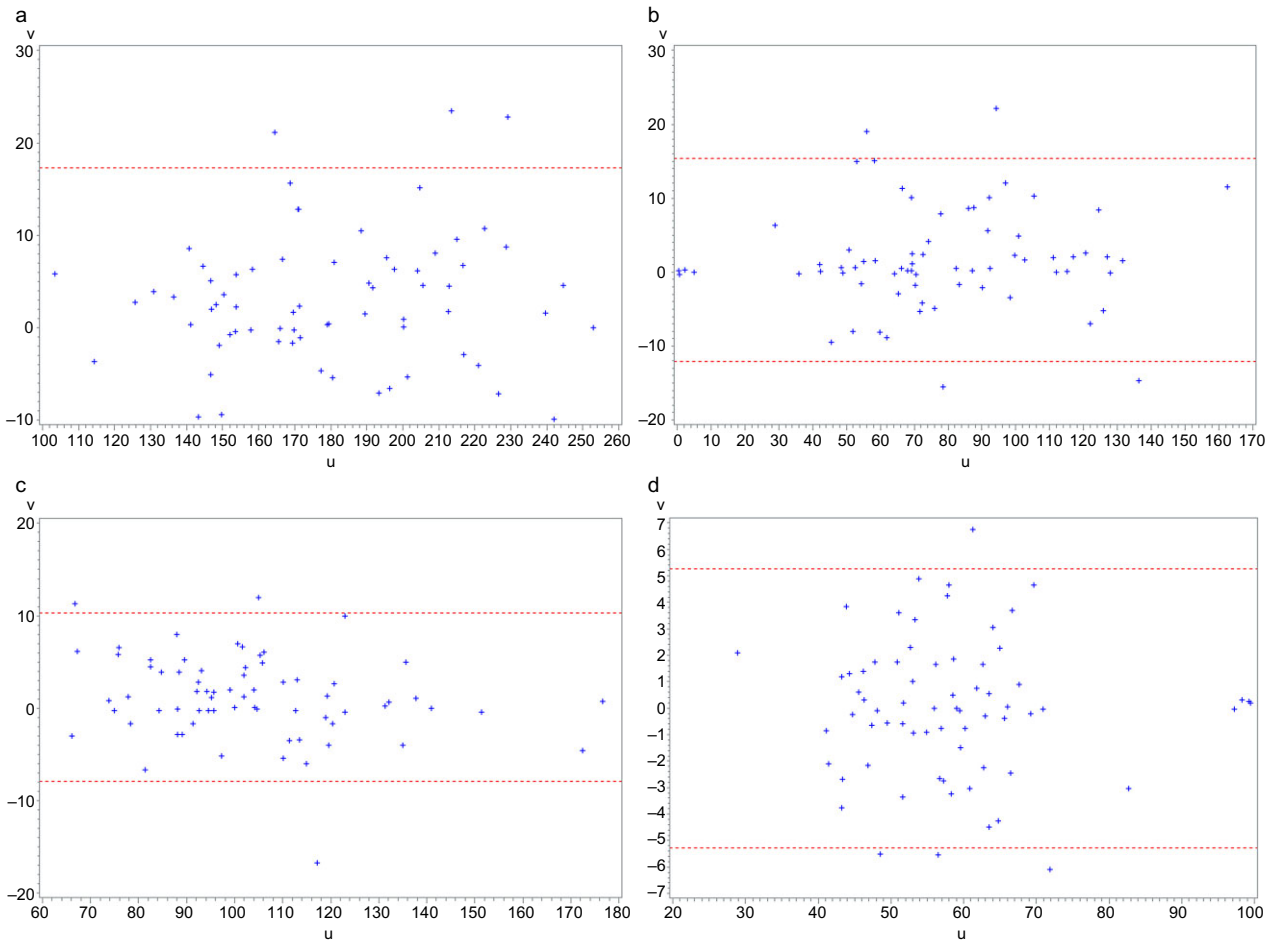

Fig. 6. Inter-reader agreement (Bland–Altman plots of mean differences and 95% confidence intervals for two readers) for right ventricular volume and function for 69 subjects. (a) End-diastolic volume. (b) End-systolic volume. (c) Stroke volume. (d) Ejection fraction.

normal ranges of LV and RV volume, function and diameter with MDCT are very important to risk-stratify patients with cardiac and cerebrovascular diseases.

Limitations

This is a retrospective study with a small sample size. There are radiation concerns that exist with MDCT, particularly when using the retrospective gating required for functional analysis, which likely relegates CT for functional analysis to either a problem-solving tool if echocardiography and MR are suboptimal and/or contraindicated or to incidental data reporting when retrospective gating has to be used. We attempted to exclude subjects with significant coronary artery disease, hypertension and hyperlipidaemia, so that our subjects represent overall healthy people free of cardiovascular disease (CVD).

Our study population included 30% obese subjects, a risk for metabolic syndrome and future cardiovascular disease; however, we stressed the importance of reporting normalised ventricular volumetric and functional values, which accounts for this limitation. As other functional assessments were not done at the same time, we could only compare our results with previously reported historical data. In the absence of a gold standard, it is not possible to estimate the accuracy of the described methodology; however, the ventricular functions served as internal controls for each other.

Conclusion

We have provided reference mean values of LV and RV volume, function and mass normalised by age, gender and body surface area for ECG-gated MDCT using threshold-based analysis software among subjects free of CVD. We stressed the importance of using reference values indexed to gender and BSA. These parameters should always be obtained and reported, especially given the availability of automated functional analysis tools

that significantly decrease the postprocessing time, and add important information that can be used in the patient's clinical management.

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