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Simple Area-based Measurement for Multidetector Computed Tomography to predict Left Ventricular Size

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Abstract

Objective—Measures of left ventricular (LV) mass and dimensions are independent predictors of morbidity and mortality. We determined whether an axial area-based method by computed tomography (CT) provides an accurate estimate of LV mass and volume.

Method—45 subjects (49% female, 56.0±12 years) with a wide range of LV geometry underwent contrast-enhanced 64-slice CT. LV mass and volume were derived from a 3D data set. 2D images were analysed to determine LV area as well the direct transverse cardiac diameter (dTCD) and the cardiothoracic ratio (CTR). Further, feasibility was confirmed in 100 Framingham Offspring Cohort subjects.

Results—2D measures of LV area, dTCD and CTR were 47.3±8 cm², 14.7±1.5 cm and 0.54±0.05, respectively. 3D-derived LV volume (end-diastolic) and mass were 148.9±45 cm³ and 124.2±34 g, respectively. Excellent inter- and intra-observer agreement were shown for 2D LV area measurements (both ICC=0.99, p<0.0001) and could be confirmed on non-contrast CT. The measured 2D LV area was highly correlated to LV volume, mass, and size (r=0.68; r=0.73; r=0.82; all p<0.0001; respectively). On the other hand, CTR was not correlated to LV volume, mass, size or 2D LV area (all p>0.27).

Conclusion—Compared with traditionally used CTR, LV size can be accurately predicted based on a simple and highly reproducible axial LV area-based measurement.

Keywords

multi-detector computed tomography; left ventricle; left ventricular size; cardio-thoracic-ratio; Framingham Heart Study

INTRODUCTION

Left ventricular (LV) size is well established as an independent predictor of cardiovascular morbidity and mortality and often used to guide patient care [1–6]. The cardiothoracic ratio (CTR) has traditionally been used to estimate LV size, while the CTR can be determined easily from plain chest x-rays [7;8]. CTR was also initially thought to be an independent predictor of all-cause mortality [9;10], but preliminary evidence has contested these results [11]. Subsequently, direct transverse cardiac diameter (dTCD), another 2D measure, was introduced, which is, in contrast to CTR, not thoracic shape depended [12;13]. Clinically, LV size is most often assessed using echocardiography, a widely available and reliable tool. However, echocardiographic assessment is sometimes limited by large body habitus and increased lung volumes, which can also make it more difficult to visualise the LV apex. Although cine magnetic resonance imaging (MRI) is considered the gold standard for LV function and size assessment [14], it is under-utilized. Recently, ECG-gated cardiac contrast-enhanced multidetector computed tomography (MDCT) measurements of LV size and function on a global and regional basis have been shown to be in excellent agreement with MRI [14;15]. Although semiautomatic software is available to measure LV mass and volume in contrast-enhanced MDCT, this procedure requires a high level of effort and time [16].

A simple, axial area-based assessment of LV size may, therefore, provide the opportunity to gather quickly additional information for cardiovascular risk stratification on contrast-enhanced MDCT, as well on non-contrast-enhanced MDCT, which were performed to assess coronary artery calcium (CAC) for risk stratification [17;18]. We assessed whether end-diastolic LV volume and size can be accurately predicted based on a simple and highly reproducible axial LV area-based measurement or based on traditionally used CTR or dTCD across a wide range of LV volumes.

METHODS

Study population for the contrast-enhanced images

45 consecutive subjects were selected to undergo contrast-enhanced MDCT in the setting of acute chest pain in the emergency department. Among these, 15 subjects had no cardiovascular risk factors, 15 had hypertension (systolic blood pressure >140 mmHg, diastolic blood pressure >90 mmHg, or currently on antihypertensive medication) and 15 had cardiovascular diseases (defined as acute coronary syndrome including STEMI, NSTEMI and UAP or apical ballooning syndrome). Overall, 33 (73%) had normal LV function, global LV function was impaired in 7 (16%) patients, regional wall motion abnormality was observed in additional 5 (11%) patients, while the ejection fraction ranged from 38% to 82%. Further details have been provided elsewhere [19]. The institutional review boards of the Massachusetts General Hospital approved the study and all subjects provided written consent.

Contrast-enhanced multi-detector computed tomography protocol

All subjects underwent imaging with 64-slice MDCT (Sensation 64, Siemens Medical Solutions, Forchheim, Germany). Images were acquired during a breath hold in inspiration with the following parameters: 64×0.6 mm slice collimation, 330 ms gantry rotation time, 120 kV tube voltage, and 850–950 mAs effective tube current. Tube current modulation - the maximum effective tube current was on during the time interval from 470 ms to 140 ms before the next expected R-wave and the tube current was reduced by 80% during the remain portion of the cardiac cycle - was used when appropriate (35/45 cases). In cases where subject heart rate was greater than 60 beats per minute, metoprolol was administered

before imaging. Contrast-enhanced images covered a region of interest from the carina to the diaphragm. The contrast agent (80–100 mL, Iodixanol 320 g/cm³, Visipaque, General Electric Healthcare, Princeton, NJ, USA) was administered at an injection rate of 5 mL/s and timed using a test bolus protocol. The images were reconstructed retrospectively using overlapping transaxial images and a medium sharp convolution kernel (B25f) with an image matrix of 512×512 pixels, and slice thickness of 1.5 mm. Ten datasets of axial images of the entire heart with a temporal resolution of 83–165 ms (automatically chosen depending on the heart rate) and a slice thickness of 1.5 mm were reconstructed at increments of 10% of the R-R interval increment, starting at 5% throughout the cardiac cycle (5%–95%) using a retrospective electrocardiogram-gated half-scan algorithm and a special cardiac reconstruction kernel (B25f).

Study population for the non-contrast-enhanced images

As a second study cohort a subset of 100 subjects were randomly selected from the Framingham Offspring Study. The Framingham Offspring Study has enrolled 3,539 spouses and children of the original Framingham Heart Study cohort [20]. Between June 2002 and April 2005, 1,418 subjects from the Framingham Offspring Study underwent non-contrast-enhanced MDCT as part of the study protocol for coronary artery calcium scoring. The study protocol was approved by the institutional review board of the Boston University Medical Centre and Massachusetts General Hospital. All subjects provided written informed consent.

Non-contrast-enhanced multi-detector computed tomography imaging protocol

The subjects of the Framingham Offspring Study underwent imaging in the supine position using eight-slice MDCT (LightSpeed Ultra, General Electric, Milwaukee, WI, USA). Helical prospective ECG-triggered CT imaging of the thorax with the centre of the acquisition at 70% of the ECG cycle was performed in a single inspiratory breath hold (tube voltage: 120 kVp, tube current: 320 mA or 400 mA in participants <220 lbs or >220 lbs; respectively). Gantry rotation time was 500 ms and temporal resolution 330 ms. Imaging covered the region from the carina to the diaphragm with a slice thickness of 2.5 mm. In a 25-cm field of view, the images were reconstructed with non-overlapping, 2.5-mm-thick slices.

Quantitative Assessment of Left Ventricular Volume, Mass and Size

Following reconstruction, dynamic cardiac contrast-enhanced MDCT images were transferred to a PC-based workstation. We assessed in 3D end-diastolic left ventricular mass and volume using dedicated cardiac function analytical software (CT QMASS; Medis Imaging Systems, Leiden, Netherlands). Short axis images were created based on the original axial images using an integrated CT-Reformatter (slice thickness of 8 mm and interslice gap of 0 mm). The endocardial and epicardial border contours were detected automatically and adjusted by manual tracing when necessary, see Fig. 1. End-diastolic and end-systolic phases were identified visually. End-diastole was defined as the maximum dilation, and end-systolic as the minimum dilation of the LV. 3D-based end-diastolic left ventricular size (EDS, in cm³) was calculated from 3D end-diastolic left ventricular volume (EDV), 3D left ventricular mass (LVM), and the specific gravity of the myocardium (SG_M, 1.05 g/cm³) using the formula: $EDS = EDV + (LVM/SG_M)$ [21]. It should be mentioned that several studies demonstrate a very high correlation between LV end-diastolic volume, mass and size in MRI and CT, studies also demonstrated a systematic overestimation of the end-diastolic volume by CT [14;22–24].

Quantitative Assessment of Left Ventricular Area, direct Transverse Cardiac Diameter and Cardiothoracic Ratio

LV area was measured in axial images at a mid-ventricular, transverse slice in the end-diastolic phase. In the first axial slice, where the left ventricle could be clearly distinguished from the left atrium, the 2D LV area was defined as the region bounded by the outer border of the left ventricle, the anterior interventricular groove (where the left anterior descending coronary artery resides) and the left posterior interventricular groove (Fig. 2). This area included both the LV mass and LV intra-cavitary volume, as well as part of the interventricular septum. These landmarks can also be readily identified on non-contrast-enhanced MDCT.

The anterior-posterior scout images, which were acquired by CT before the cardiac imaging, were used to assess the direct transverse cardiac diameter (dTCD) and the cardiothoracic ratio (CTR). The dTCD represents the maximal transverse diameter of the cardiac silhouette. The CTR was calculated as the ratio of the maximal transverse diameter of the cardiac silhouette to the distance between the internal margins of the ribs at the level of the right hemidiaphragm. All measurements of the 2D LV area, the dTCD and the CTR were made on a dedicated offline workstation.

Determination of inter- and intra-observer variability of the left ventricular area

Two experienced observers independently measured the 2D LV area in a random order to assess inter-observer variability. One reader repeated the analysis at a later time to assess intra-observer variability.

Statistical evaluation

Inter- and intra-observer reproducibility was assessed using the intraclass correlation coefficient (ICC). A value close to 1 indicates excellent agreement between the two readings. In addition, the significance of the mean difference between the two readings was assessed using the paired t-test. Pearson correlation coefficients (r) and simple linear regression analysis were used to determine correlation between the 2D- and 3D-derived variables. A p value <0.05 was considered to indicate statistical significance.

RESULTS

The first study cohort consisted of 45 subjects (49% female, mean age: 56.0 ± 12 years, mean BMI 30.6 ± 7 kg/m²) who underwent contrast-enhanced MDCT. 2D-derived measures of LV area was on average 47.3 ± 8 cm² (range: 33.6 to 67.9), mean dTCD was 14.7 ± 2 cm (range: 11.4 cm to 18.3), and mean CTR was 0.54 ± 0.05 (range: 0.44 to 0.67), Table 1. 3D-derived LV volume, mass and size were 148.9 ± 44.5 cm³, 124.2 ± 34.4 g and 267.2 ± 65.8 cm³, respectively. The interclass correlation for inter- and intra-observer agreement of the 2D LV area method was high (ICC=0.99, $p<0.0001$; ICC=0.98, $p<0.0001$; respectively) and the relative mean difference low (delta $0.5 \pm 4.5\%$, $p=0.49$; delta $0.02 \pm 3.3\%$, $p=0.75$; respectively).

The 2D LV area was highly correlated with 3D end-diastolic LV volume, mass and size ($r=0.68$, $p<0.0001$; $r=0.73$, $p<0.0001$; $r=0.82$, $p<0.0001$, respectively, Table 2). Also dTCD is correlated with 3D end-diastolic LV volume, mass and size (all $p \leq 0.009$, Table 2), but all those correlations were inferior as compared to the correlation between 2D LV area and the 3D measures. On the other hand, CTR was not correlated with end-diastolic LV volume, mass, or size ($r=0.17$, $p=0.32$; $r=0.01$, $p=0.94$; $r=0.12$, $p=0.51$; $r=-0.19$, $p=0.27$, respectively, Table 2). Interestingly, LV area was not significantly correlated with CTR ($r=0.16$, $p=0.35$).

An association between 2D LV area and 3D LV size was demonstrated using simple linear regression analysis (β : 7.4 cm^3 , 95%-CI: $6.1\text{--}8.76$, $p<0.0001$), and a derived formula can be used to calculate 3D LV size from 2D LV area (see Equation 1). The differences between the measured 3D LV size and the calculated LV size based on 2D LV area are illustrated in a Bland Altman scatter plot (Fig. 3). The mean difference was $-6.8 \times 10^{-5} \text{ cm}^3$ (95%-CI: -10.2 to 10.2). A slight underestimation of calculated LV size was seen in subjects with LV size over 350 cm^3 . However, the mean difference between measured and calculated LV size was not different for subjects with or without LV dysfunction (0.64 vs. -0.12 cm^3 , $p=0.96$ for presence and absence of global LV dysfunction, respectively).

The second study cohort, a subgroup of the Offspring cohort of the Framingham Heart Study ($n=100$) consisted of 49% female patients with an average age of 59.9 ± 13 years, and an average BMI of $27.8 \pm 5 \text{ kg/m}^2$. This subgroup did not differ significantly from the overall Offspring cohort with respect to gender, age and BMI (all $p>0.25$). While the subjects of the Framingham Heart Study underwent non-contrast-enhanced MDCT for the purpose of calcium scoring, we repeated our new 2D LV area method to evaluate their feasibility and reproducibility. The average measured 2D LV area was $38.6 \pm 7 \text{ cm}^3$. Similar to the previously described observer agreement on contrast-enhanced MDCT, we also demonstrated excellent inter- and intra-observer agreement on non-contrast-enhanced MDCT (ICC=0.99, $p<0.0001$; ICC=0.99, $p<0.0001$, respectively). In addition, the relative mean difference was low ($\text{delta}=0.95\%$, $p=0.04$; $\text{delta}=0.74\%$, $p=0.74$, for inter- and intra-observer variability retrospectively).

DISCUSSION

Our study demonstrates that a quick 2D area-based measurement is highly correlated with 3D-based measurements and accurately predicts LV mass and size in subjects with and without CAD and/or hypertension. This method is also highly reproducible with low inter- and intra-observer variability. These findings were confirmed on non-contrast MDCT of the Framingham Heart Study. Further, we derived a precise formula to calculate 3D LV size based on the 2D LV area measurements. On the other hand, CTR was not correlated with LV mass, size or 2D LV area measurements.

It is well established that LV hypertrophy is an independent risk factor for cardiac mortality. LV hypertrophy determined by echocardiography [5;25] and electrocardiography [2] is associated with a 1.5- to 4-fold increase in mortality. In addition, a study by Woo et al. highlighted the significant impact of left ventricular size on morbidity and mortality, demonstrating that LV hypertrophy is more highly associated with both angiographic coronary disease and future coronary events than coronary artery calcium and other traditional risk factors [26].

However, the cardiothoracic ratio (CTR), another 2D measurement, is regarded as an unspecific marker for cardiac hypertrophy with questionable clinical value [11;27]. Like other studies evaluating the clinical significance of CTR, this study did not reveal a correlation between CTR and end-diastolic left ventricular volume, mass or size. One possible explanation is that CTR measures are also dependent on the geometry of the thoracic shape as well the right ventricle, which we did not include in our analysis. Even so direct transverse cardiac diameter (dTCD) was predicting LV geometry; 2D LV area was superior in the correlation to end-diastolic volume, mass and size.

On the other hand, this study indicates that 2D LV area-derived measurements of end-diastolic left ventricular size are both accurate and precise and may play a role in risk stratification for cardiovascular disease. Future research in population-based, prospective

studies will evaluate the utility of this novel method for measuring end-diastolic left ventricular size. With an average performance time of less than 1 min, these 2D LV area-derived measurements may be applied quickly and easily in both large population-based cohort research studies and clinical practice. Similar approaches are currently evaluated to right ventricular area for the prediction of outcome in patients with pulmonary embolism [28;29].

Using axial 2D area for the prediction of LV size is further limited by its dependency on the position and the shape of the heart. Further, this approach cannot distinguish between the LV cavity and LV wall tissue. While this method can accurately assess LV size, it cannot differentiate between patients with cardiac dilatation and those with increased ventricular filling volumes secondary to myocardial hypertrophy. While both are predictors of increased risk of cardiovascular events, further diagnostic studies, including contrast-enhanced MDCT or echocardiography, would be necessary to clarify the predictive value of increased LV size. In addition, that CTR was not correlated to LV geometry must be stated under the limitation we derived CTR from images, which were acquired in supine position.

CONCLUSION

Compared with the traditional CTR measure, 3D end-diastolic LV volume and size can be accurately determined using a straightforward and highly reproducible 2D LV area measurement applicable across a wide range of LV volumes. This 2D LV area method could provide additional information on the risk of cardiovascular events on imaging already performed to detect coronary artery calcification. Future studies will aim to determine the impact of 2D LV area-derived measurements on risk stratification.

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Figure 1.

Two short axis images of a contrast-enhanced cardiac CT (A + B, slice thickness 8 mm; green contour: epicardial border; red contour: endocardial border) and the 3D reconstruction of the end-diastolic left ventricular mass and volume using CT QMASS (C; green contour: epicardial border; red contour: endocardial border).

Figure 2.

2D LV area measurements on contrast-enhanced (**A**, 2D LV Area = 43 cm²) and non-contrast-enhanced (**B**, 2D LV area = 41 cm²) images. 2D LV area was defined as the region bounded by the outer border of the left ventricle, the anterior interventricular groove (where the left anterior descending coronary artery resides) and the left posterior interventricular groove.

Figure 3. Bland Altman Plot showing the difference (in cm^3) between 3D measured end-diastolic left ventricular (LV) size and end-diastolic LV size, calculated based on 2D LV area and the derived formula (Equation 1).

$$3D\text{ LV size}_{\text{calculated}} = 2D\text{ LV area} \times 7.4\text{cm} - 82.0\text{cm}^3$$

Equation 1.

Formula to calculate 3D LV size from the measured 2D LV area.

Table 1

Demographics and LV parameters of forty-five subjects who underwent contrast-enhanced MDCT; SD: standard deviation.

Variable	Mean $\pm$ SD, or Percentage (Frequency)	Minimum	Maximum
Gender (female)	49% (22)	---	---
Age (years)	56.0 $\pm$ 12	33	85
2D Left Ventricular Area, end-diastolic (cm ²)	47.5 $\pm$ 8	33.6	67.9
3D Left Ventricular Volume, end-diastolic (cm ³)	148.9 $\pm$ 45	84.4	284.2
3D Left Ventricular Mass, end-diastolic (g)	124.2 $\pm$ 34	67.2	227.7
3D Left Ventricular Size, end-diastolic (cm ³)	267.2 $\pm$ 66	158.7	427.8
direct Transverse Cardiac Diameter (dTCD, cm)	14.7 $\pm$ 2	11.4	18.3
Cardiothoracic ratio (CTR)	0.54 $\pm$ 0.05	0.44	0.67

Table 2

Pearson correlation between the 2D-derived measurements (LV Area, dTCD, CTR) and traditional 3D-based LV parameters

	3D Left Ventricular Volume			3D Left Ventricular Mass			3D Left Ventricular Size			2D Left Ventricular Area		
	r	p		r	p		r	p		r	p	
2D Left Ventricular Area	0.68	<.0001		0.73	<.0001		0.82	<.0001		---	---	---
direct Transverse Cardiac Diameter (dTCD)	0.47	0.004		0.44	0.008		0.52	0.001		0.51	0.001	0.001
Cardiothoracic Ratio (CTR)	0.17	0.32		0.01	0.94		0.12	0.51		0.16	0.35	0.35