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Characterization and normal measurements of the left ventricular outflow tract by ECG-gated cardiac CT: implications for disorders of the outflow tract and aortic valve.

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Abstract

Objectives: To demonstrate the morphology of the left ventricular outflow tract (LVOT) on ECG-gated coronary CTA (cCTA) and to establish normal values for LVOT measurements.

Background: Normal values for LVOT area on cCTA have not been established in the literature. Recent studies suggest that cCTA provides clear definition of the LVOT, and that normal LVOT morphology may not be round as is routinely assumed when the continuity equation is applied during echocardiography.

Methods: Institutional review board approval was obtained for retrospective review of cCTA studies. Two independent readers measured antero-posterior (AP) and transverse diameters of the LVOT, and performed LVOT planimetry. Measurements were correlated with maximum aortic root diameter and patient body surface area.

Results: Excellent interobserver agreement was observed for all measurements. The LVOT was ovoid, with a larger transverse diameter compared to AP diameter during diastole and systole ($p < 0.001$). However, the ratio of AP to transverse diameter was closer to 1.0 during systole ($p < 0.001$). Mean indexed LVOT area was minimally larger in systole as compared to diastole ($p = 0.01-0.04$), and was larger in males as compared to females during diastole ($p \leq 0.001$) and systole ($p \leq 0.01$). Mean LVOT area indexed to body surface area is $2.3 \pm 0.5 \text{cm}^2/\text{m}^2$ in females and $2.6 \pm 0.7 \text{cm}^2/\text{m}^2$ in males. LVOT area demonstrated significant correlation with aortic root diameter.

Conclusions: The normal LVOT is ovoid in shape. Although the LVOT is more circular during systole, the AP diameter remains smaller than the transverse diameter throughout the cardiac cycle. The oval shape of the LVOT has important implications when LVOT area is calculated

from LVOT diameters. Normal LVOT area values established in this study should facilitate diagnosis of the fixed component of LVOT obstruction.

Condensed Abstract

In this study we demonstrate the morphology of left ventricular outflow tract (LVOT) on ECG-gated CT and establish normal values for LVOT measurements. Two independent readers

measured antero-posterior (AP) and transverse diameters of LVOT, and performed LVOT planimetry. Although the LVOT is more circular during systole, the AP diameter remains smaller than the transverse diameter throughout the cardiac cycle. Tables of normal LVOT area are provided to assist in the diagnosis of LVOT obstruction.

Abbreviations

LVOT = left ventricular outflow tract

LVOTd = left ventricular outflow tract diameter

cCTA = coronary CT angiography

TTE = transthoracic Doppler echocardiography

AP = anteroposterior diameter

TRV = transverse diameter

BSA = body surface area

Introduction

A diagnosis of left ventricular outflow tract (LVOT) obstruction is suggested by an elevated gradient in the LVOT in the setting of a normal aortic valve. LVOT obstruction is classified into two categories – dynamic and fixed, which may coexist. Dynamic LVOT obstruction is classically associated with primary hypertrophic cardiomyopathy, a genetic disorder of sarcomeric proteins (1). Many of these patients demonstrate asymmetrical hypertrophy of the ventricular septum and dynamic left ventricular contraction, which draw the anterior mitral valve leaflet or its chordal apparatus into the LVOT during mid-late systole (2). Fixed LVOT obstruction is a congenital abnormality where reduced outflow tract area may be related to fibromuscular narrowing, a discrete fibrous ring or a membrane. A dynamic component that changes in severity during ventricular ejection can coexist with fixed obstruction, complicating the assessment and treatment of LVOT obstruction (3).

Two-dimensional transthoracic Doppler echocardiography (TTE) is widely used for diagnosis of LVOT obstruction by measuring Doppler-derived pressure gradients (4). Decisions regarding the timing of surgery for fixed LVOT obstruction are based on Doppler-derived gradient measures (5,6). However, this method has inherent limitations, such as variation in gradients with changes in cardiac output, and the challenge of separating fixed from dynamic components of gradients measured in the LVOT. Accurate depiction of the shape and size of the LVOT is critical in this decision process. Thus, the ability to produce high resolution static and dynamic images of the LVOT throughout the cardiac cycle with ECG-gated CT angiography provides a unique opportunity for evaluation of LVOT obstruction.

Quantification of blood flow through the LVOT and aortic valve by TTE is based upon a combination of grayscale measurements of LVOT diameter and Doppler measurements of LVOT and aortic valve gradients. The method involves measuring LVOT diameter (LVOTd) in the anterior-posterior dimension in the parasternal long axis view during midsystole. Current recommendations suggest that LVOTd measurements should be averaged from three or more beats (7). Based upon the assumption of a circular LVOT, LVOTd is used to calculate LVOT area (πr^2). Doppler-derived measurements of LVOT blood flow are combined with LVOT area to estimate cardiac output and shunt flow. In the setting of aortic stenosis, the same Doppler-derived measurements of LVOT blood flow are used to calculate aortic valve area based upon the continuity equation (8). As LVOT area is related to the square of LVOTd, any error in calculating LVOT area will be magnified in terms of blood flow and valve area calculations.

To our knowledge, there are no established normal reference values for LVOT area in the cardiology literature. Furthermore, a recent study using ECG-gated CTA suggests that estimates of aortic valve area based upon the continuity equation may be incorrect based upon a flawed assumption of a circular LVOT (9). We designed this study to demonstrate the true morphology of the normal LVOT and to establish normal values for LVOT measurements during systole and diastole.

Methods

Study Population

Institutional review board approval was obtained for retrospective review of coronary CT angiographic (cCTA) examinations. The requirement for written informed consent was waived for this retrospective analysis. Consecutive patients from April 2008 through July 2011 who had undergone cCTA with helical technique for evaluation of coronary anatomy were identified. Inclusion criteria included normal left ventricular function and a normal aortic valve on the clinical interpretation of the cCTA (n=110). Patients with an abnormal aortic valve (n = 2 with calcified aortic valve) or replaced aortic valve (n = 2 with a prosthetic aortic valve) were excluded from the series. The remaining 106 patients were included in the analysis.

CT Scan Protocol

Imaging was performed with a 256-MDCT scanner (Brilliance iCT, Philips Medical Systems). Standard scanning parameters were set to 120 kVp and 600 mAs/slice. Patients who weighed more than 200 lb (91 kg) based on weight reported by the patient underwent scanning at 700-1,000 mAs/slice.

All patients with initial heart rates greater than 60 beats/minute were treated with intravenous metoprolol (5-20 mg) to a target heart rate of 50-60 beats/minute. Sublingual nitroglycerin spray (800 µg) was administered 2-4 minutes before scanning. Biphasic injection protocol was used with 60-70 ml of ioversol (Optiray 350, Mallinckrodt Imaging) followed by 40 ml of 0.9% saline

solution injected at approximately 5.5 ml/s. ECG-based tube current modulation was used for patients with a regular cardiac rhythm and rate below 65 beats/minute.

CT Imaging Analysis

Reconstructed images with a 3 mm slice thickness were obtained through the aortic root and LVOT with a 25-cm field of view at 10% intervals throughout the cardiac cycle. All measurements were performed on a 3D laboratory workstation (Extended Brilliance Workspace (EBW), Philips Medical Systems). Short axis views of the LVOT and aortic root were obtained at end systole and end diastole (40% and 80% of the R-R interval, respectively) by identifying the LVOT on a standard three chamber long axis view and rotating the volume 90°. The short axis orientation was confirmed by aligning two perpendicular planes parallel to the LVOT and aortic outflow at the level of the aortic valve (Figure 1). Measurements were performed with the left atrium positioned at the bottom of the EBW monitor screen. In order to duplicate the LVOT measurement technique used during echocardiography for the continuity equation, anterior-posterior (AP) and transverse (TRV) diameter measurements of the LVOT were obtained immediately below the level of the aortic valve/annulus (10,11). Planimetry of the LVOT was obtained at this same level by a freehand tracing of the LVOT. Indexed LVOT was computed by normalizing LVOT area to BSA (Mosteller's formula) (12). Maximum aortic root diameter was measured at end-diastole at the level of the sinuses of Valsalva, between the aortic annulus and the sinotubular junction. All measurements were performed by two independent readers – a board-certified radiology fellow with several months of experience on cardiovascular rotation and an undergraduate student with several months of experience performing measurements of the

aortic valve for a prior study. Each reader was independently trained with the CT imaging analysis of 20 cases (independent of the cases included in this study) under the supervision of an attending radiologist.

Statistical Analysis

Statistical analysis was performed using Stata software (version 11.0, StatCorp). Means and standard deviations were calculated for continuous variables, including LVOT diameter and area. To evaluate interobserver agreement between the two readers, Bland-Altman plots were constructed and correlation coefficients were computed on continuous measures. The intraclass correlation coefficient was computed in addition to the Pearson correlation coefficient, as the intraclass correlation is influenced by linear transformations in the data while the Pearson correlation coefficient is insensitive to differences that result from linear transformations. Pearson correlation coefficients were computed to demonstrate correlation of LVOT area with BSA and maximum aortic root diameter. Paired t-tests were used for comparison of AP and TRV diameters, for comparison of AP:TRV diameter ratios between systole and diastole, and for comparison of LVOT areas between systole/diastole, males/females, and Caucasians/African Americans. Hispanics ($n = 2$) and Asians ($n = 1$) were not included in the analysis of ethnicities due to lack of statistical power. All comparisons were performed with paired two-tailed Student's t tests. A value of $p < 0.05$ was considered statistically significant.

Results

Study Population

Of 110 consecutive cases included in this retrospective review, two cases with mechanical aortic valves and two cases with aortic valve calcification were excluded. The remaining 106 patients in the study population included 54 males and 52 females with a mean \pm standard deviation age of 56.7 ± 12.7 years (range 20.3 – 84.0 years). Ethnicities included 74 Caucasians, 27 African Americans, two Hispanics, and one Asian. Ethnicities of two patients were unknown. The BSA mean \pm standard deviation of the patients was 2.0 ± 0.3 m², with a range of 1.3 – 2.9 m².

Interobserver Agreement

The LVOT and aortic root were clearly visualized on all cCTAs. Mean measurement values were very similar between the two independent readers, with limits of agreement of -2.9 to 3.3 mm for AP diameter, -4.7 to 4.9 mm for transverse diameter and -0.92 to 0.99 cm² for area by planimetry (see Figure 2 for Bland-Altman plots). Both intraclass correlation coefficients and Pearson's correlation coefficients demonstrated good to excellent interobserver agreement for all measurements acquired by the two independent readers with values ranging from 0.78 to 0.93 (Table 1), indicating that the measurements of our two readers are in close agreement.

Antero-posterior and Transverse LVOT Measurements

The adult LVOT is ovoid in shape. As demonstrated in Table 2, the TRV diameter is larger as compared to the AP diameter ($p < 0.001$). The difference between the TRV diameter and AP diameter is smaller during systole, but remains significant ($p < 0.001$). The ratio of AP:TRV diameter increases during systole as compared with diastole ($p < 0.001$), suggesting that the LVOT shape is less ovoid (or conversely, more round) during systole.

LVOT Planimetry Area

LVOT areas are summarized in Table 3. The mean normal LVOT area by planimetry during systole was minimally larger than during diastole (Reader #1: $\Delta = 0.06 \text{ cm}^2$, $p = 0.01$; Reader #2: $\Delta = 0.12 \text{ cm}^2$, $p = 0.04$). Mean LVOT for males was significantly larger than the mean LVOT for females during diastole ($p < 0.001$ for Readers #1 and #2) and systole ($p < 0.001$ for Readers #1 and #2).

There was a significant correlation ($p < 0.01$) between LVOT area and BSA, with a correlation coefficient of 0.49 - 0.60. LVOT areas indexed to BSA are summarized in Table 4. Mean LVOT indexed to BSA was minimally larger in systole in comparison to diastole (Reader #1: $\Delta = 0.4 \text{ cm}^2/\text{m}^2$, $p = 0.01$; Reader #2: $\Delta = 0.06 \text{ cm}^2/\text{m}^2$, $p = 0.04$). When stratified by sex, indexed LVOT was larger for males than females during diastole (Reader #1: $p < 0.001$; Reader #2: $p = 0.001$) and systole (Reader #1: $p = 0.001$; Reader #2: $p = 0.01$). There was no significant difference in mean indexed LVOT area between Caucasian and African American patients.

Maximum Aortic Root Diameter and LVOT Planimetry Area

Pearson correlation coefficients for maximum aortic root diameter and LVOT planimetry were 0.61 (Reader #1) and 0.64 (Reader #2) during diastole, and 0.62 (Reader #1) and 0.63 (Reader #2) during systole. The correlation between maximum aortic root diameter and indexed LVOT planimetry was lower (0.45 (Readers #1 and #2) during diastole; 0.44 (Reader #1) and 0.43 (Reader #2) during systole), but remained statistically significant ($p < 0.001$).

LVOT Planimetry Area Compared to Area Assuming a Circular LVOT (πr^2)

Mean systolic LVOT area by planimetry was larger than mean area calculated from the AP diameter assuming a circular LVOT (Reader #1: 4.9 vs. 4.1, $p < 0.0001$; Reader #2: 5.0 vs. 3.9, $p < 0.0001$). Underestimation of LVOT area by the geometric calculation (πr^2) was 16% for reader #1 and 22% for reader #2.

Discussion

Estimates of aortic valve area by ECG-gated CT angiography tend to be larger than those obtained by TTE using the continuity equation (9). A recent review of the CT literature suggests that “the oval rather than round shape of the LVOT is the most likely factor behind this systematic difference” (13). Several small studies using real-time three-dimensional echocardiography have demonstrated the eccentric shape of the LVOT (14,15). The present report is the largest published clinical study of LVOT anatomy using ECG-gated CTA, and establishes normal values for the dimensions and area of LVOT during systole and diastole. Our study confirms that the normal LVOT is ovoid in shape and that a circular estimate of LVOT area based upon the systolic AP diameter results in underestimation of the true LVOT area by 16-22%. Based upon the linear relationship between LVOT area and aortic valve area in the continuity equation, it is obvious that TTE estimates using the continuity equation will also underestimate the true aortic valve area by 16-22%.

Knowing the normal range for LVOT size has direct clinical applications. Using the normal values for LVOT size established by our study, we reassessed two recently encountered patients with suspected LVOT obstruction based upon an increased LVOT gradient of unclear origin (Figures 3 and 4). Neither patient had ventricular hypertrophy, dynamic left ventricular function or a definite explanation for the elevated LVOT gradient found by echocardiographic evaluation. The first of these patients had a mildly elevated fixed gradient in the outflow tract with an anatomically small outflow tract confirmed by CT planimetry (Figure 3). The second patient had elevated dynamic and fixed gradients in the outflow tract which were explained by the combination of a small outflow tract with systolic anterior motion of mitral chordal structures (Figure 4). LVOT measurements of our study explained the reason for the fixed LVOT gradients

in both patients by confirming the outflow tracts were anatomically small. CT imaging also demonstrated the anatomic basis for both the fixed and dynamic obstruction in the second patient.

Normal ranges for echocardiographic measurements are frequently provided as gender specific values indexed to BSA. The normal range for gender specific indexed LVOT area is narrower as compared to the normal range for non-indexed LVOT area, while still allowing for variation of LVOT area based upon patient size. For example, based upon the reported values by Reader #1 in table 4, a theoretical 50 kg female with a height of 168 cm (BSA = 1.52 m²) would have an expected LVOT area of 3.38 ± 0.62 cm², while a 90 kg male with a height of 178 cm (BSA = 1.95 m²) would have an expected LVOT area of 5.01±1.09 cm². The LVOT area of 3.59 cm² demonstrated in figure 3 is 1.6 standard deviations below the mean for the male patient in figure 3 with a BSA of 2.14 m². The LVOT area of 2.41 cm² demonstrated in figure 4 is 2.7 standard deviations below the mean for the male patient in figure 4 with a BSA of 2.28 m².

Use of gender-specific indexed values of LVOT area is supported by significant differences in LVOT area between males and females, and by the significant correlation between LVOT area and BSA. As illustrated in the example above, gender specific values will provide a more sensitive diagnosis of reduced LVOT, particularly in larger male patients. However, since ECG-gated CTA scans are usually interpreted without knowledge of BSA, non-indexed values for LVOT area are also reported in this study. Based upon our experience, we suggest that planimetry of the LVOT should be useful for evaluation of the fixed component of LVOT obstruction when present alone or concurrently with dynamic LVOT obstruction.

The observed correlation between LVOT area and maximum aortic root diameter suggests that it might be useful to provide normal range values for LVOT indexed to maximum aortic root diameter as well. However, cardiac measurements are not generally indexed to aortic size. Furthermore, variations in aortic size may be related to other pathologic conditions such as aneurysmal dilatation, which should not necessarily impact the normal LVOT size. For these reasons, LVOT measurements were not indexed to aortic size in this study.

Our study has several limitations. The patient sample was retrospectively identified, raising the possibility of selection bias impacting LVOT area. To minimize obvious sources of bias, patients with a visible abnormality in the LVOT or aortic valve were excluded. Second, our two observers had limited experience in evaluating ECG-gated CTAs prior to this study. Nonetheless, the excellent interobserver agreement in this study suggests that measurements of LVOT areas can be accurately reproduced from ECG-gated CTAs on a 3D laboratory workstation with some basic training.

We conclude that measurement of LVOT area from ECG-gated CTA is reproducible with a high degree of interobserver agreement, and can be useful for the assessment of suspected LVOT obstruction. Furthermore, cine CTA images obtained throughout the cardiac cycle can explain the anatomic basis for both fixed and dynamic components of LVOT obstruction. Our confirmation of the non-circular shape of the LVOT might lead to changes in the way LVOT areas and flows are calculated with TTE and the continuity equation, improving the accuracy with which valve area, cardiac output and shunt calculations are made echocardiographically, and potentially altering the decision tree for treatment of LVOT obstruction.

Table 1. Correlation Coefficients for Interobserver Agreement

		Antero- Posterior Diameter of LVOT	Transverse Diameter of LVOT	LVOT Area by Planimetry	Maximum Aortic Root Diameter
End Diastole	Pearson	0.88	0.79	0.94	0.91
	Intraclass	0.88	0.79	0.93	0.90
End Systole	Pearson	0.81	0.84	0.91	---
	Intraclass	0.78	0.82	0.90	

Table 2. AP:TRV Ratios of LVOT*

		Anteroposterior Diameter (mm)	Transverse Diameter (mm)	AP:TRV Ratio
End Diastole	Reader #1	20.77 ± 2.93	28.33 ± 3.57	0.74 ± 0.07
	Reader #2	20.89 ± 3.24	28.39 ± 3.77	0.73 ± 0.09
End Systole	Reader #1	22.68 ± 3.09	27.02 ± 3.50	0.84 ± 0.08
	Reader #2	21.93 ± 3.54	27.73 ± 3.80	0.79 ± 0.09

*All values are mean ± standard deviation.

Table 3. LVOT Planimetry Area*

		Overall	Gender		Ethnicity	
		(n = 106)	Females (n = 52)	Males (n = 54)	African Americans (n = 27)	Caucasians (n = 74)
End Diastole	Reader #1	4.81 ± 1.24	4.08 ± 0.81	5.52 ± 1.18	4.43 ± 0.96	4.95 ± 1.33
	Reader #2	4.86 ± 1.33	4.11 ± 0.84	5.57 ± 1.34	4.48 ± 1.09	4.99 ± 1.42
End Systole	Reader #1	4.88 ± 1.25	4.18 ± 0.86	5.55 ± 1.20	4.52 ± 1.00	5.01 ± 1.32
	Reader #2	4.98 ± 1.41	4.28 ± 0.97	5.65 ± 1.45	4.47 ± 1.13	5.17 ± 1.47

*All values are mean ± standard deviation in cm².

Table 4. LVOT Planimetry Area Indexed to BSA*

		Overall	Gender		Ethnicity	
		(n = 106)	Females (n = 52)	Males (n = 54)	African Americans (n = 27)	Caucasians (n = 74)
End Diastole	Reader #1	2.38 ± 0.50	2.20 ± 0.39	2.55 ± 0.53	2.27 ± 0.40	2.42 ± 0.54
	Reader #2	2.40 ± 0.58	2.22 ± 0.46	2.58 ± 0.63	2.29 ± 0.47	2.44 ± 0.63
End Systole	Reader #1	2.41 ± 0.52	2.25 ± 0.41	2.57 ± 0.56	2.32 ± 0.44	2.45 ± 0.56
	Reader #2	2.47 ± 0.63	2.31 ± 0.50	2.62 ± 0.70	2.29 ± 0.52	2.54 ± 0.67

*All values are mean ± standard deviation in cm²/m².

Figure Titles/Legends

Figure 1. Measurement of the normal LVOT from ECG-gated CT angiography. A.

Coronary CT angiographic image in the long axis of the left ventricle and ascending aorta. The plane of the LVOT is defined just below the level of the aortic valve. **B.** Coronary CT angiographic image at 90° to the image in part A. The plane of the LVOT is again defined parallel to and just below the aortic valve. **C.** Short axis coronary CT angiographic image immediately below aortic valve/annulus defined by the planes in A and B, shows LVOT in cross section. Note the oval shape of the LVOT. The transverse diameter is longer when the left atrium lies posterior to the LVOT. **D.** Diameter measurements. Anteroposterior diameter of LVOT corresponds to the minor axis, and transverse diameter of LVOT corresponds to major axis of LVOT. **E.** Planimetry of the LVOT was obtained by a freehand tracing of the LVOT.

Figure 2. Bland-Altman plots for: (A) anteroposterior diameter, (B) transverse diameter, and (C) planimetry of left ventricular outflow tract measured at end-systole. Plots show the mean of the two readers' measurements on the x-axis, and the difference between the two readers' measurements on the y-axis.

Figure 3. 40-year-old man (BSA 2.14m²) with unclear history of repaired congenital aortic stenosis. Transesophageal echocardiography demonstrated an elevated velocity of 1.9m/s through the LVOT at rest despite a normal opening of the aortic valve (2.7cm² by planimetry). **A.** Coronary CT angiographic image in three-chamber view shows normal systolic opening of the aortic valve with no evidence for systolic anterior motion of the mitral valve. **B.** Short axis

shows LVOT in cross section with anteroposterior diameter (minor axis) of 1.8 cm and transverse diameter (major axis) of 2.6 cm. **C.** Short axis with free hand tracing of LVOT for planimetry demonstrates an LVOT area of 3.59 cm^2 (indexed area = $3.59/2.14 = 1.68$) which is approximately 1.6 standard deviations below the expected mean male LVOT area (see Table 4).

Figure 4. 61-year-old man (BSA 2.28m^2) with normal left ventricular systolic function. A fixed LVOT gradient of 55 mmHg as well as a second dynamic gradient of 54 mmHg were measured by transthoracic echocardiography. The aortic valve was mildly thickened with normal motion. **A.** Coronary CT angiographic image in three-chamber view demonstrates coaptation of the mitral valve. The coapted leaflet tips are tilted toward the interventricular septum; cine images (not shown) were interpreted as demonstrating systolic anterior motion of the associated chordal structures. **B.** Short axis coronary CT angiographic image shows LVOT in cross section with anteroposterior diameter (minor axis) of 1.6 cm and transverse diameter (major axis) of 2.1 cm. **C.** Short axis coronary CT angiographic image shows free hand tracing of LVOT in cross section with planimetry measure of 2.41cm^2 (indexed area = $2.41/2.28 = 1.06$) which is 2.7 standard deviations below the expected mean male LVOT area (see Table 4). The CTA was helpful in demonstrating both the dynamic and fixed components of the LVOT obstruction.

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