

Use of Advanced CT Technology to Evaluate Left Atrial Indices in Patients with a High Heart Rate or with Heart Rate Variability: The Converge Registry

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We intended to assess the ability of current-generation 256-slice coronary CT angiography (CCTA) to measure left atrial volume (LAV), comparing patients with a high heart rate (HiHR) of at least 70 bpm and patients with heart rate variability such as atrial fibrillation (AFib). **Methods:** Using the prospective Converge Registry of patients undergoing 256-detector CCTA on a Revolution scanner, we enrolled 121 HiHR patients (74 men; mean age, 62.7 ± 12.5 y) and 102 AFib patients (72 men; mean age, 60.5 ± 11.0 y) after obtaining informed consent. Quantitative data analysis of LAV was performed using automated methods, and end-systolic phases were chosen for measurements from CCTA. A Student *t* test, Wilcoxon rank-sum test, or χ^2 test assessed baseline parameters. Univariate and multivariate linear regression analysis was used to assess LAV and LAV index (LAVI) while adjusting potentially confounding variables. **Results:** Mean LAV was significantly higher in AFib subjects (148.6 ± 57.2 mL) than in HiHR subjects (102.1 ± 36.5 mL) ($P < 0.0001$). Similarly, mean LAVI was significantly higher in AFib subjects (72.4 ± 28.1 mL/m²) than in HiHR subjects (51.5 ± 19.0 mL/m²) ($P < 0.0001$). After adjusting for age, body mass index, sex, diabetes, hypertension, hyperlipidemia, and smoking, subjects with AFib had, on average, LAV measures higher by 41.2 ± 6.7 mL and LAVI values higher by 23.1 ± 3.4 mL/m² ($P < 0.0001$). **Conclusion:** Misalignment and motion artifacts in CCTA images affect diagnostic CT performance, especially in patients with elevated heart rates or profound arrhythmia. However, the new-generation Revolution CCTA provides detailed information on left-atrium-complex morphology and function, in addition to coronary anatomy, in HiHR and AFib patients without additional radiation, scanning, or contrast requirements.

Key Words: left atrial volume; heart rate variability; high heart rate; arrhythmia; motion artifacts

CT technology has significantly improved since its introduction into clinical practice in 1972 (1). Coronary CT angiography (CCTA) is a rapidly evolving, noninvasive imaging technique to evaluate the presence, extent, and severity of coronary artery disease (2). In cardiac CT imaging modalities such as coronary artery calcium scoring and CCTA, the patient's high, irregular, or high and irregular heart rate variation plays an important role in imaging quality. Prescan β -blockers are commonly administered to achieve a resting heart rate of less than 65 bpm, thereby reducing the number of motion artifacts. However, previous studies have demonstrated a significant negative correlation between mean heart rate and image quality ($r = 0.80$, $P < 0.001$) (3). During the scanning, a significant variation in heart rate (e.g., from 41 to 100 bpm, equivalent to an R–R interval ranging from 1,463 to 600 ms) results in improper recording of electrocardiogram-gated data and severe discontinuities in the reconstructed cardiac images, especially in individuals with atrial fibrillation (AFib) or other arrhythmia (4). The temporal window suited for imaging (e.g., mid- to end-diastole) is shortened by the increased motion speed of coronary vessels in high-heart-rate (HiHR) patients, whereas the temporal variability of the diastolic phase is increased between contiguous cardiac cycles in individuals with AFib. This inaccurate locating of temporal windows creates motion artifacts and prevents adequate visualization and assessment of coronary vessels. However, progressive improvements in the temporal resolution and electrocardiogram-gated capability of new-generation CT scanners minimize motion-related imaging artifacts and may reduce the need for prescan β -blockers (5,6). Electrocardiogram gating with tube-current-modulation capability

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automatically acquires images at the diastolic phase for lower heart rates, as well as acquiring images at both the systolic and the diastolic phases for higher heart rates.

Recent advancements in cardiovascular imaging modalities and their clinical application have contributed significantly to the assessment of left-atrium-complex morphology and function and their interrelationship with the left ventricle, aorta, and pulmonary artery along the coronary arteries. Previous studies have shown that 3-dimensional echocardiography has better accuracy and reproducibility than 2-dimensional echocardiography; however, 3-dimensional echocardiography is not widely used in clinical practice (5). The echocardiographic parameters of the left atrium include left atrial anteroposterior diameter, left atrial area, and left atrial volume (LAV). These parameters are more globally descriptive, and they remain normal in the early phases of disease. Furthermore, LAV measured by echocardiograms is highly dependent on image quality and has been shown to be underestimated when compared with LAV measured by contrast-enhanced cardiac CT or cardiac MRI (6).

The aim of the present study was to investigate the ability of a current-generation coronary CT angiography (CCTA) scanner to measure LAV in patients with a high and irregular heart rate.

MATERIALS AND METHODS

Study Population

Using the prospective Converge Registry of patients undergoing 256-detector CCTA on the Revolution scanner (GE Healthcare), we identified 121 HiHR patients with sinus rhythm (74 men [71%]; mean age, 62.7 ± 12.5 y) and 102 patients with AFib (72 men [61%]; mean age, 60.5 ± 11.0 y). In total, 223 eligible participants (146 men [65%]; mean age, 61.7 ± 11.9 y), with an age of 25–80 y, a weight of less than 136 kg (300 lb), a heart rate of at least 70 bpm, and a clinical indication for CCTA, were enrolled after providing written informed consent using a form that was approved by the Institutional Review Board of the Lundquist Institute. The study was conducted according to the principles expressed in the Declaration of Helsinki.

We excluded patients with insufficient CCTA image quality ($n = 4$) or a known history of valvular diseases ($n = 1$), cancer ($n = 1$), chronic kidney disease (estimated glomerular filtration rate < 60 mL/min/1.73 m² within 30 d of the CT) ($n = 3$), or intravenous contrast allergy ($n = 2$).

Evaluation of Cardiovascular Risk Factors

Before CCTA, demographics were obtained for each participant, along with blood pressure, height, weight and a focused history of cardiovascular risk factors. Clinical history was ascertained through a patient interview and a clinical questionnaire. Previous history of hypertension, diabetes mellitus, or hyperlipidemia was determined, along with the medications targeted at managing them. Current cigarette smokers or those who quit smoking within 3 mo of testing were recorded as having a positive smoking history. A clinically significant family history of coronary artery disease was defined as that occurring in a female relative younger than 65 y or a male relative younger than 55 y.

CCTA Scan and Image Acquisition

Both contrast and non-contrast scans were performed to evaluate the extent of coronary artery calcium and coronary plaque

volume, as previously published (7–10). Prescan oral metoprolol was used to achieve a resting heart rate of less than 65 bpm, and we enrolled those individuals whose heart rate was at least 70 bpm even after β -blockade therapy. Sublingual nitroglycerin, 0.4 mg, was administered immediately before contrast injection. The contrast medium (Omnipaque 350; GE Healthcare) was injected at a rate of 5.0 mL/s using a triple-phase protocol: 60 mL of contrast followed by 20 mL of contrast plus 30 mL of saline followed by a 50-mL saline flush. For the contrast-enhanced CCTA scan, we used electrocardiogram gating, with the scan beginning 20 mm above the level of the left main artery and continuing to 20 mm below the inferior myocardial apex. The scan parameters were a rotation speed of 0.28 s/rotation (with no table motion), 256-slice CT \times 0.625-mm collimation, tube voltage of 120 kVp, and an effective amperage of 122–740 mA based on the body mass index of the patient, which was automatically determined by the system as previously published (7–10). The autogating capability of the Revolution scanner automatically acquires the diastolic phase for lower heart rates and both the systolic and the diastolic phases for higher heart rates. Each scan was done in a single-beat acquisition within 1 cardiac cycle, regardless of heart rate. After scan completion, multiphase reconstruction of the CCTA scans was performed, with reconstructed images from 70% to 80% by 5% increments and from 5% to 95% by 10% increments.

Before CCTA, a prospective non-contrast coronary calcium scan was performed. For quantitative assessment of coronary artery calcium, the Agatston score was calculated using a 3-mm-thick CT slice and a detection threshold of at least 130 HU involving at least a 1-mm² area per lesion (3 pixels) (11).

LAV Analysis

Quantitative data analyses were performed using automated methods on an Advantage Workstation (version 4.6; GE Healthcare) with software that used a Hounsfield unit–based technique to detect the endocardial border. Volumes were calculated using the Simpson method (12). Images were reconstructed with a 1.25-mm slice thickness. The end-systolic phases were chosen for measurements of LAV. The left atrial appendage and pulmonary veins were not included in the LAV measurement. After adjustment for body surface area, the LAV index (LAVI) was estimated using the formula of Du Bois and Du Bois (13).

Statistical Analysis

Continuous variables are expressed as mean \pm SD, whereas categorical variables are stated as count and percentage. A Student *t* test, Wilcoxon rank-sum test, or χ^2 test assessed differences in all baseline parameters between AFib and HiHR subjects. Univariate and multivariate linear regression analysis was used to examine the relationship between LAV and LAVI while adjusting for potentially confounding variables. A *P* value of less than 0.05 was considered significant. SAS software (version 9.4) performed all statistical analyses.

RESULTS

Baseline demographics and clinical characteristics are summarized in Table 1. Age, sex, smoking use, and hyperlipidemia did not significantly differ between the AFib and HiHR groups, but ethnicity, body mass index, body surface area, self-reported chest pain, diabetes mellitus, and hypertension did.

Mean LAV was significantly higher in AFib subjects (148.6 ± 57.2 mL) than in HiHR subjects (102.1 ± 36.5 mL)

TABLE 1
Baseline Characteristics

Characteristic	Total (n = 223)	HiHR (n = 121)	AFib (n = 102)	P
Age (y)	61.7 ± 11.9	62.7 ± 12.5	60.5 ± 11.0	0.16
Men	146 (65)	74 (61)	72 (71)	0.14
Chest pain	42 (19)	29 (24)	13 (13)	0.03
Hypertension	157 (70)	72 (60)	85 (83)	0.0001
Dyslipidemia	140 (63)	81 (67)	59 (58)	0.16
Diabetes mellitus	67 (30)	24 (20)	43 (42)	0.0003
History of myocardial infarction	31 (14)	10 (8)	21 (21)	0.008
Current smoking	19 (9)	7 (6)	12 (12)	0.11
Body mass index (kg/m ²)	30.6 ± 6.7	28.7 ± 5.9	32.8 ± 6.9	<0.0001
Body surface area (m ²)	2.0 ± 0.3	2.0 ± 0.3	2.1 ± 0.3	0.03
Heart rate (bpm)	71.4 ± 9.8	71.4 ± 9.8	66.5 ± 10.1	0.01
Systolic blood pressure (mm Hg)	131.3 ± 19.2	136.1 ± 18.6	125.5 ± 18.4	<0.0001
Diastolic blood pressure (mm Hg)	78.8 ± 10.9	78.2 ± 11.1	79.5 ± 10.8	0.3893
Coronary artery calcium score	631.65 ± 1,294.9	724.6 ± 1,416.8	524.1 ± 1,135.4	0.227
LAV (mL)	123.4 ± 52.4	102.1 ± 36.5	148.6 ± 57.2	<0.0001
LAVI (mL/m ²)	61.1 ± 25.7	51.5 ± 19.0	72.4 ± 28.1	<0.0001

All comparisons between HiHR and AFib groups were performed using Student *t* test, Wilcoxon rank-sum test, or χ^2 test. Qualitative data are number followed by percentage in parentheses; continuous data are mean ± SD.

($P < 0.0001$). Similarly, mean LAVI was significantly higher in AFib subjects (72.4 ± 28.1 mL/m²) than in HiHR subjects (51.5 ± 19.0 mL/m²) ($P < 0.0001$). After adjusting for age, body mass index, sex, diabetic status, hypertension, hyperlipidemia, history of myocardial infarction, and smoking habits, subjects with AFib had, on average, an LAV higher by 41.2 ± 6.7 mL and an LAVI higher by 23.1 ± 3.4 mL/m² ($P < 0.0001$) (Table 2).

DISCUSSION

This study was, to the best of our knowledge, the first to assess the ability of the 256-slice Revolution CT scanner to measure LAV in patients with high and irregular heart rates. We found significantly higher LAV measurements among individuals with AFib than in HiHR patients ($P < 0.0001$).

Heart rate variability plays a vital role in the diagnostic accuracy of CCTA, and the interexamination heart rate variability results in an inaccurate temporal window of R–R intervals, impairing the electrocardiogram-gated reconstruction image technique. Leschka et al. (14) showed that heart rate variability positively correlated with image quality and that the diagnostic accuracy of CCTA was reduced with increasing heart rate variability ($r = 0.61$, $P < 0.01$). Brodoefel et al. reported a negative correlation between heart rate variability and image quality for all coronary segments and individual coronary arteries, whereas heart rate variability did not affect the diagnostic specificity of dual-source CCTA (15). Ropers et al. (16) demonstrated that the diagnostic accuracy of CCTA was not influenced by heart rate. Furthermore, Zhang et al. (17) concluded that average heart rate had no effect on the diagnostic accuracy of cardiac CT; whole-heart-rate variability was found to have a significant effect on the sensitivity and specificity of CCTA. Misalignment and motion artifacts in CTA images affect the

CT diagnostic performance, especially in patients with elevated heart rates or profound arrhythmia. In the past few years, advances in software (e.g., automatic recognition and editing of heart rhythm irregularities) and scanner technology (e.g., faster rotation times or increased temporal resolution) have allowed for effective and efficient imaging to provide accurate measurements of cardiac volumes and function, compared with prior generations of CCTA devices. All these previous studies assessed the diagnostic accuracy and image quality of cardiac CT for coronary arteries. In the present study, we evaluated the ability of cardiac CT to measure LAV in individuals with a variable heart rate.

CCTA provides full volumetric data on all 4 cardiac chambers, making LAV measurement possible without the need for any geometric assumption about the left atrial parameters (18). The determination of left atrial function simultaneously with left ventricle function, aortic function, and pulmonary artery hemodynamics will provide a better

TABLE 2
Relationship Between Left Atrial Measurements and HiHR or AFib Subjects

Parameter	Univariate, unadjusted			Multivariate, adjusted*		
	β	SE	P	β	SE	P
LAV	-46.42	6.33	<0.0001	-41.18	6.76	<0.0001
LAVI	-20.86	3.17	<0.0001	-23.10	3.39	<0.0001

*Adjusted for age, body mass index, sex, diabetic status, hypertension, hyperlipidemia, history of myocardial infarction and smoking habits.

β = standardized regression coefficient.

understanding of the role of the left atrium in cardiovascular homeostasis in healthy subjects and patients with cardiovascular diseases. CCTA measures the LAV more accurately than cardiac MR does (19). Because of the high contrast-to-noise ratio, CCTA provides high image quality with spatial temporal resolution, excellent endocardial border definition, and software-based motion correction (20). The iterative reconstruction ability of new-generation CT scanners reduces image noise without compromising diagnostic quality, thus permitting a significant reduction in effective radiation dose. Andreini et al. (21) reported a 98.5% diagnostic accuracy for a Revolution scanner equipped with 0.23-mm spatial resolution, a 0.28-s gantry rotation time, and an intracycle motion correction algorithm, in the detection of coronary artery disease in AFib patients with a mean heart rate of 83 bpm. We used similar parameters for the Revolution scanner to measure LAV in our study population. Additionally, a previous study demonstrated that the new-generation Revolution scanner obtains better-quality images at a lower radiation than is possible with the Aquilion ONE ViSION CT scanner (Toshiba) ($1.50 + 0.75$ mSv vs. 1.9 mSv; interquartile range, 1.7–2.7 mSv; $P = 0.01$) (20).

Previous studies have shown that LAV measurements are more accurate than linear-dimension measurements in evaluating asymmetric left atrial remodeling and are considered a strong predictor of cardiovascular disease (22). Leschka et al. (23) demonstrated that dual-source CCTA provides the best image quality at diastole (70% of the R–R interval) at various heart rates (35–117 bpm). Walker et al. (24) reported normal LAVI values of 20.8 to 49.8 mL/m² for cardiac CT at the mid-diastolic phase at slow and regular heart rates (LAV was reported as 37.7–98.7 mL), and Osawa et al. (25) reported LAVI values of 35.2 ± 10.9 mL/m² in young adults with suspected coronary artery disease. These studies excluded the AFib population, and moreover, the mean heart rate of their study populations was less than approximately 70 bpm. The mid-diastolic-phase mean values of LAV (HiHR, $102.1 + 36.5$ mL; AFib, $148.6 + 57.2$ mL) and LAVI (HiHR, $51 + 19.0$ mL/m²; AFib, $72.4 + 28.1$ mL/m²) in our study population were slightly larger, possibly because our HiHR and AFib population had documented coronary artery disease.

Left atrial enlargement has emerged as a strong predictor of common cardiovascular disease outcomes such as AFib, stroke, congestive heart failure, and cardiovascular death (26). Left atrial dilation promotes stasis of blood, which in turn increases the risk of thrombus formation and the potential for embolization. Several studies have shown the clinical usefulness of Doppler-derived left ventricular diastolic function in predicting cardiovascular mortality and morbidity (27,28). However, due to the significant left ventricle measurements, attention was drawn toward diastolic dysfunction markers, such as LAV. Tsang et al. demonstrated a strong association between LAV and left ventricular diastolic dysfunction (26). The Stroke Prevention in Atrial Fibrillation study (29) and the Cardiovascular Health Study (30) reported a significant association between stroke

and left atrial dimensions. Early detection of left atrial dysfunction is proposed to provide insight into the pathophysiology and clinical management of several diseases in which left atrial dysfunction may be present.

The current study had several limitations. First, the LAV measured from CCTA was not compared with simultaneous echocardiography or MRI or with previous-generation CT scanners. Second, left ventricular function, aortic function, and pulmonary artery hemodynamics were not determined along with LAV. Third, we did not assess any follow-up measurements of LAV. Fourth, we did not show the relationship between LAV and conventional risk factors. Additional research is necessary to determine the importance of volumetric LAV in predicting mortality and morbidity in high-risk individuals such as those with AFib, stroke, congestive heart failure, or cardiovascular death.

CONCLUSION

Misalignment and motion artifacts in CCTA images affect diagnostic CT performance, especially in patients with elevated heart rates or profound arrhythmia. However, the new-generation Revolution CCTA provides detailed information on left-atrium-complex morphology and function, in addition to coronary anatomy, in HiHR and AFib patients without additional radiation, scanning, or contrast requirements.

DISCLOSURE

Matthew Budoff performs work for the National Institutes of Health and GE Healthcare. The study was funded by GE Healthcare. No other potential conflict of interest relevant to this article was reported.

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