



Left atrial volume, a simple measure but strong predictor of cardiovascular events in non-contrast computed tomography

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Left atrial volume (LAV) emerged as a marker of cardiovascular disease many years ago with a large body of supporting scientific evidence. Since then, it has found clinical utility in the cardiovascular field, especially in cardiology and neurology. It remains of great interest as to why so simple a measure carries such a strong prognostic impact for a wide variety of cardiovascular diseases [1,2]. Among these disorders are ischemic heart disease, heart failure (HF) [3–6], hypertrophic cardiomyopathy (HCM) [7], atrial fibrillation (AFib) and even for predicting stroke in the absence of AFib. To understand why LAV is so sensitive [8], we look to the mechanisms of left atrial remodeling with a common endpoint of increased LAV, left atrium (LA) dilatation and hypocontractility, and eventually resulting in AFib [1] (Table 1). Identifying increased LAV will allow early detection of LA dysfunction [1] and alert clinicians to treat the patient in a timely manner to reduce the negative consequences of long-standing incompletely treated diseases or pathologic states (Table 1).

The power of LAV has been tested in long-term follow up of patients, underscoring its predictive nature [9]. This predictive capability has been largely validated with echocardiography (Echo), where its value

was originally confirmed, and with other newer and more accurate methods such as cardiovascular magnetic resonance (CMR) and contrast-enhanced cardiac computed tomography (CT). The latter has traditionally been performed using retrospective acquisition of coronary computed tomography angiography (CCTA) images in different pathologic states (such as those described in Table 1).

The accuracy of the different imaging modalities has been largely documented, however two-dimensional echocardiographic (2D-echo) methods are somewhat limited, [10] three-dimensional (3D) echocardiography (3D-echo) has better accuracy and reproducibility but is not widely used in routine clinical practice (despite newer rapid imaging and analysis strategies that improve its utilization) [10], atrial strain imaging can detect LA dysfunction before the manifestation of LA structural changes since its parameters are influenced by loading conditions, rhythm irregularity and fibrosis [11], but, as it is for 3D-echo, is not widely used in routine clinical practice. CMR is the gold standard method for the assessment of cardiac structure and function [12] due to its strong accuracy and reproducibility, and LAV reference ranges are published and validated for different gender and ages [13]. CCTA, based on its retrospective acquisition, allows 3D visualization of the LA and is readily available for analysis without additional testing with high spatial resolution across the cardiac cycle [14].

In the real world, obtaining this strong predictor in asymptomatic population is limited, since it is not feasible to perform 3D-echo, CMR and CCTA just to obtain the LAV in this group. 3D-echo and CMR are not ubiquitous, and CCTA requires somewhat greater radiation doses, even with dose-limiting protocols [15], since it necessitates retrospective acquisition and the use of contrast media.

Thus, given the clinical relevance of LAV assessment, it would be preferable to have a highly accurate and reproducible method such as those described, but also one that is widely used and that overcomes the real-world limitations described.

Toward this end, Cardona et al. developed a method to test whether a highly reproducible and accurate LAV could be obtained on more commonly-performed non-contrast coronary artery calcium (CAC) scans. Their study is particularly clinically relevant since CAC scans are widely available, have a well-established operator-independent protocol, do not require contrast media, and are acquired with radiation doses significantly lower than CCTA.

Cardona et al. in their recent publication [16] provide a valuable contribution by measuring LAV using the standard CAC protocol,

Abbreviations: LAV, left atrial volume; HF, heart failure; HCM, hypertrophic cardiomyopathy; AFib, atrial fibrillation; LA, left atrium; Echo, echocardiography; CMR, cardiovascular magnetic resonance; CT, computed tomography; CCTA, coronary computed tomography angiography; 2D-echo, two-dimensional echocardiographic; 3D, three-dimensional; 3D-echo, three-dimensional echocardiography; CAC, coronary artery calcium.

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Table 1
Underlying pathophysiologic mechanisms that affect LA size and function.

Pathophysiologic mechanism	Effect on LA	Examples of diseases and pathologic states
Pressure and/or volume overload	Hypertrophy, necrosis, apoptosis and fibrosis at cellular and extracellular matrix levels [1]	• LV systolic dysfunction (HFrEF) [3,4] • LV diastolic dysfunction (HEpEF) [5,6] • Ischemic heart disease [3,4] • Post-myocardial infarction [3,4] • Hypertension • Aortic stenosis • Aortic insufficiency • HCM [7] • Mitral stenosis • Mitral regurgitation • LV dilatation [3,4] • LV myocardial scar [3,4]
	Neurohumoral activation such as atrial natriuretic peptide (ANP) [1,18]	• Iron deposition on the myocardium • Sarcoidosis • Amyloidosis • Obesity • LV hypertrophy on athletes • Aging • Dilated cardiomyopathies • Obstructive Sleep Apnea • AFib
Tachycardia		• Hyperthyroidism • Drug induced tachycardia • Energetic beverages • Caffeine in excess

Abbreviations: **HFrEF:** Heart failure with reduced ejection fraction, **HEpEF:** Heart failure with preserve ejection fraction, **HCM:** Hypertrophic cardiomyopathy, **LV:** Left ventricle, **AFib:** Atrial fibrillation.

and proving that it is feasible and highly accurate compared with the reference standard of CCTA. They overcame certain technical limitations that are attributed to non-contrast CT studies, including not having to modify the standard acquisition protocol, and developing a method to use the mitral valve plane as a landmark in a multiplanar reformatting approach. This new method reduced an important source of variability and low reproducibility, and provided excellent interobserver and intra-observer reproducibility. The authors identified several additional technical characteristics of the non-contrast gated CT scan and of the LA anatomy that allows this approach to be feasible. These included the fact that both CAC scan and CCTA are ECG-gated, that the LA is surrounded by easily identifiable structures on non-contrast CT images, the lower density of the interatrial septum, and that the mitral annulus has specific and easily identifiable landmarks (fat in the auriculo-ventricular groove, the circumflex artery and the coronary sinus).

There is a difference between LAV from CAC scan and from the reference standard on CCTA, due to technical reasons such the potential inclusion of part of the esophageal wall, the overestimation related to the thicker slices of the CAC scans, and the decreased endocardial border definition of the non-contrast enhanced study. Even though these differences were statistically significant, they had little clinical relevance since they only represent 4% of the average measured LA volume.

Normal reference values will need to be established for this approach in an asymptomatic population since the reported values are measured at end-systole and not in mid-diastole as for CAC scans. Likewise, the technique will require validation in symptomatic individuals with pathologic states (Table 1), and in long-term follow-up cohorts to validate its predictive strength.

Cardona et al. have advanced the field by proving that standard CAC scans can be used to quantify LAV. This tool allows the benefit of LAV measurements to be applied to routine CAC scans, and should help to improve cardiovascular risk prediction in asymptomatic populations mainly for those subjects with new-onset AFib [17]. It is likely that

using this method will reclassify the cardiovascular risk of an individual, above and beyond the metric of the CAC score and in addition to conventional risk stratification scales.

Conflict of interest

The author declare that there is no conflict of interest.

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