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STATE-OF-THE-ART PAPER

Left Atrial Size and Function

Role in Prognosis

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The author examines the ability of left atrial size and function to predict cardiovascular outcomes. Data are sufficient to recommend evaluation of left atrial volume in certain populations, and although analysis of atrial reservoir, conduit, and booster pump function trails in that regard, the gap is rapidly closing. In this state-of-the-art paper, the author reviews the methods used to assess left atrial size and function and discusses their role in predicting cardiovascular events in general and referral populations and in patients with atrial fibrillation, cardiomyopathy, ischemic heart disease, and valvular heart disease. (J Am Coll Cardiol 2014;63:493–505) © 2014 by the American College of Cardiology Foundation

The principal role of the left atrium is to modulate left ventricular (LV) filling and cardiovascular performance by functioning as a *reservoir* for pulmonary venous return during ventricular systole, a *conduit* for pulmonary venous return during early ventricular diastole, and a *booster pump* that augments ventricular filling during late ventricular diastole. It is important to recognize the interplay that exists among these atrial functions and ventricular performance throughout the cardiac cycle. For example, although reservoir function is governed by atrial compliance during ventricular systole (and, to a lesser extent, by atrial contractility and relaxation), it is influenced by descent of the LV base during systole and by LV end-systolic volume (1). Conduit function is influenced by atrial compliance and is reciprocally related to reservoir function but by necessity is closely related to LV relaxation and compliance. Finally, atrial booster pump function reflects the magnitude and timing of atrial contractility but is dependent on the degree of venous return (atrial pre-load), LV end-diastolic pressures (atrial afterload), and LV systolic reserve.

Atrial size and function can be assessed with echocardiography, cardiac computed tomography (CCT), and cardiac magnetic resonance (CMR). Although echocardiography is best suited for these tasks because of its availability, safety, versatility, and ability to image in real time with high temporal and spatial resolution, CCT and CMR are complementary in specific clinical instances (2).

The resurgence of interest in atrial size and function has enhanced our understanding of the atrial contributions to cardiovascular performance in health and disease. Although the reasons responsible for this renaissance are multifactorial and include the use of left atrial (LA) volume as a biomarker integrating the magnitude and duration of diastolic LV function and the development of sophisticated, noninvasive indexes of LA size and function, the increasingly recognized importance of LA size and function in determining prognosis and risk stratification is critical and is the focus of this state-of-the-art paper.

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Measuring LA Size

Quantifying LA size is difficult, in part because of the left atrium's complex geometry and intricate fiber orientation and the variable contributions of its appendage and pulmonary veins. LA size is most often measured from M-mode and 2-dimensional echocardiography (2DE). Among these measurements, maximal left atrial volume (LAV) indexed to body surface area (LAVi) is most strongly associated with cardiovascular disease and is the most sensitive in predicting cardiovascular outcomes and providing uniform and accurate risk stratification (3). In 317 patients in normal sinus rhythm, LAVi measured from biplane 2-dimensional (2D) apical views was superior to 4-chamber LA area and M-mode LA dimension in predicting the development of first atrial fibrillation (AF), congestive heart failure (CHF), stroke (cerebrovascular accident [CVA]), transient ischemic attack, acute myocardial infarction (AMI), coronary revascularization, and cardiovascular death over 3.5 years of follow-up. In addition, a graded relationship between cumulative event-free survival and the categorical increment of LA size was demonstrated for LAVi. In that study, the ability of LA size to predict cardiovascular events in patients with AF was poor, irrespective of the quantitative method used (3). Despite these data and the American Society of Echocardiography's recommendation of LAVi for the quantification of LA size

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Abbreviations and Acronyms

AF = atrial fibrillation

AMI = acute myocardial infarction

CCT = cardiac computed tomography

CHF = congestive heart failure

CMR = cardiac magnetic resonance

CVA = cerebrovascular accident

ε = strain

HCM = hypertrophic cardiomyopathy

LA = left atrial

LAKE = left atrial kinetic energy

LAV = left atrial volume

LAVi = left atrial volume indexed to body surface area

LV = left ventricular

MR = mitral regurgitation

RT3DE = real-time 3-dimensional echocardiography

SR = strain rate

STE = speckle-tracking echocardiography

TDI = tissue Doppler imaging

VTI = velocity-time integral

3D = 3-dimensional

2D = 2-dimensional

2DE = 2-dimensional echocardiography

(4), individual echocardiography laboratories continue to report a variety of 1-dimensional linear and 2D area measurements (5).

The normal LAVi using echocardiography is 22 ± 6 ml/m^2; thus, on the basis of the sensitivity and specificity for predicting cardiac events (3,6–8), the American Society of Echocardiography considers LA enlargement as >28 ml/m^2 (i.e., 1 SD from the mean). However, for the purpose of identifying LV diastolic dysfunction, an LAV cut point >34 ml/m^2 (i.e., 2 SD) was endorsed (9).

Inaccuracies owing to geometric assumptions and foreshortening of the LA cavity with 2D biplane volume methods are overcome with real-time 3-dimensional (3D) echocardiography (RT3DE) (Fig. 1), which has been shown to accurately and reproducibly estimate LAV compared with CMR (10). However, it is difficult to extrapolate cut points derived from the large body of outcome data that were obtained using biplane 2DE, because data using RT3DE are relatively scant. Suh et al. (11) found that RT3DE was a better predictor of cardiovascular events than biplane 2DE in a group of patients with severe LV dysfunction followed for approximately 1 year; in that study, unlike on 2DE, LAVi on RT3DE was an independent risk factor on multivariate analysis. Caselli et al. (12) also reported a better correlation with major adverse cardiovascular events when LAVs were obtained with RT3DE compared with biplane 2DE in 178 outpatients followed for 45 months. Although these data need to be confirmed, they do suggest a clinically important incremental benefit of risk assessment using RT3DE.

LAVs can be accurately measured from acquired 3D datasets using CCT (13,14). However, the radiation exposure and need for iodinated contrast medium relegate CCT largely to an important adjunctive role in LA ablation procedures; moreover, the relatively poor temporal resolution of CCT may preclude accurate measurements of phasic LAVs and atrial function. CMR (considered the "gold standard") provides accurate measurements of LAV with acceptable temporal resolution but is limited by increased costs, decreased availability, an inability to measure phasic volumes with gated 3D sequences, and problems related to gadolinium contrast and an inability to scan patients with intracardiac devices. Because absolute LAVs measured with 2DE are smaller than those measured with CCT or CMR (15,16), it is important to compare volume estimates with reference values that exist for each imaging modality.

Assessing LA Functions

LA function is most often assessed echocardiographically using volumetric analysis; spectral Doppler of transmitral, pulmonary venous, and LA appendage flow; and tissue Doppler and deformation analysis (strain [ε] and strain rate [SR] imaging) of the LA body (Tables 1 to 3, Fig. 2). Although atrial pressure-volume loops can be generated in humans using invasive and semi-invasive means (17,18), these methods are cumbersome, time-consuming, and difficult to apply. CMR can quantify scar and has been useful in predicting the risk for recurrence of AF after LA ablation (19). CCT plays an important role in the pre-procedural, intraprocedural, and post-procedural stages of LA ablation. Both CCT and CMR have been used to assess volumetric LA functions (20–26).

Volumetric methods. A volumetric assessment of LA reservoir, conduit, and booster pump functions can be obtained from LAVs at their maximums (at end-systole, just before mitral valve opening) and minimums (at end-diastole, when the mitral valve closes) and immediately before atrial systole (before the electrocardiographic P-wave). From these volumes, total, passive, and active ejection (or emptying) fractions can be calculated (Fig. 1, Tables 1 to 3).

Spectral Doppler. Doppler waveforms of LA filling (pulmonary venous flow) and LA emptying (transmitral flow) can be used to estimate relative atrial functions. Advantages are their availability and simplicity in acquisition and interpretation. The ratios of peak transmitral early (E) and late (A) velocities (or their velocity-time integrals [VTIs]) and the atrial filling fraction (Avti/[Evti+Avti]) estimate the relative contribution of atrial booster pump function, and the ratio of systolic (S) to diastolic (D) pulmonary venous flow estimates relative reservoir-to-conduit function. The magnitude and duration of reversed pulmonary flow during atrial contraction is used to estimate atrial contractility and LV diastolic pressures (27). Atrial ejection force, the force exerted by the left atrium to accelerate blood into the left ventricle, is another marker of atrial systolic function (28). LA work can be expressed by left atrial kinetic energy (LAKE), which incorporates LA stroke volume and the transmitral Doppler peak atrial velocity (29). Low LA appendage velocities (usually on transesophageal echocardiography) reflect reduced appendage contractile function and predict the risk for thromboembolism and maintenance of sinus rhythm after cardioversion (30,31). Interpretation of spectral Doppler indexes can be difficult with sinus tachycardia, conduction system disease, and arrhythmia (especially AF), and obtaining high-quality pulmonary venous recordings may