

# Clinical and Echocardiographic Correlates of Left Atrial Function Index: The Framingham Offspring Study

Mayank Sardana, MBBS, Gregory Nah, MA, Connie W. Tsao, MD, Adedotun A. Ogunsua, MPH, Eric Vittinghoff, PhD, Randell C. Thomas, MD, Susan Cheng, MD, Aditya Vaze, MD, Jayashri R. Aragam, MD, Gary F. Mitchell, MD, Emelia J. Benjamin, MD, ScM, Ramachandran S. Vasani, MD, Gerard P. Aurigemma, MD, Nelson B. Schiller, MD, David D. McManus, MD, ScM, and Nisha I. Parikh, MD, MPH, *Worcester, Boston, Framingham, West Roxbury, and Norwood, Massachusetts, and San Francisco, California*

**Background:** Left atrial (LA) remodeling is a predictor of cardiovascular disease (CVD). We performed measurement of the LA function index (LAFI), a composite measure of LA structure and function, in a community-based cohort and here report the distribution and cross-sectional correlates of LAFI.

**Methods:** In 1,719 Framingham Offspring Study participants (54% women, mean age  $66 \pm 9$  years), we derived LAFI from the LA emptying fraction, left ventricular (LV) outflow tract velocity time integral, and indexed maximal LA volume. We used multivariable linear regression to assess the clinical and echocardiographic correlates of LAFI adjusting for age, sex, anthropometric measurements, and CVD risk factors.

**Results:** The average LAFI was  $35.2 \pm 12.1$ . Overall, LAFI declined with advancing age ( $\beta = -0.27, P < .001$ ). LAFI was significantly higher ( $37.5 \pm 11.6$ ) in a subgroup of participants free of CVD and CVD risk factors compared with those with either of these conditions ( $34.5 \pm 12.2$ ). In multivariable models, LAFI was inversely related to antihypertensive use ( $\beta = -1.26, P = .038$ ), prevalent atrial fibrillation ( $\beta = -4.46, P = .001$ ), heart failure ( $\beta = -5.86, P = .008$ ), and coronary artery disease ( $\beta = -2.01, P = .046$ ). In models adjusting for echocardiographic variables, LAFI was directly related to LV ejection fraction ( $\beta = 14.84, P < .001$ ) and inversely related to LV volume ( $\beta = -7.03, P < .001$ ).

**Conclusions:** LAFI was inversely associated with antihypertensive use and prevalent CVD and was related to established echocardiographic traits of LV remodeling. Our results offer normative ranges for LAFI in a white

From the Cardiology Division, Department of Medicine, University of Massachusetts Medical School, Worcester, Massachusetts (M.S., A.A.O., A.V., G.P.A., D.D.M.); Cardiology Division, Department of Medicine, University of California, San Francisco, San Francisco, California (G.N., E.V., R.C.T., N.B.S., N.I.P.); Cardiovascular Division, Department of Medicine, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, Massachusetts (C.W.T.); Boston University's and National Heart, Lung, and Blood Institute's Framingham Heart Study, Framingham; and Section of Preventive Medicine and Epidemiology and Cardiovascular Medicine, Department of Medicine, and Department of Epidemiology, Boston University Schools of Medicine and Public Health, Boston, Massachusetts (S.C., G.F.M., E.J.B., R.S.V.); Cardiology Division, Department of Medicine, Brigham and Women's Hospital, Massachusetts (S.C., J.R.A.); Veterans Administration Medical Center, West Roxbury, and Harvard Medical School, Boston, Massachusetts (J.R.A.); and Cardiovascular Engineering, Norwood, Massachusetts (G.F.M.).

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Reprint requests: Nisha I. Parikh, MD, MPH, 555 Mission Bay Blvd South, Division of Cardiology, University of California San Francisco, San Francisco, CA 94158 (E-mail: [nparikh@medicine.ucsf.edu](mailto:nparikh@medicine.ucsf.edu)).

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community-based sample and suggest that LAFI represents a marker of pathological atrial remodeling. (J Am Soc Echocardiogr 2017; ■: ■-■.)

**Keywords:** Left atrial function, Left atrial function index, Cardiovascular diseases, Atrial fibrillation, Epidemiology, Echocardiography

#### Abbreviations

<b>CVD</b> = Cardiovascular disease
<b>LA</b> = Left atrial
<b>LAFI</b> = Left atrial function index
<b>LAm<sub>ax</sub></b> = Maximum left atrial volume
<b>LAm<sub>in</sub></b> = Minimum left atrial volume
<b>LV</b> = Left ventricular
<b>LVEDD</b> = Left ventricular end-diastolic diameter
<b>LVEDV</b> = Left ventricular end-diastolic volume
<b>LVEF</b> = Left ventricular ejection fraction
<b>LVESD</b> = Left ventricular end-systolic diameter
<b>LVESV</b> = Left ventricular end-systolic volume
<b>LVOT</b> = Left ventricular outflow tract
<b>PWT</b> = Posterior wall thickness
<b>SWT</b> = Septal wall thickness
<b>VTI</b> = Velocity-time integral

Adverse left atrial (LA) remodeling is associated with increased risk of cardiovascular disease (CVD) and CVD-specific and all-cause mortality.<sup>1-4</sup> Increased LA volume and abnormalities in phasic function are examples of echocardiographic traits that capture aspects of adverse structural and functional LA remodeling and have prognostic significance, particularly as predictors of incident or recurrent atrial fibrillation, heart failure, and cerebrovascular accident.<sup>1-4</sup> Although LA volume is the recommended LA echocardiographic trait for clinical practice,<sup>5</sup> its prognostic value diminishes when ventricular systolic and diastolic function are considered concomitantly.<sup>6-8</sup>

A subtle decline in LA function, as detected by impaired LA phasic function (atrial reservoir phase, passive atrial emptying, and atrial systole), is associated with incident and recurrent CVD, adjusting for ventricular function, but such measures are not routinely collected as part of a standard echocardiographic examination.<sup>3,5,9-14</sup> Left atrial function index (LAFI) is a composite measure of LA structure and function that combines

information about atrial reservoir function as well as LA size, body habitus, and left ventricular (LV) function (as measured by stroke volume).<sup>15</sup> LAFI might characterize LA remodeling better than currently used volumetric echocardiographic measures. In select populations with CVD, a lower LAFI is associated with an increased risk of incident heart failure, cerebrovascular events, atrial fibrillation recurrence, and all-cause mortality.<sup>16-19</sup> In this retrospective investigation, we describe the distribution of LAFI and the cross-sectional clinical and echocardiographic correlates of LAFI in a community-based sample.

during examination cycle 8 (2005-8).<sup>21</sup> Participants who were in atrial fibrillation at the time of their echocardiographic examination, who had significant mitral regurgitation on echocardiogram, and who had inadequate atrial images were excluded. We also created a subgroup free of CVD/CVD risk factors ( $n = 415$ ) within the general study sample for analysis. This included nonobese participants, free of prevalent hypertension, diabetes, atrial fibrillation, coronary heart disease, cerebrovascular accident, transient ischemic attack, or heart failure. Participants who had one or more of these conditions were included in the subgroup with CVD/CVD risk factors. Laboratory parameters and echocardiographic measures were not considered for creation of CVD/CVD risk factors subgroups. Development of the general study sample and various subgroups is depicted in [Supplemental Figure 1](#) (available at [www.onlinejase.com](http://www.onlinejase.com)).

The study protocol was approved by the Boston University Medical Center Institutional Review Board, the University of California, San Francisco, School of Medicine Review Board, and the University of Massachusetts Medical School Review Board, and all participants provided written informed consent.

#### Left Atrial Volumetric Assessment

We performed offline analysis of echocardiographic images from 1,795 participants with LA imaging of sufficient quality to enable LA volumetric measurement from apical two and four-chamber views. Prior studies have demonstrated that the presence of atrial fibrillation rhythm at the time of echocardiogram affects LA contractile function and significantly decreases LAFI.<sup>19</sup> We therefore excluded the participants who were in atrial fibrillation at the time of echocardiogram ( $n = 40$ ). Since atrial fibrillation is strongly associated with LA remodeling, the participants with history of atrial fibrillation who were in sinus rhythm during the echocardiogram were included in the current study to assess the ability of LAFI to capture LA remodeling associated with atrial fibrillation. Participants with moderate or higher degrees of mitral regurgitation on the echocardiogram ( $n = 36$ , quantified using color Doppler by the maximum systolic proximal mitral regurgitation jet height)<sup>22</sup> were also excluded, leading to the final sample size of 1,719. The baseline characteristics of included and excluded participants are presented in [Supplemental Table 1](#) (available at [www.onlinejase.com](http://www.onlinejase.com)). Excluded participants had significantly higher body mass index (29 kg/m<sup>2</sup> vs 28 kg/m<sup>2</sup> for included participants;  $P = .001$ ), use of antihypertensive medications (57% vs 52% in included participants;  $P = .002$ ), prevalence of atrial fibrillation (10% vs 5% in included participants;  $P < .001$ ), and heart failure (4% vs 2% in the included participants;  $P = .003$ ). Other clinical and demographic variables were similarly distributed between the included and excluded participants.

Two sonographers performed LA volume measurement. Serial quality control iterations were performed to maximize the inter- and intraobserver correlation. During each of these iterations, the maximal and minimal LA volumes were measured for 20 randomly selected participants by both sonographers. Sonographers were trained between serial iterations, and the interobserver coefficients of variation between the sonographers measured during the final

**MATERIALS AND METHODS**

#### Study Sample

The design and sampling of the Framingham Offspring study were published previously.<sup>20</sup> Briefly, starting in 1971, the children of the original Framingham Heart Study cohort were enrolled and evaluated approximately every 4-8 years. A total of 2,888 participants underwent transthoracic echocardiography with digital image acquisition

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