

Potential Usefulness and Clinical Relevance of Adding Left Atrial Strain to Left Atrial Volume Index in the Detection of Left Ventricular Diastolic Dysfunction

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ABSTRACT

OBJECTIVES The purpose of this study was to analyze the potential usefulness and clinical relevance of adding left atrial (LA) strain to left atrial volume index (LAVI) in the detection of left ventricular diastolic dysfunction (LVDD) in patients with preserved left ventricular ejection fraction (LVEF).

BACKGROUND Recent studies have suggested that LA strain could be of use in the evaluation of LVDD. However, the potential utility and clinical significance of adding LA strain to LAVI in the detection of LVDD remains uncertain.

METHODS Using 2-dimensional speckle-tracking echocardiography, we analyzed a population of 517 patients in sinus rhythm at risk for LVDD such as those with arterial hypertension, diabetes mellitus, or history of coronary artery disease and preserved LVEF.

RESULTS In patients with LV diastolic alterations and estimated elevated LV filling pressures, the rate of abnormal LA strain was significantly higher than an abnormal LAVI (62.4% vs. 33.6%, $p < 0.01$). In line with this, in patients with normal LAVI, high rates of LV diastolic alterations and abnormal LA strain were present (rates 80% and 29.4%, respectively). In agreement with these findings, adding LA strain to LAVI in the current evaluation of LVDD increased significantly the rate of detection of LVDD (relative and absolute increase 73.3% and 9.9%; rate of detection of LVDD: from 13.5% to 23.4%; $p < 0.01$). Regarding the clinical relevance of these findings, an abnormal LA strain (i.e., $< 23\%$) was significantly associated with worse New York Heart Association functional class, even when LAVI was normal. Moreover, in a retrospective post hoc analysis an abnormal LA strain had a significant association with the risk of heart failure hospitalization at 2 years (odds ratio: 6.6 [95% confidence interval: 2.6 to 16.6]) even adjusting this analysis for age and sex and in patients with normal LAVI.

CONCLUSIONS The findings from this study provide important insights regarding the potential usefulness and clinical relevance of adding LA strain to LAVI in the detection of LVDD in patients with preserved LVEF. (J Am Coll Cardiol Img 2017; ■:■-■) © 2017 by the American College of Cardiology Foundation.

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**ABBREVIATIONS
AND ACRONYMS****ASE** = American Society of Echocardiography**av. E/e'** = ratio of mitral early diastolic inflow velocity (E) using pulsed wave Doppler to average of septal and lateral mitral annular early-diastolic peak velocity (e') using tissue Doppler imaging**E/A** = ratio of mitral early diastolic inflow velocity (E) to mitral late diastolic inflow velocity (A) using pulsed wave Doppler**LA** = left atrial or left atrium**LAVI** = maximal left atrial volume index**LV** = left ventricular or left ventricle**LVDD** = left ventricular diastolic dysfunction**PCWP** = pulmonary capillary wedge pressure**Septal or lateral e'** = septal or lateral mitral annular early-diastolic peak velocity using tissue Doppler imaging**TR** = tricuspid regurgitation jet peak velocity

The volumetric analysis of the left atrium (LA) using the maximal LA volume index (LAVI) is an adequate analysis to estimate the cumulative effect of increased left ventricular (LV) filling pressures over time (1,2). However, LAVI has limitations to detect early LV diastolic alterations because this volumetric parameter reflects mainly the chronic effect of increased LV filling pressures (1,2). Despite these limitations, in the clinical practice LAVI remains the unique recommended LA parameter to analyze changes caused by LV diastolic alterations on the LA (1,2). Notwithstanding, recent findings have found that a new LA functional parameter, LA strain, has a strong correlation to invasive gold standard diastolic measurements and LV filling pressures, even better than LAVI (3-6). In addition, recent studies have found that LA strain is significantly correlated to the severity of LV diastolic dysfunction (LVDD) and that this parameter could reflect earlier changes on the LA than LAVI in patients with LVDD (7-10). Nonetheless, despite these interesting and promising studies (Online Table 1), whether LA strain could help to detect higher rates of LVDD than using only

LAVI or help to detect LV diastolic alterations when LAVI is normal remains uncertain.

Therefore, the aim of the present study was to analyze a large cohort of patients at risk for LVDD and preserved LV ejection fraction (LVEF) to determine the potential usefulness and clinical relevance of adding LA strain to LAVI in the detection of LVDD.

METHODS

STUDY POPULATION. We included patients in sinus rhythm with some risk factor for LVDD such as those with arterial hypertension (systolic and diastolic blood pressure $\geq 140/90$ mm Hg), diabetes mellitus (fasting plasma glucose ≥ 126 mg/dl), or history of coronary artery disease (history of acute coronary syndrome, stable angina, or coronary revascularization) and preserved LVEF (LVEF $>50\%$) referred to the Laboratory of Echocardiography of the Charité University Hospital for detection of LVDD between May 2009 and October 2014 (some of these patients were enrolled in previous studies of our research group) (11-13).

Regarding the exclusion criteria of the study population, in line with the recommendations for LV diastolic measurements of the American Society of

Echocardiography (ASE) (2), patients with at least mild valvular heart stenosis, moderate or severe aortic or mitral regurgitation, severe pulmonary or tricuspid regurgitation (TR), valvular heart surgery or intervention, significant mitral annular calcification (≥ 5 mm), ventricular paced rhythm, left bundle branch block, or LV assist devices were excluded. In addition, to avoid underestimations of LA strain values, patients with poor 2-dimensional imaging quality in ≥ 1 LA segments, history or presence of atrial fibrillation, supraventricular arrhythmias, or unavailable electrocardiogram in the past 90 days as well as those with hypermobile interatrial septum or interatrial septal aneurysm, were excluded from this study. Furthermore, with the purpose of excluding noncardiac causes of dyspnea, patients with severe pulmonary disease such as those with requirement of supplemental oxygen or need of treatment with corticoids, patients with severe kidney disease such as those with dialysis requirement or indication for renal transplantation, and patients with severe liver disease such as those with Child-Pugh class B and C or indication for liver transplantation were also excluded from this study.

The ethic committee from the Charité University Hospital approved this research project, and informed consent was obtained from all subjects.

MEASUREMENTS USING CONVENTIONAL TRANSTHORACIC ECHOCARDIOGRAPHY.

All patients were examined at rest using a Vivid 7 or E9 (GE Healthcare, Horton, Norway) ultrasound system. Two-dimensional (2D) and Doppler measurements were performed as recommended by the ASE (1,2,14). Abnormal values of conventional LV diastolic parameters were determined according to the recent 2016 ASE criteria for LVDD (2): 1) septal or lateral mitral annular early-diastolic peak velocity (e') <7 cm/s or <10 cm/s using tissue Doppler imaging, respectively; 2) mitral average septal-lateral (av.) E/e' ratio >14 ; 3) LAVI >34 ml/m² (using the biplane Simpson method); and 4) TR jet peak velocity >2.8 m/s. In line with these criteria of the ASE, LVDD was determined when $>50\%$ of the aforementioned criteria were positive and normal LV diastolic function when $<50\%$ of these criteria were positive (Online Figure 1). In addition, indeterminate LV diastolic function was defined when only 50% of the criteria were positive (Online Figure 1). Likewise, the severity of LVDD was determined according to the 2016 ASE criteria for the grading of LVDD (Online Figure 1). Furthermore, we analyzed patients with LV diastolic alterations without including LAVI as diagnostic criteria to compare head-to-head LA strain

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