JACC: CARDIOVASCULAR IMAGING
VOL. 6, NO. 10, 2013

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER INC.
http://dx.doi.org/10.1016/j.jcmg.2013.08.002

ORIGINAL RESEARCH

Prognostic Value of LA Volumes Assessed by Transthoracic 3D Echocardiography

Comparison With 2D Echocardiography

Victor Chien-Chia Wu, MD,* Masaaki Takeuchi, MD,* Hiroshi Kuwaki, MD,* Mai Iwataki, MD,* Yasufumi Nagata, MD,* Kyoko Otani, MD,* Nobuhiko Haruki, MD,* Hidetoshi Yoshitani, MD,* Masahito Tamura, MD,* Haruhiko Abe, MD,* Kazuaki Negishi, MD,† Fen-Chiung Lin, MD,‡ Yutaka Otsuji, MD*

Kitakyushu, Japan; Hobart, Tasmania, Australia; and Taipei, Taiwan

OBJECTIVES The hypothesis of this study was that minimal left atrial volume index (LAVImin) by 3-dimensional echocardiography (3DE) is the best predictor of future cardiovascular events.

BACKGROUND Although maximal left atrial volume index (LAVImax) by 2-dimensional echocardiography (2DE) is a robust index for predicting prognosis, the prognostic value of LAVImin and the superiority of measurements by 3DE over 2DE have not been determined in a large group of patients.

METHODS In protocol 1, we assessed age and sex dependency of LAVIs using 2DE and 3DE in 124 normal subjects and determined their cutoff values (mean + 2 SD). In protocol 2, 2-dimensional (2D) and 3-dimensional (3D) LAVImax/LAVImin were measured in 556 patients with high prevalence of cardiovascular disease. After excluding patients with atrial fibrillation, mitral valve disease, and age <18 years, 439 subjects were followed to record major adverse cardiovascular events (MACE). Patients were divided into 2 groups by the cutoff criteria of LAVI in each method.

RESULTS In protocol 1, there was no significant age and sex dependency for each 2D and 3D LAVI. In protocol 2, during a mean of 2.5 years of follow-up, MACE developed in 88 patients, including 32 cardiac deaths. Kaplan-Meier survival analyses showed that all 4 LAVI cutoff criteria had significant predictive power of MACE. After variables were adjusted for clinical variables and left ventricular ejection fraction, all 4 methods were still independently and significantly associated with MACE, but 3D-derived LAVImin had the highest risk ratio. 3D LAVImin also had an incremental prognostic value over 3D LAVImax.

CONCLUSIONS LAVIs by both 2DE and 3DE are powerful predictors of future cardiac events. 3D LAVImin tended to have a stronger and additive prognostic value than 3D LAVImax. (J Am Coll Cardiol Img 2013;6:1025–35) © 2013 by the American College of Cardiology Foundation

From the *Second Department of Internal Medicine, University of Occupational and Environmental Health, School of Medicine, Kitakyushu, Japan; †Menzies Research Institute Tasmania, Hobart, Tasmania, Australia; and the ‡Department of Second Section of Cardiology, Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Taipei, Taiwan. All authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received June 1, 2013; revised manuscript received August 2, 2013, accepted August 9, 2013.

Remodeling of the left atrium caused by pressure and/or volume overload reflects severity and chronicity of underlying pathologic conditions rather than instantaneous left ventricular (LV) diastolic dysfunction and filling pressure (1–3). Thus, the degree and extent of left atrial (LA) dilation are closely coupled with disease severity. Several previous studies demonstrated that left atrial volume (LAV) measured by 2-dimensional echocardiography (2DE) is a robust index for predicting future cardiovascular events in various clinical scenarios (4–7). Although normal range and cutoff values of LAV using 2DE have been described in guidelines, the values established only maximal LAV and maximal LAV corrected to body surface area (maximal left atrial volume index [LAVImax]) (2). Recently, many researchers have focused on the importance of minimal LAV because its size is determined by the direct exposure of LV diastolic pressure and reflects more reliably underlying pathology (8). Biplane 2DE determination of LAV is convenient and currently the standard method of choice (9). However, it is sometimes inaccurate due to the complexity of LA shape and the inability to obtain optimal cutting planes (10).

Transthoracic 3-dimensional echocardiography (3DE) has the potential for more accurate determination of LAV because it does not rely on geometric assumptions (11,12). However, few studies investigated the prognostic utility of LAV measurement by 3DE (13). We hypothesized that minimal left atrial volume index (LAVImin) measured by 3DE is the best index for predicting future cardiovascular events.

Accordingly, the aims of this study were to establish a normal range of LAVImax and LAVImin and their cutoff values (mean + 2 SD) in normal controls using 2DE and 3DE and to evaluate the utility of these cutoff criteria to predict future major cardiovascular events (MACE) and cardiac death in a larger number of patients.

ABBREVIATIONS AND ACRONYMS

2D = 2-dimensional
3D = 3-dimensional
2DE = 2-dimensional echocardiography
3DE = 3-dimensional echocardiography
CKD = chronic kidney disease
HF = heart failure
ICC = intraclass correlation coefficient
LA = left atrial
LAV = left atrial volume
LAVI = left atrial volume index
LAVImax = maximal left atrial volume index
LAVImin = minimal left atrial volume index
LAVmax = maximal left atrial volume
LAVmin = minimal left atrial volume
LV = left ventricular
LVEF = left ventricular ejection fraction
MACE = major adverse cardiac events

METHODS

Study subjects. In protocol 1, 124 healthy subjects >18 years of age (mean age 44 ± 16 years; range 18 to 85 years; 56 men) were enrolled as a normal control group. They were recruited from hospital employees and their relatives and volunteers through advertising. In protocol 2, a total of 556 patients who underwent both clinically indicated 2DE and 3DE for underlying cardiac diseases were randomly selected from our 3DE database. Exclusion criteria included atrial fibrillation, mitral valve disease, and age <18 years. Clinical characteristics including hypertension, diabetes mellitus, hyperlipidemia, smoking, chronic kidney disease (CKD) and coronary artery disease were evaluated for all patients based on established criteria. CKD was defined as an estimated glomerular filtration rate <60 ml/min/1.73 m^2. The study was approved by the ethics committee of the University of Occupational and Environmental Health Hospital, and written informed consent was obtained from all subjects at the time of echocardiographic examinations.

2D echocardiography. 2DE was performed using a commercially available ultrasound machine and transducer (iE33 and S4/S5-1 transducer, Philips Medical Systems, Andover, Massachusetts). Three consecutive beats in the apical 4- and 2-chamber views including the entire left atrium were acquired, with specific attention directed at ensuring that the long axis of the left atrium was maximally delineated and the difference between long-axis diameter from the 2 imaging planes was <5 mm. LAVs were determined using the biplane Simpson method at end-systolic frames just before mitral valve opening (maximal left atrial volume [LAVmax]) and at end-diastolic frames coincided with the R-wave on the electrocardiogram (minimal left atrial volume [LAVmin]). In each view, the LA wall was traced, excluding the LA appendage and pulmonary veins. LAV was calculated using the following formula on the Xcelera workstation (Philips Medical Systems):

$$LAV(mL) = \frac{\pi}{4}\sum_{i=1}^{20} Ai \times Bi \times \frac{L}{20}$$

where A and B are the diameters of transverse axis perpendicular to the long axis of the left atrium from the apical 4- and 2-chamber views, and L is the long-axis diameter. Values were then indexed to the body surface area (LAVImax and LAVImin).

3D echocardiography. A fully sampled matrix-array transducer (X3-1 or X5-1) (Philips Medical Systems) was used to acquire the 3-dimensional (3D) full-volume datasets from apical approach during held respiration. To ensure inclusion of the entire LAV within the pyramidal scan volume with a relatively higher volume rate, the datasets were acquired using multibeat acquisition, wherein 4 wedge-shaped subvolumes (93° × 21°) were acquired during a single 5-s to 7-s breath hold. A 3D