VENTRICULAR AND ATRIAL FUNCTION

Comprehensive Analysis of Left Ventricular Geometry and Function by Three-Dimensional Echocardiography in Healthy Adults

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Background: Recent European Association of Echocardiography and American Society of Echocardiography guidelines on three-dimensional echocardiography state that normal values of left ventricular (LV) parameters for age and body size remain to be established.

Methods: In 226 consecutive healthy subjects (125 women; age range, 18–76 years), comprehensive three-dimensional echocardiographic analyses of LV parameters were performed, and values were compared with those obtained by conventional echocardiography.

Results: Upper reference values (mean + 2 SDs) for three-dimensional LV end-diastolic and end-systolic volumes were 85 and 34 mL/m^2 in men and 72 and 28 mL/m^2 in women, respectively. Indexing LV volumes to body surface area did not eliminate gender differences. Lower reference values (mean − 2 SDs) for ejection fraction were 54% in men and 57% in women and for stroke volume were 25 and 24 mL/m^2, respectively. Upper reference values for LV mass were 97 g/m^2 in men and 90 g/m^2 in women and for end-diastolic sphericity index were 0.49 and 0.48, respectively. Significant age dependency of LV parameters was identified and reported across age groups. Three-dimensional echocardiographic LV volumes were larger, ejection fraction was similar, and LV stroke volume and mass were significantly smaller in comparison with the corresponding values obtained by conventional echocardiography.

Conclusions: The investigators report a comprehensive analysis of LV geometry and function using three-dimensional echocardiography in a relatively large cohort of healthy Caucasian subjects with a wide age range. These may serve to establish age-specific and gender-specific reference ranges, which are crucial for the routine implementation of three-dimensional echocardiography to detect LV remodeling and dysfunction in clinical practice. (J Am Soc Echocardiogr 2013;26:618-28.)

Keywords: Echocardiography, Three-dimensional, Left ventricle, Reference values, Normal subjects

The quantification of left ventricular (LV) size, geometry, and function represents the most frequent indication for an echocardiographic study and is pivotal for patient evaluation and management. Indication for cardiac surgery, suitability for device implantation, indication for medical treatment in systolic heart failure, and suspension of cardiotoxic agents in patients with cancer are among the most critical decisions that rely on accurate assessments of LV geometry and function.[1]

Three-dimensional echocardiography (3DE) enables comprehensive, accurate, and reproducible LV quantitation.[2,3] The superiority of 3DE over conventional two-dimensional (2D) echocardiography (2DE) for LV volume measurement in comparison with cardiac magnetic resonance (CMR) has been well documented.[4-6] Although there seems to be a small underestimation of LV volumes using 3DE, this modality provides LV volumes significantly closer to those measured with CMR than 2DE, and no less important, it has been proved to be more robust than 2DE when tested for intraobserver, interobserver, and test-retest reproducibility.[3]

The identification of reference values for LV volumes, mass, and function is a prerequisite for the routine clinical application of quantitative 3DE. Indeed, both the European Association of Echocardiography and the American Society of Echocardiography recommend 3DE rather than 2DE for the routine clinical assessment of LV volumes.[3] However, they also acknowledge that limited normative data are available, particularly because of the lack of gender-based and anthropometric analysis. These aspects have significantly contributed to the limited adoption of 3DE in routine clinical practice.

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Abbreviations

BSA = Body surface area

BSA_{DB} = Body surface area (Dubois and Dubois)

BSA_{H} = Body surface area (Haycock *et al.*)

CMR = Cardiac magnetic resonance

ICC = Intraclass correlation coefficient

LV = Left ventricular

3D = Three-dimensional

3DE = Three-dimensional echocardiography

2D = Two-dimensional

2DE = Two-dimensional echocardiography

Accordingly, we designed this prospective, single-center, observational study to (1) perform a comprehensive analysis of LV geometry and function using state-of-the-art 3D echocardiographic equipment in a relatively large cohort of healthy subjects, (2) assess the effects of age and gender on LV 3D echocardiographic parameters, and (3) compare the values measured by 3DE with those obtained by conventional echocardiography in the same subjects.

METHODS

Study Population

Between October 2011 and February 2013, 257 healthy Caucasian volunteers were prospectively recruited at a single tertiary center among hospital employees, fellows in training, their relatives, and individuals who underwent medical visits for driving or working licenses and met the inclusion criteria. The sample size of the study was determined according to Altman,[7] who set 200 subjects as the minimum number to enroll in a study aiming to assess reference values for biologic variables. Prospective criteria for recruitment included age > 17 years, no history of cardiovascular or lung disease, no symptoms, absence of cardiovascular risk factors (i.e., systemic hypertension, smoking, diabetes, dyslipidemia), no cardioactive or vasoactive treatment, and normal results on electrocardiography and physical examination. Exclusion criteria were athletic training, pregnancy, body mass index > 30 kg/m^2, and poor apical acoustic window, defined as more than two LV segments not adequately visualized without contrast infusion.

Blood pressure was measured in all subjects immediately before the echocardiographic examination. Height and weight were measured using a calibrated stadiometer and scale, and body surface area (BSA) was calculated according to the formulas of both Dubois and Dubois[8] (BSA_{DB}) and Haycock *et al.*[9] (BSA_{H}) (modified by Sluysmans and Colan[10]).

The study was approved by the University of Padua ethics committee (protocol 2380 P, approved on October 6, 2011), and written informed consent was obtained from all volunteers before screening for eligibility in the study.

Image Acquisition

Using a standardized protocol, all examinations were performed by three cardiologists with experience in research echocardiography (L.D.B., D.M., and L.P.B.) using a commercially available Vivid E9 ultrasound machine (GE Vingmed Ultrasound AS, Horten, Norway) equipped with M5S and 4V probes for 2DE and 3DE, respectively. All patients were examined in the left lateral position using grayscale second-harmonic 2D imaging, with the adjustment of image contrast, frequency, depth, and sector size for adequate frame rate and optimal LV border visualization. Care was taken to avoid LV foreshortening in both apical views, and image acquisition was done during breath holding to minimize respiratory movements.

Standard transthoracic echocardiography included (1) 2D-guided M-mode tracings of LV wall thickness and cavity diameter to calculate LV mass; (2) a zoom image of the LV outflow tract obtained from the parasternal 2D long-axis view; (3) spectral recordings of LV outflow tract flow sampled using a pulsed-wave Doppler sample volume positioned just proximal to the aortic valve, so that the location of the velocity recording could match the LV outflow tract measurement; and (4) apical four-chamber and two-chamber view recordings for LV volume measurements, taking care to maximize LV length and to reduce depth by excluding the left atrium to achieve the highest frame rate.[11] All tracings and recordings contained at least three cardiac cycles to allow averaging of measurements.

Three-dimensional echocardiographic full-volume LV data sets obtained by stitching together four or six consecutive electrocardiographically gated subvolumes were acquired by the same examiner at the end of the standard 2D echocardiographic examination. Using multislice display of the 3D LV data set, special care was taken to adequately visualize all LV segments and to exclude any stitching artifacts between subvolumes. Data sets were stored digitally in raw-data format and exported to a separate workstation for analysis (EchoPAC BT 11; GE Vingmed Ultrasound AS).

Image Analysis

Image quality check and analysis were performed offline by two independent observers (D.M. and L.P.B.) with 3 years of experience with the software package used in this study. LV mass was calculated using measurements performed on 2DE-guided M-mode tracings[12] according to the American Society of Echocardiography's leading-edge convention.[13] To calculate LV stroke volume, LV outflow tract diameter was measured in the parasternal long-axis view in midsystole, inner edge to inner edge, parallel and proximal (within 0.5 cm) to the aortic valve plane. End-diastole and end-systole were identified from 2D echocardiographic cine loops using frame-by-frame analysis of the apical four-chamber and two-chamber LV views as the largest and smallest cavity during the cardiac cycle, respectively. Then, manual tracing of endocardial border was performed in both frames, paying attention to include the papillary muscles within the LV cavity. LV volumes were calculated using the biplane disk-summation algorithm (modified Simpson's rule), and ejection fraction was calculated as 1 − end-systolic volume/end-diastolic volume. Two-dimensional echocardiographic end-diastolic sphericity index was calculated from LV end-diastolic volume and LV longitudinal axis (averaged from the LV longitudinal axes in four-chamber and two-chamber views) by applying the same formula as for 3D echocardiographic sphericity index (see below).

Quantification of 3D LV volumes and ejection fraction was performed using a commercially available software (4D AutoLVQ; GE Vingmed Ultrasound AS) previously validated against CMR and extensively described elsewhere[14] (Figure 1). Initialization of LV endocardial border tracing was manually performed by the operator, by identifying two points on the four-chamber view image at end-diastole and then at end-systole (one point in the middle of the mitral annulus and a second point at the LV apex). Manual editing of the semiautomatically generated endocardial contours was routinely applied to include the LV outflow, as well as papillary muscles and trabeculae within the LV cavity, because this approach was found to reduce bias in comparison with CMR.[14,15] Editing involved the systematic addition of several attractor points, within a range of one to five points for the endocardium and two to eight points for the epicardium.

In addition, this software enabled the automatic calculation of LV sphericity index (Figure 1) and LV mass (Figure 2). LV sphericity index