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ORIGINAL RESEARCH

# Normalized Echocardiographic Values From Guideline-Directed Dedicated Views for Cardiac Dimensions and Left Ventricular Function

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## ABSTRACT

**BACKGROUND** Continuous technologic development and updated recommendations for image acquisitions creates a need to update the current normal reference ranges for echocardiography. The best method of indexing cardiac volumes is unknown.

**OBJECTIVES** The authors used 2- and 3-dimensional echocardiographic data from a large cohort of healthy individuals to provide updated normal reference data for dimensions and volumes of the cardiac chambers as well as central Doppler measurements.

**METHODS** In the fourth wave of the HUNT (Trøndelag Health) study in Norway 2,462 individuals underwent comprehensive echocardiography. Of these, 1,412 (55.8% women) were classified as normal and formed the basis for updated normal reference ranges. Volumetric measures were indexed to body surface area and height in powers of 1 to 3.

**RESULTS** Normal reference data for echocardiographic dimensions, volumes, and Doppler measurements were presented according to sex and age. Left ventricular ejection fraction had lower normal limits of 50.8% for women and 49.6% for men. According to sex-specific age groups, the upper normal limits for left atrial end-systolic volume indexed to body surface area ranged from 44 mL/m$^2$ to 53 mL/m$^2$, and the corresponding upper normal limit for right ventricular basal dimension ranged from 43 mm to 53 mm. Indexing to height raised to the power of 3 accounted for more of the variation between sexes than indexing to body surface area.

**CONCLUSIONS** The authors present updated normal reference values for a wide range of echocardiographic measures of both left- and right-side ventricular and atrial size and function from a large healthy population with a wide age-span. The higher upper normal limits for left atrial volume and right ventricular dimension highlight the importance of updating reference ranges accordingly following refinement of echocardiographic methods. (J Am Coll Cardiol Img 2023;16:1501-1515) © 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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**ABBREVIATIONS AND ACRONYMS**

**AF** = atrial fibrillation

**BMI** = body mass index

**BSA** = body surface area

**EDV** = end-diastolic volume

**EF** = ejection fraction

**ESV** = end-systolic volume

**EV** = ejection volume

**LA** = left atrial

**LV** = left ventricular

**MOD** = method of discs summation

**RA** = right atrial

**RV** = right ventricular

The basis for all diagnostics is separating normal findings from pathology. This also holds true for echocardiography. Reference data for adult echocardiography exist from large initiatives,[1-5] but as technologic development is continuously ongoing, there is a need to update the current normal reference ranges, because they are limited by: 1) being based on echocardiograms recorded by scanners that have been or are being replaced;[6-8] 2) low numbers of old subjects;[1,9] 3) lack of details of the technology used;[4,10] and 4) not all publications having included indexed volumetric measurements of chamber size.

In recent years, innovations to improve image quality have been implemented, that is, change from hardware-based to software-based beam forming, and nonlinear beam-forming techniques enhancing the myocardial structures. This influences both 2-dimensional (2D) and 3-dimensional (3D) imaging. In addition, expert recommendations now advocate specific views, such as right ventricular (RV) focused views for RV measurements and dedicated views for the left atrium (LA).[9,11] It has been shown that the measurement size is closely related to the view used for the measurement,[10,12,13] but updated normal reference values are not yet implemented in the recommendations.[9] Recent studies have challenged the indexing of chamber volumes to body surface area (BSA).[14,15] Thus, there is a need for updated normal reference values. The aim of the present study was to provide updated normal reference data of cardiac dimensions by 2D and 3D imaging, as well as volumetric and Doppler-based measurements of left ventricular (LV) systolic and diastolic function from a large cohort of Caucasians obtained with a novel high-end echocardiographic system. We also aimed to evaluate the importance of body mass and systolic blood pressures on the normal reference values for cardiac size and function.

## METHODS

**POPULATION.** The fourth wave of HUNT4, the longitudinal population study in the northern part of Trøndelag County, Norway, was performed in the years 2017 to 2019.[16] In total, 56,042 individuals (54% of those that were invited) participated in the HUNT4 baseline study. After completing the HUNT4 baseline examination, a subset of 5,763 participants were invited to the HUNT4 Fitness and Echocardiography study. Participants were invited if they participated in the HUNT4 baseline examination had participated in the HUNT3 (2006-2008) Fitness or Echocardiography studies or had validated atrial fibrillation (AF) from HUNT3 or self-reported AF from HUNT4. In total, 3,174 responded to the invitation, and 2,462 persons participated in the HUNT4 echocardiographic study. The HUNT4 baseline examinations included self-reported questionnaires, blood samples, and anthropometric and clinical measurements. In this study of updated normalized values from guideline-directed dedicated echocardiographic views, exclusion criteria were self-reported diabetes, AF, previous myocardial infarction or angina, antihypertensive treatment, malignant or pulmonary disease, and echocardiographic pathologic findings, such as LV hypertrophy, LV dilation, hypokinetic or akinetic segments, and more than mild valvular regurgitation or stenosis. All participants provided comprehensive self-reports on risk factors and daily life activities and were evaluated by echocardiography and a cardiopulmonary exercise test. Vascular ultrasound was performed in a subgroup. In the echocardiographic normal values study we excluded 14 without readable echocardiograms, 259 with known heart disease, 203 being treated for hypertension, 39 with diabetes, and 535 with valid AF. Thus, a total of 1,412 (55.8% women) were included in the main analysis (Figure 1). Of these, 1,192 also had body mass index (BMI) $\leq$30 kg/m$^2$ and systolic blood pressure $\leq$160 mm Hg and were included in the sensitivity analyses. The mean age for all included persons was 58 $\pm$ 12 years.

Variability of echocardiographic variables was assessed in 40 randomly selected individuals, with testing in 2 separate data sets by 4 operators. The study was approved by the Regional Committee for Medical and Health Research Ethics of Mid-Norway (REC ID 13083) and was conducted in compliance with the ethical principles of the Declaration of Helsinki. Personal data security and data handling were approved by the institutional personal data officer at St Olav's Hospital and Norwegian University of Science and Technology.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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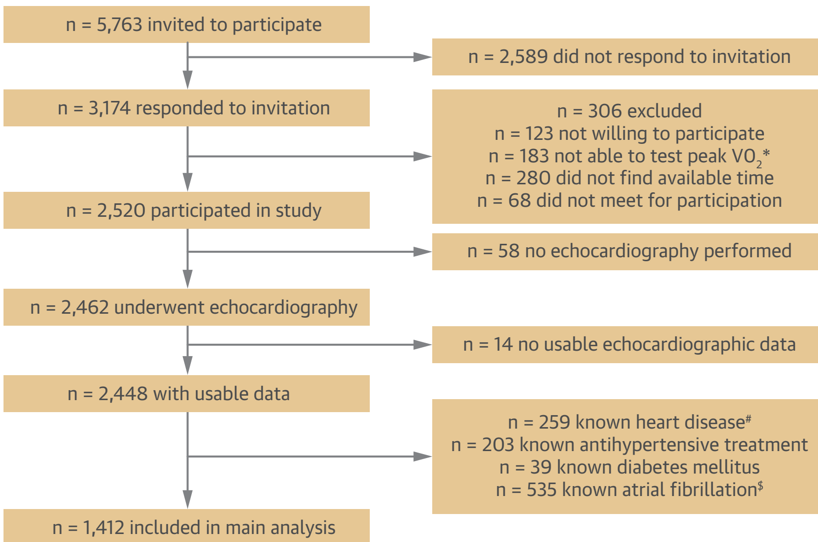
**FIGURE 1 Flowchart of the Study Participants**




*n = 64, not able to walk on treadmill; n = 57, no $VO_2$-test due to pacemaker or cardiovascular diseases; n = 62, other reasons. #Known angina, previous myocardial infarction, significant valvular pathology, or incident findings revealed by echocardiography. $Validated by an experienced cardiologist.

**DATA COLLECTION.** Previous medical history was assessed by interview and self-reported questionnaires from the baseline examination. Self-reports of AF were validated by reviewing of electronic medical records and electrocardiograms by an experienced cardiologist. Details of clinical measurements are included in the Supplemental Methods.

Echocardiography was performed with a Vivid E95 scanner (GE Vingmed Ultrasound) using a phased-array transducer (M5S). All recordings and measurements were performed by experienced personnel according to current recommendations.[9] Analyses and measurements were done in EchoPAC SWO (version 203, GE Ultrasound). 2D recordings included parasternal long- and short-axis views, 3 standard apical LV views, dedicated LA 2- and 4-chamber views to limit foreshortening of the LA, and RV-focused views for assessment of RV dimensions and RA volumes. Full 3D volumes of the LV and LA were recorded by limiting the sampled volume to the chambers while ensuring inclusion of the whole myocardial wall. Stitching of 2 to 4 cardiac cycles during breath-hold was done to ensure a proper volume rate.

Dimensions were measured according to recommendations, and volumes were calculated by tracing the endocardial borders of LV, LA, and RA in dedicated views.[9] LV volume was measured at end-diastole and end-systole, tracing the endocardial border with the use of Simpson's method of discs summation (MOD). Left ventricular ejection fraction (LVEF) was calculated. For 2D quantification of LA volume, the LA endocardial border was traced in 2- and 4-chamber views in end-systole, excluding the pulmonary veins and the LA appendage and with the mitral valve annulus closed by a straight line. Atrial length was measured in 2- and 4-chamber views and calculated by the area-length method and by MOD. LV and LA volumes were also measured with the use of the 4D auto LVQ and LAQ packages in EchoPAC 204 (GE Ultrasound). The automatically identified endocardial border was manually corrected by the reader if necessary. Special attempts were made to delineate the LV endocardial border at end-diastole and end-systole. For LA evaluation, we delineated the LA endocardial border also just before atrial contraction (pre-A). End-diastolic and end-systolic volumes as well as EF were measured in the LV. LA volume was quantified at prespecified time points: LA end-systolic volume (ESV), LA end-diastolic volume (EDV), and LA pre-A. LA ejection volume (EV) and LA ejection fraction (EF) (LA EV/LA ESV × 100) were calculated. LV and LA chamber volumes were indexed to BSA, height, height-squared, and height-cubed. Further details of the

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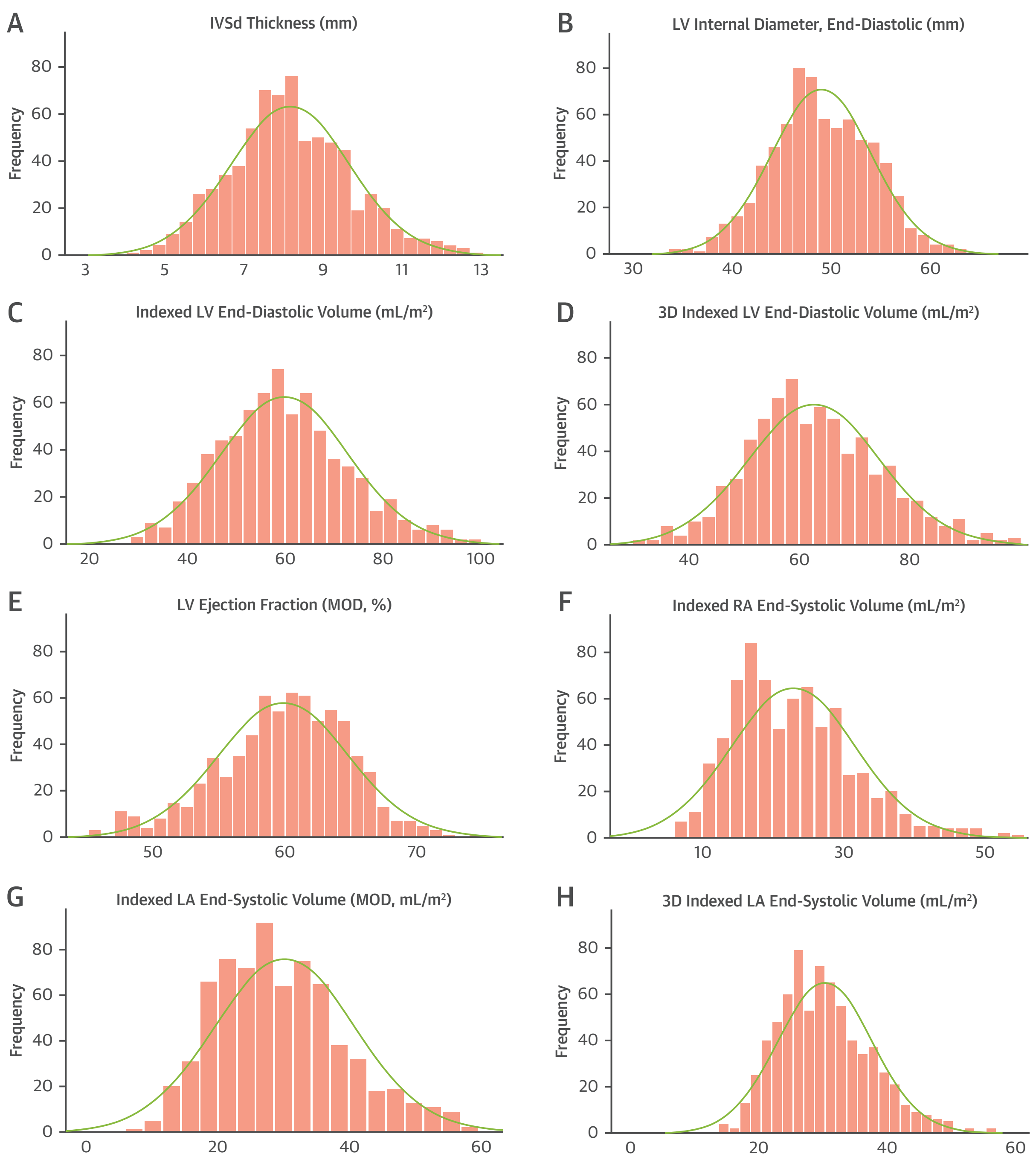
**FIGURE 2** **Distribution of Different Echocardiographic Measurements**




(A to H) Presented data are from 2-dimensional (2D) echocardiography if not stated elsewhere. 3D = 3-dimensional; IVSd = interventricular septum thickness; LA = left atrial; LV = left ventricular; MOD = method of disc summation; RA = right atrial.

echocardiographic measurements are included in the Supplemental Methods.

Reproducibility was evaluated in 40 randomly selected participants. Two experienced operators (cardiologist and sonographer) performed separate recordings, and these were later analyzed by 4 experienced operators. Diastolic reproducibility data have been published.[17] Repeatability was best for the mitral inflow and tissue Doppler measures, with intraclass correlations (ICCs) from 0.88 to 0.97, while LA volumes (ICCs of 0.71 by 2D and 0.84 by 3D), LVEF (ICCs 0.53 by 2D and 0.56 by 3D), and RV basal diameter (ICC: 0.62) showed somewhat poorer reproducibility.

**STATISTICS.** Data distributions were assessed by means of histograms (Figure 2), and by evaluating skewness and kurtosis. Normally distributed variables are presented as mean ± SD. Skewed variables are presented as median (IQR). Frequency variables are presented as n (%). Normal reference values according to age groups and sex were calculated as mean ± 1.96 SD, with assumptions of 95% of the observations of a normally distributed variable can be expected to lie within such a range (prediction interval). Tabulated data was presented according to age groups (20-39, 40-59, 60-79, and ≥80 years). Upper and lower normal values were defined as mean + 1.96 SD and mean − 1.96 SD as appropriate. We used linear regression analyses to estimate continuous reference ranges (means with 95% prediction intervals) according to age and sex, treating age as a continuous variable. Differences between age groups were evaluated by 1-way ANOVA with post hoc Bonferroni correction. Differences between sexes were tested by Student's *t*-test and Mann-Whitney *U*-test. We performed a specific sensitivity analysis excluding individuals with BMI >30 kg/m$^2$ or systolic blood pressure >160 mm Hg (or both). Reproducibility was tested by analyses in a 2-way random ICC model with testing for absolute agreement.[17] Comparison of 2D and 3D imaging was done by paired Student's *t*-test. A value of $P < 0.05$ was considered to be significant. Statistical analyses were performed with the use of SPSS (version 27) and R (packages lm, lme4, and ggplot2).

## RESULTS

**POPULATION.** Basic characteristics of the study population are presented in Table 1 and Supplemental Table 1. Mean age was 57.5 ± 12.4 years. Half of the population had BMI ≥25 kg/m$^2$, the proportion with systolic blood pressure 140-160 mm Hg was 16.0% in women and 19.5% in men, and kidney function and lipid levels were within normal ranges.

**ECHOCARDIOGRAPHIC DIMENSIONS.** Dimensions of the atria and ventricles stratified for age and sex are shown in Table 2 and Supplemental Table 2. All dimensions were significantly larger for men. Ventricular dimensions were lower with higher age, but the LV outflow tract diameters were not different between different age groups. LV wall was thicker in the older age groups ($P < 0.001$) and 1 mm thicker in men than women ($P < 0.001$).

**TABLE 1 Basic Characteristics of the Study Population**

| | Main Analyses | | Sensitivity Analyses | | |
|---|---|---|---|---|---|
| | Women (n = 788) | Men (n = 624) | Women (n = 674) | Men (n = 527) | All (N = 2,448) |
| Age, y | 57.2 ± 12.4 | 57.8 ± 12.4 | 56.8 ± 12.6 | 57.4 ± 12.6 | 61.1 ± 12.8 |
| Height, cm | 166 ± 6 | 179 ± 6 | 166 ± 6 | 179 ± 6 | 172 ± 9 |
| Weight, kg | 67 ± 12 | 85 ± 12 | 67 ± 8 | 83 ± 9 | 79 ± 14 |
| BMI, kg/m$^2$[a] | 25 ± 4 | 26 ± 3 | 24 ± 3 | 26 ± 2 | 26 ± 4 |
| BSA, m$^2$ | 1.8 ± 0.1 | 2.0 ± 0.1 | 1.7 ± 0.1 | 2.0 ± 0.1 | 1.9 ± 0.2 |
| Systolic blood pressure, mm Hg[a] | 127 ± 18 | 131 ± 17 | 123 ± 15 | 128 ± 13 | 131 ± 18 |
| Diastolic blood pressure, mm Hg | 72 ± 9 | 78 ± 10 | 71 ± 8 | 76 ± 9 | 76 ± 10 |

Values are mean ± SD. [a]In the sensitivity analyses individuals with BMI >30 kg/m$^2$ and SBP >160 mm Hg were excluded. All characteristics differed by sex ($P < 0.001$, except age [$P \geq 0.46$]).
BSA = body surface area; BMI = body mass index.

**ECHOCARDIOGRAPHIC VOLUMES.** Normal reference values for absolute volumes of the LV and left and right atria are presented in Table 3. All volumes were 20% to 47% smaller in women ($P < 0.001$), and LV volumes were approximately 10% lower per each 20 years older age group ($P < 0.001$). LVEF was not significantly altered by age group ($P = 0.141$), but absolute values were marginally higher in women ($P = 0.006$). LA volumes at end-diastole and at pre-A were larger with higher age, but there were no significant differences of LA ESV by age.

Normal reference values for indexed LV volumes by 2D and 3D imaging are presented in Table 4. The differences by age and sex were consistent after indexing for BSA, height, and height-squared. By indexing LV volumes for height-cubed, the differences were between sexes were reduced but still significant. Similar findings were found for age groups. Compared with indexing to BSA, indexing to height, height-squared, and height-cubed removed differences in LV volumes between the 2 youngest age groups in men (Table 4).

Table 5 presents normal reference values for indexed LA and RA volumes by 2D and 3D imaging according to methods, age, and sex. After indexing LA ESV to height-cubed, no significant difference was found between sexes. For the other time points for assessment of LA, the different methods of indexing did not substantially alter the results. Figure 3 shows prediction plots for key echocardiographic measurements according to sex and age. The corresponding equations are given in Supplemental Table 3.

**CARDIAC VOLUMES BY 2D VS 3D IMAGING.** Figure 4 shows the high agreement in paired

**TABLE 2 Dimensions of Cardiac Chambers According to Age and Sex**

| | Women, y | | | | Men, y | | | | *P* Value | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 20-39 (n = 64) | 40-59 (n = 357) | 60-79 (n = 355) | ≥80 (n = 12) | 20-39 (n = 49) | 40-59 (n = 284) | 60-79 (n = 279) | ≥80 (n = 12) | Age | Sex |
| IVS thickness, end-diastolic, mm | 6.8 ± 1.2 | 7.4 ± 1.3 | 8.1 ± 1.5 | 8.2 ± 1.0 | 7.9 ± 1.3 | 8.7 ± 1.3 | 9.2 ± 1.5 | 9.3 ± 1.7 | <0.001 | <0.001 |
| LV internal diameter, end-diastolic, mm | 49 ± 4 | 48 ± 4 | 45 ± 5 | 41 ± 2 | 52 ± 4 | 52 ± 5 | 50 ± 5 | 48 ± 6 | <0.001 | <0.001 |
| LVPW thickness, end-diastolic, mm | 6.6 ± 0.9 | 6.9 ± 1.0 | 7.5 ± 1.1 | 7.7 ± 1.2 | 7.3 ± 1.0 | 8.0 ± 1.2 | 8.3 ± 1.2 | 8.2 ± 0.8 | <0.001 | <0.001 |
| LV end-diastolic length, 4-chamber view, cm | 8.5 ± 0.6 | 8.3 ± 0.6 | 7.9 ± 0.6 | 7.1 ± 0.5 | 9.7 ± 0.6 | 9.2 ± 0.6 | 8.9 ± 0.6 | 8.5 ± 0.5 | <0.001 | <0.001 |
| LV end-diastolic length, 2-chamber view, cm | 8.6 ± 0.8 | 8.4 ± 0.6 | 7.9 ± 0.6 | 7.3 ± 0.6 | 9.7 ± 0.6 | 9.4 ± 0.7 | 8.9 ± 0.7 | 8.4 ± 0.5 | <0.001 | <0.001 |
| LV internal diameter, end-systolic, mm | 33.3 ± 4.0 | 33.0 ± 3.7 | 30.9 ± 4.2 | 28.1 ± 3.0 | 35.2 ± 4.3 | 35.9 ± 4.5 | 33.9 ± 4.8 | 34.6 ± 3.9 | <0.001 | <0.001 |
| LV outflow tract diameter, mm | 20.6 ± 1.8 | 20.5 ± 1.8 | 20.4 ± 1.8 | 20.0 ± 1.8 | 22.7 ± 2.1 | 23.1 ± 1.9 | 23.0 ± 2.1 | 21.7 ± 1.6 | 0.425 | <0.001 |
| LA end-systolic length, 4-chamber view, cm | 5.0 ± 0.7 | 5.0 ± 0.6 | 4.9 ± 0.7 | 4.9 ± 0.9 | 5.1 ± 0.6 | 5.3 ± 0.8 | 5.3 ± 0.8 | 5.8 ± 0.9 | 0.189 | <0.001 |
| LA end-systolic length, 2-chamber view, cm | 4.9 ± 0.6 | 5.0 ± 0.7 | 5.1 ± 0.6 | 5.0 ± 0.7 | 5.2 ± 0.5 | 5.3 ± 0.7 | 5.4 ± 0.7 | 5.8 ± 1.0 | 0.027 | <0.001 |
| LA end-systolic area, 4-chamber view, $cm^2$ | 17.2 ± 3.9 | 17.5 ± 3.5 | 16.6 ± 3.8 | 15.7 ± 4.9 | 18.4 ± 3.4 | 19.4 ± 4.2 | 19.5 ± 4.8 | 23.0 ± 6.6 | 0.093 | <0.001 |
| LA end-systolic area, 2-chamber view, $cm^2$ | 16.9 ± 3.9 | 17.4 ± 3.9 | 17.3 ± 4.0 | 16.4 ± 4.6 | 19.2 ± 3.6 | 20.2 ± 4.5 | 20.3 ± 4.9 | 23.0 ± 6.6 | 0.256 | <0.001 |
| RV basal diameter, cm | 3.3 (2.9-3.8) | 3.3 (3.0-3.7) | 3.2 (2.9-3.6) | 2.8 (2.4-3.3) | 4.0 (3.7-4.3) | 3.9 (3.5-4.4) | 3.8 (3.3-4.3) | 4.0 (3.7-4.2) | 0.020 | <0.001 |
| RV mid-diameter view, cm | 2.4 ± 0.5 | 2.4 ± 0.5 | 2.2 ± 0.5 | 2.2 ± 0.5 | 3.0 ± 0.4 | 2.9 ± 0.5 | 2.7 ± 0.5 | 2.8 ± 0.5 | <0.001 | <0.001 |
| RA end-systolic length view, cm | 4.6 ± 0.6 | 4.8 ± 0.5 | 4.8 ± 0.5 | 4.4 ± 0.3 | 5.2 ± 0.5 | 5.4 ± 0.6 | 5.4 ± 0.6 | 5.4 ± 0.8 | 0.004 | <0.001 |
| RA end-systolic area view, $cm^2$ | 13.8 ± 2.9 | 14.6 ± 3.0 | 13.9 ± 3.1 | 11.7 ± 2.1 | 18.0 ± 3,9 | 18.6 ± 4.1 | 18.0 ± 4.5 | 18.9 ± 4.3 | 0.098 | <0.001 |

Values are mean ± SD or median (IQR).

IVS = interventricular septum; LA = left atrial; LV = left ventricular; LVPW = left ventricular posterior wall; RA = right atrial; RV = right ventricle.

measurements by 2D and 3D imaging. Overall, volumes were significantly higher by 3D measurements, except for LA ESV indexed to BSA, where there was no significant difference (Supplemental Table 4). Indexing to height, height-squared, or height-cubed did not significantly alter the results. The differences between 2D and 3D measurements were 5.7 mL (5.2%) for LV EDV and 3.3 mL (7.4%) for LV ESV (both $P < 0.001$). For the average LV EDV and LV ESV indexed to BSA, the corresponding differences were 3.0 mL/$m^2$ (5.1%) and 1.7 mL/$m^2$ (7.2%), respectively (both $P < 0.001$).

**DOPPLER MEASUREMENTS.** Doppler measurements of blood flow and tissue velocities by age and sex are presented in **Tables 6 to 8**. Mitral inflow early (E-wave) and late (A-wave) diastolic velocities were 10% higher in women (both $P < 0.001$). The E/A ratio was 50% lower in the oldest vs the youngest age group ($P < 0.001$), and the E/e′ ratio was

**TABLE 3 Atrial and Ventricular Volumes According to Age, Sex, and Methods**

| | Women, y | | | | Men, y | | | | *P* Value | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 20-39 (n = 64) | 40-59 (n = 357) | 60-79 (n = 355) | ≥80 (n = 12) | 20-39 (n = 49) | 40-59 (n = 284) | 60-79 (n = 279) | ≥80 (n = 12) | Age | Sex |
| LV EDV, 2D (MOD), mL | 114 ± 26 | 102 ± 19 | 84 ± 19 | 67 ± 7 | 145 ± 28 | 136 ± 29 | 119 ± 27 | 104 ± 18 | <0.001 | <0.001 |
| LV ESV, 2D (MOD), mL | 46 ± 11 | 40 ± 9 | 33 ± 8 | 26 ± 4 | 61 ± 13 | 55 ± 13 | 48 ± 13 | 42 ± 10 | <0.001 | <0.001 |
| LVEF, 2D (MOD), % | 60 ± 4 | 61 ± 5 | 60 ± 5 | 62 ± 3 | 58 ± 6 | 60 ± 5 | 60 ± 5 | 59 ± 5 | 0.141 | 0.006 |
| LV EDV, 3D, mL | 119 ± 21 | 110 ± 20 | 92 ± 19 | 77 ± 12 | 153 ± 21 | 140 ± 27 | 125 ± 24 | 109 ± 20 | <0.001 | <0.001 |
| LV ESV, 3D, mL | 48 ± 9 | 43 ± 10 | 37 ± 8 | 33 ± 5 | 64 ± 12 | 58 ± 13 | 52 ± 11 | 46 ± 11 | <0.001 | <0.001 |
| LVEF, 3D, % | 60 ± 5 | 61 ± 4 | 60 ± 5 | 58 ± 4 | 58 ± 4 | 58 ± 5 | 58 ± 4 | 58 ± 6 | 0.139 | <0.001 |
| LA ESV, 2D (MOD), mL | 48 ± 16 | 50 ± 15 | 48 ± 15 | 44 ± 20 | 56 ± 15 | 61 ± 19 | 62 ± 21 | 78 ± 29 | 0.082 | <0.001 |
| LA ESV, 2D (A-L), mL | 53 ± 17 | 55 ± 16 | 52 ± 17 | 47 ± 22 | 60 ± 16 | 66 ± 20 | 66 ± 23 | 84 ± 31 | 0.084 | <0.001 |
| LA ESV, 3D, mL | 54 ± 16 | 52 ± 12 | 50 ± 12 | 52 ± 8 | 56 ± 11 | 62 ± 16 | 63 ± 17 | 71 ± 21 | 0.468 | <0.001 |
| LA pre-A volume, 3D, mL | 34 ± 11 | 37 ± 9 | 38 ± 10 | 39 ± 9 | 36 ± 8 | 45 ± 13 | 49 ± 15 | 58 ± 16 | <0.001 | <0.001 |
| LA EDV, 3D, mL | 22 ± 7 | 23 ± 7 | 23 ± 8 | 28 ± 8 | 22 ± 6 | 27 ± 9 | 29 ± 11 | 41 ± 17 | <0.001 | <0.001 |
| LA EF, 3D, % | 59 ± 9 | 56 ± 8 | 55 ± 9 | 46 ± 10 | 60 ± 7 | 56 ± 9 | 54 ± 9 | 44 ± 8 | <0.001 | 0.503 |
| RA ESV, 2D (MOD), mL | 33 (26-41) | 35 (28-45) | 32 (25-41) | 27 (17-33) | 49 (37-66) | 51 (38-65) | 46 (34-61) | 53 (38-73) | 0.044 | <0.001 |
| RA ESV, 2D (A-L), mL | 35 (27-43) | 36 (28-46) | 33 (26-42) | 27 (17-35) | 52 (39-69) | 53 (41-67) | 49 (36-64) | 54 (40-78) | 0.131 | <0.001 |

Values are mean ± SD or median (IQR). LA and LV volumes by 2D are means of 4- and 2-chamber views. RA volume is from RV/RA-focused views.

2D = 2-dimensional recordings; 3D = 3-dimensional full volume recordings; A-L = area-length method; EDV = end-diastolic volume; EF = ejection fraction; ESV = end-systolic volume; LVEF = left ventricular ejection fraction; MOD = method of disc summation; pre-A = pre-atrial contraction; other abbreviations as in **Table 2**.

**TABLE 4 Indexed LV Volumes by Methods, Sex, and Age**

| | Scaling Parameter | Women, y | | | | Men, y | | | | *P* Value | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 20-39 (n = 64) | 40-59 (n = 357) | 60-79 (n = 355) | ≥80 (n = 12) | 20-39 (n = 49) | 40-59 (n = 284) | 60-79 (n = 279) | ≥80 (n = 12) | Age, Women/Men | Sex |
| LV EDV, 2D (MOD), mL | BSA, $m^2$ | 65 ± 13 | 57 ± 11 | 48 ± 10[a] | 41 ± 5 | 70 ± 13 | 66 ± 14 | 59 ± 13[a] | 55 ± 9 | <0.001/<0.001 | <0.001 |
| | Height, m | 68 ± 14 | 61 ± 11 | 51 ± 11[a] | 42 ± 4 | 80 ± 15[a] | 75 ± 15 | 67 ± 15[a] | 59 ± 10 | <0.001/<0.001 | <0.001 |
| | $Height^2$, $m^2$ | 40 ± 8 | 37 ± 7 | 31 ± 7[a] | 26 ± 3 | 44 ± 9[a] | 41 ± 8 | 37 ± 9[a] | 34 ± 6 | <0.001/<0.001 | <0.001 |
| | $Height^3$, $m^3$ | 24 ± 5 | 22 ± 4 | 19 ± 4[a] | 16 ± 2 | 24 ± 5[a] | 23 ± 5 | 21 ± 5[a] | 19 ± 4 | <0.001/<0.001 | <0.001 |
| LV ESV, 2D (MOD), mL | BSA, $m^2$ | 26 ± 6 | 22 ± 5 | 19 ± 4[a] | 16 ± 2 | 29 ± 6 | 26 ± 6 | 24 ± 6[a] | 22 ± 4 | <0.001/<0.001 | <0.001 |
| | Height, m | 27 ± 6 | 24 ± 5 | 20 ± 5 | 16 ± 3 | 33 ± 7 | 30 ± 7 | 27 ± 7[a] | 24 ± 5 | <0.001/<0.001 | <0.001 |
| | $Height^2$, $m^2$ | 16 ± 4 | 14 ± 3 | 12 ± 3[a] | 10 ± 2 | 18 ± 4[a] | 17 ± 4 | 15 ± 4[a] | 14 ± 3 | <0.001/<0.001 | <0.001 |
| | $Height^3$, $m^3$ | 10 ± 2 | 9 ± 2 | 7 ± 2[a] | 6 ± 1 | 10 ± 2[a] | 9 ± 2 | 9 ± 2[a] | 8 ± 2 | <0.001/<0.001 | <0.001 |
| LV EDV, 3D, mL | BSA, $m^2$ | 67 ± 10 | 62 ± 10 | 53 ± 10[a] | 49 ± 8 | 75 ± 11 | 68 ± 12 | 62 ± 11[a] | 57 ± 10 | <0.001/<0.001 | <0.001 |
| | Height, m | 71 ± 11 | 66 ± 12 | 56 ± 11[a] | 48 ± 7 | 84 ± 12 | 77 ± 14 | 70 ± 13[a] | 62 ± 11 | <0.001/<0.001 | <0.001 |
| | $Height^2$, $m^2$ | 42 ± 6 | 39 ± 7 | 34 ± 6[a] | 30 ± 4 | 46 ± 7 | 43 ± 8 | 39 ± 7[a] | 35 ± 6 | <0.001/<0.001 | <0.001 |
| | $Height^3$, $m^3$ | 25 ± 4 | 24 ± 4 | 21 ± 4[a] | 19 ± 3 | 26 ± 4 | 24 ± 4 | 22 ± 4[a] | 20 ± 4 | <0.001/<0.001 | 0.002 |
| LV ESV, 3D, mL | BSA, $m^2$ | 27 ± 4 | 24 ± 5 | 21 ± 4[a] | 21 ± 3 | 31 ± 6 | 28 ± 6 | 26 ± 5[a] | 24 ± 5 | <0.001/<0.001 | <0.001 |
| | Height, m | 28 ± 5 | 26 ± 6 | 22 ± 5[a] | 20 ± 3 | 35 ± 6 | 32 ± 7 | 29 ± 6[a] | 26 ± 6 | <0.001/<0.001 | <0.001 |
| | $Height^2$, $m^2$ | 17 ± 3 | 15 ± 3 | 14 ± 3[a] | 13 ± 2 | 20 ± 4 | 18 ± 4 | 16 ± 4[a] | 15 ± 3 | <0.001/<0.001 | <0.001 |
| | $Height^3$, $m^3$ | 10 ± 2 | 9 ± 2 | 8 ± 2[a] | 8 ± 1 | 11 ± 2[a] | 10 ± 2 | 9 ± 2[a] | 8 ± 2 | <0.001/<0.001 | <0.001 |

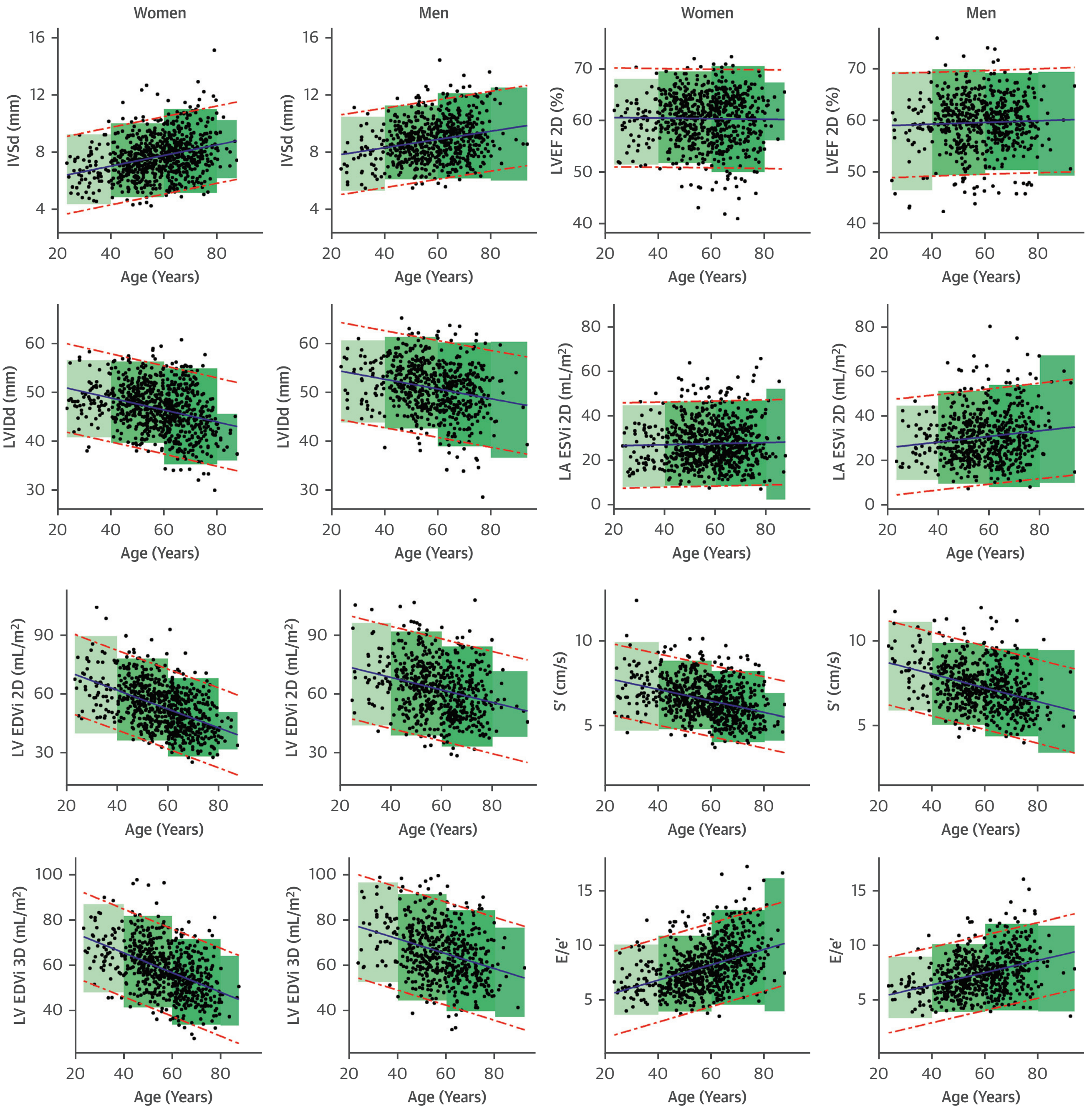
Values are mean ± SD. [a]Not significantly different from nearby group of higher age.
Abbreviations as in Tables 1 to 3.

**TABLE 5 Indexed LA and RA Volumes by Methods, Sex, and Age**

| | Scaling Parameter | Women, y | | | | Men, y | | | | *P* Value | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 20-39 (n = 64) | 40-59 (n = 357) | 60-79 (n = 355) | ≥80 (n = 12) | 20-39 (n = 49) | 40-59 (n = 284) | 60-79 (n = 279) | ≥80 (n = 12) | Age, Women/Men | Sex |
| LA ESV, 2D (MOD), mL | BSA, $m^2$ | 27 ± 9[a] | 28 ± 10[a] | 28 ± 10[a] | 27 ± 13 | 28 ± 9[a] | 31 ± 11[a] | 31 ± 11[a] | 39 ± 15 | 0.80/0.03 | <0.001 |
| | Height, m | 29 ± 9[a] | 30 ± 9[a] | 29 ± 9[a] | 27 ± 13 | 31 ± 8[a] | 34 ± 11[a] | 35 ± 12 | 44 ± 16 | 0.27/0.03 | <0.001 |
| | $Height^2$, $m^2$ | 17 ± 5[a] | 18 ± 5[a] | 18 ± 6[a] | 17 ± 8 | 17 ± 5[a] | 19 ± 6[a] | 20 ± 7 | 25 ± 9 | 0.43/<0.001 | 0.01 |
| | $Height^3$, $m^3$ | 10 ± 3[a] | 11 ± 3[a] | 11 ± 3[a] | 11 ± 5 | 9 ± 3[a] | 10 ± 3[a] | 11 ± 4 | 14 ± 5 | 0.46/<0.001 | 0.77 |
| LA ESV, 3D, mL | BSA, $m^2$ | 30 ± 9[a] | 29 ± 6[a] | 29 ± 7[a] | 32 ± 6 | 27 ± 6[a] | 30 ± 8[a] | 31 ± 8[a] | 37 ± 10 | 0.51/0.01 | 0.002 |
| | Height, m | 32 ± 9[a] | 31 ± 7[a] | 31 ± 7[a] | 32 ± 5 | 31 ± 6[a] | 34 ± 9[a] | 35 ± 9[a] | 40 ± 12 | 0.63/0.02 | <0.001 |
| | $Height^2$, $m^2$ | 19 ± 6[a] | 19 ± 4[a] | 19 ± 4[a] | 20 ± 3 | 17 ± 3[a] | 19 ± 5[a] | 20 ± 5[a] | 23 ± 7 | 0.82/0.004 | 0.51 |
| | $Height^3$, $m^3$ | 11 ± 3[a] | 11 ± 3[a] | 11 ± 3[a] | 12 ± 2 | 9 ± 2[a] | 11 ± 3[a] | 11 ± 3[a] | 13 ± 4 | 0.82/<0.001 | 0.03 |
| LA pre-A volume, 3D, mL | BSA, $m^2$ | 19 ± 5 | 21 ± 5 | 22 ± 6 | 24 ± 7 | 17 ± 4 | 22 ± 6 | 24 ± 7[a] | 30 ± 8 | 0.002/<0.001 | <0.001 |
| | Height, m | 20 ± 6[a] | 22 ± 5[a] | 23 ± 6[a] | 24 ± 6 | 20 ± 4 | 25 ± 7 | 27 ± 8[a] | 33 ± 9 | 0.04/<0.001 | <0.001 |
| | $Height^2$, $m^2$ | 12 ± 4 | 13 ± 3[a] | 14 ± 4[a] | 15 ± 4 | 11 ± 2 | 14 ± 4 | 15 ± 5[a] | 19 ± 5 | <0.001/<0.001 | 0.02 |
| | $Height^3$, $m^3$ | 7 ± 2 | 8 ± 2[a] | 8 ± 2[a] | 9 ± 2 | 6 ± 1 | 8 ± 2 | 9 ± 3[a] | 11 ± 3 | <0.001/<0.001 | 0.21 |
| LA EDV, 3D, mL | BSA, $m^2$ | 12 ± 4[a] | 13 ± 4[a] | 13 ± 4[a] | 17 ± 6 | 11 ± 3[a] | 13 ± 4 | 15 ± 5 | 21 ± 8 | 0.03/<0.001 | 0.002 |
| | Height, m | 13 ± 4[a] | 14 ± 4[a] | 14 ± 5[a] | 17 ± 5 | 12 ± 3 | 15 ± 5[a] | 16 ± 6 | 23 ± 10 | 0.10/<0.001 | <0.001 |
| | $Height^2$, $m^2$ | 8 ± 3[a] | 8 ± 2[a] | 8 ± 3[a] | 11 ± 3 | 7 ± 2 | 8 ± 3 | 9 ± 3 | 13 ± 6 | 0.04/<0.001 | 0.02 |
| | $Height^3$, $m^3$ | 5 ± 2[a] | 5 ± 1[a] | 5 ± 2[a] | 7 ± 2 | 4 ± 1 | 5 ± 2 | 5 ± 2 | 7 ± 3 | 0.01/<0.001 | 0.21 |
| | | **Women, y** | | | | **Men, y** | | | | | |
| | | **20-39 (n = 54)** | **40-59 (n = 284)** | **60-79 (n = 256)** | **≥80 (n = 8)** | **20-39 (n = 39)** | **40-59 (n = 230)** | **60-79 (n = 225)** | **≥80 (n = 8)** | | |
| RA ESV, 2D (MOD), mL | BSA, $m^2$ | 19 ± 6[a] | 21 ± 7[a] | 20 ± 7[a] | 17 ± 6 | 25 ± 10[a] | 26 ± 10[a] | 24 ± 10[a] | 29 ± 9 | 0.045/0.26 | <0.001 |
| | Height, m | 20 ± 6[a] | 22 ± 8[a] | 21 ± 7[a] | 16 ± 5 | 29 ± 11[a] | 29 ± 11[a] | 27 ± 11[a] | 31 ± 10 | 0.01/0.22 | <0.001 |
| | $Height^2$, $m^2$ | 12 ± 4[a] | 13 ± 5[a] | 12 ± 4[a] | 10 ± 3 | 16 ± 6[a] | 16 ± 6[a] | 15 ± 6[a] | 18 ± 5 | 0.02/0.34 | <0.001 |
| | $Height^3$, $m^3$ | 7 ± 2[a] | 8 ± 3[a] | 8 ± 3[a] | 6 ± 2 | 9 ± 3[a] | 9 ± 3[a] | 9 ± 3[a] | 10 ± 3 | 0.046/0.46 | <0.001 |

Values are mean ± SD. [a]Not significantly different from nearby group of higher age.
Abbreviations as in Tables 1 to 3.

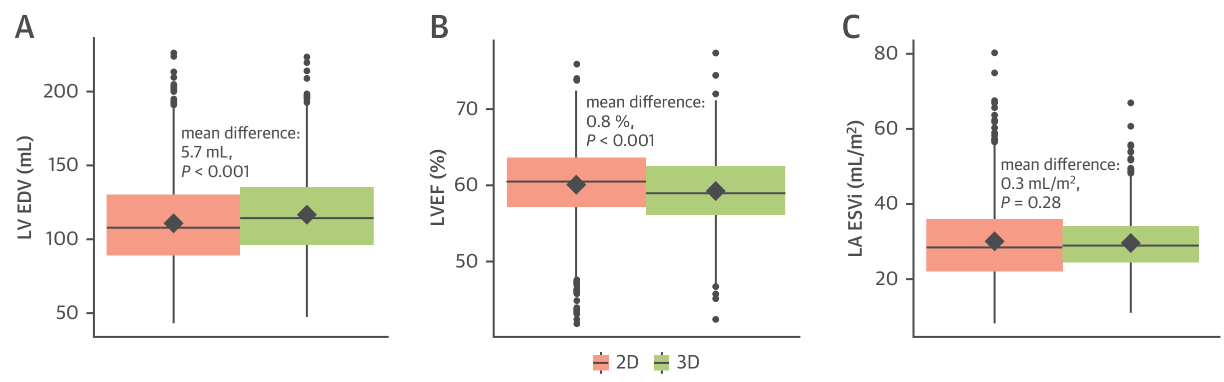
**FIGURE 3 Prediction Plots for Different Echocardiographic Measurements According to Sex and Age**




All measurements are shown according to age and sex. Regression line (blue) and prediction lines for lower and upper normal limits (red). Green indicates normal reference limits by age categories. E = mitral early inflow; e′ = mitral annular early diastolic velocity; EDVi = indexed end-diastolic volume; ESVi = indexed end-systolic volume; LVEF = left ventricular ejection fraction; LVIDd = left ventricular end-diastolic internal diameter; S′ = peak systolic mitral annular velocity; other abbreviations as in Figure 2.

approximately 1 unit higher per older age group ($P < 0.001$). The E/A ratio did not differ significantly between sexes, whereas the E/e′ ratio was approximately 0.5 unit higher in women ($P < 0.001$). The lower limit of lateral e′ was below 10 cm/s for all age groups in both sexes, and septal e′ was >7 cm/s only in individuals ≤39 years. Furthermore, one-half of the population above the age of 60 years had E/e′ >8,

**FIGURE 4** **Comparison of 2D and 3D LV and LA Measurements**




Boxplots of LV EDV, LVEF, and LA ESVi by 2D (red) and 3D (green) echocardiography. EDV = end-diastolic volume; other abbreviations as in Figures 2 and 3.

and except for women >80 years, the upper normal limit for E/e′ was <14. The upper normal limits for maximal tricuspid regurgitant velocity were < 2.8 m/s for women in all age groups and 2.83 and 2.84 for men aged 40-59 and 60-79, respectively.

**THE IMPORTANCE OF BLOOD PRESSURE AND BODY SIZE.** In the sensitivity analyses excluding those with BMI >30 kg/m² or systolic blood pressure >160 mm Hg, we found no clinically meaningful difference in LV end-diastolic diameter, RV basal diameter or LV, LA, and RA volumes between the main analyses and the sensitivity group. There was a significant difference between septal and lateral e′, as well as E/e′, between the 2 groups (Supplemental Table 5). Compared with those without obesity or elevated systolic blood pressure, the subpopulation excluded from the sensitivity analyses were an average 1.5 years younger. However, the sex distribution was similar between the groups.

## DISCUSSION

This study provides updated normal reference values for 2D and 3D assessment of dimensions and volumes of cardiac chambers, as well as blood flow and tissue Doppler measurements of healthy adults recruited from the general population (**Central Illustration**). These updated normal values add new knowledge as the upper normal limits as, eg, LA volumes and RV dimensions were significantly higher than indicated in the present recommendations. This indicates that normal reference values should be updated regularly according to technologic development and refined echocardiographic methods. Normal reference values indexed to height-cubed accounted for most of the variation of LA and LV volumes by sexes, as well as some of the differences between age groups.

**ASPECTS RELATED TO THE STUDY POPULATION.** One of the major challenges in defining normal values in echocardiography is to define a “normal” population. The studied population should be free from cardiac diseases, but it is somewhat controversial if cardiac risk factors should be regarded as exclusion criteria.[18] In this study, we excluded individuals with cardiovascular diseases (ischemic heart disease, heart failure, valvular disease, and AF), risk factors that could influence size and function of cardiac structures (hypertension and diabetes), and echocardiographic findings of evident pathology such as myocardial dysfunction (hypokinesia or akinesia) and structural changes of the left ventricular (eg, dilated or hypertrophic cardiomyopathy). To avoid creating supranormal reference values, we did not exclude individuals with further suboptimal health characteristics. The presented population was 11 to 12 years older than in the NORRE (Normal Reference Ranges for Echocardiography) study,[1] and the age-span was larger than for the EchoNORMAL (Echocardiographic Normal Ranges Meta-Analysis of the Left Heart Collaboration) meta-analysis.[19] Our large study, with inclusion of 245 healthy individuals over the age of 70 years, adds to the data regarding normal reference values for that age group. Robust normal data have previously been missing in that age group,[20] and compared with the NORRE study, more than twice the number of individuals were included for a central measure such as LVEF.[1]

**TABLE 6 Blood Flow Measurements by Pulsed-Wave Doppler**

| | Women, y | | | | Men, y | | | | *P* Value | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 20-39 (n = 64) | 40-59 (n = 357) | 60-79 (n = 355) | ≥80 (n = 12) | 20-39 (n = 49) | 40-59 (n = 284) | 60-79 (n = 279) | ≥80 (n = 12) | Age | Sex |
| Mitral E, cm/s | 93 ± 16 | 77 ± 15 | 68 ± 15 | 63 ± 13 | 84 ± 16 | 70 ± 14 | 61 ± 14 | 53 ± 13 | <0.001 | <0.001 |
| Mitral A, cm/s | 60 ± 12 | 66 ± 14 | 76 ± 16 | 87 ± 19 | 51 ± 11 | 60 ± 13 | 70 ± 15 | 66 ± 21 | <0.001 | <0.001 |
| Mitral E/A ratio | 1.6 ± 0.4 | 1.2 ± 0.3 | 0.9 ± 0.2 | 0.8 ± 0.2 | 1.7 ± 0.4 | 1.2 ± 0.3 | 0.9 ± 0.2 | 0.9 ± 0.3 | <0.001 | 0.314 |
| LVOT Vmax, m/s | 1.1 ± 0.2 | 1.1 ± 0.2 | 1.1 ± 0.2 | 1.1 ± 0.2 | 1.1 ± 0.2 | 1.1 ± 0.2 | 1.1 ± 0.2 | 0.9 ± 0.2 | 0.004 | 0.394 |
| LVOT VTI, cm | 23 ± 3 | 23 ± 4 | 22 ± 4 | 23 ± 4 | 22 ± 4 | 22 ± 4 | 22 ± 4 | 19 ± 3 | 0.027 | <0.001 |
| Tricuspid E, cm/s | 58 ± 11 | 50 ± 9 | 46 ± 9 | –[a] | 64 ± 19 | 48 ± 9 | 45 ± 10 | 45 ± 20 | <0.001 | 0.179 |
| Tricuspid A, cm/s | 37 ± 5 | 39 ± 10 | 39 ± 9 | –[a] | 42 ± 12 | 37 ± 10 | 38 ± 8 | 44 ± 16 | 0.357 | 0.216 |
| Tricuspid E/A ratio | 1.6 ± 0.4 | 1.3 ± 0.3 | 1.2 ± 0.3 | –[a] | 1.5 ± 0.2 | 1.4 ± 0.3 | 1.2 ± 0.2 | 1.0 ± 0.2 | <0.001 | 0.925 |
| RVOT Vmax, cm/s | 81 ± 13 | 78 ± 15 | 76 ± 13 | –[a] | 80 ± 15 | 76 ± 13 | 75 ± 13 | 72 ± 11 | 0.115 | 0.305 |
| RVOT VTI, cm | 18 ± 3 | 17 ± 3 | 16 ± 3 | –[a] | 16 ± 3 | 16 ± 3 | 15 ± 3 | 17 ± 2 | 0.004 | 0.029 |
| TR Vmax, m/s | 2.1 ± 0.3 | 2.2 ± 0.3 | 2.3 ± 0.2 | 2.3 ± 0.2 | 2.2 ± 0.3 | 2.2 ± 0.3 | 2.3 ± 0.3 | 2.4 ± 0.4 | <0.001 | 0.964 |
| Pulmonary S, cm/s | 58 ± 12 | 61 ± 12 | 67 ± 13 | 67 ± 15 | 57 ± 10 | 63 ± 13 | 67 ± 12 | 69 ± 14 | <0.001 | 0.345 |
| Pulmonary D, cm/s | 59 ± 11 | 51 ± 12 | 45 ± 10 | 40 ± 11 | 60 ± 11 | 53 ± 12 | 45 ± 10 | 40 ± 9 | <0.001 | 0.484 |
| Pulmonary S/D ratio | 1.0 ± 0.2 | 1.2 ± 0.3 | 1.5 ± 0.3 | 1.8 ± 0.5 | 0.9 ± 0.2 | 1.2 ± 0.3 | 1.5 ± 0.4 | 1.8 ± 0.4 | <0.001 | 0.543 |

Values are mean ± SD. [a]Too few with available measurements to get meaningful normal data.

A = peak late diastolic blood flow velocity; E = peak early diastolic blood flow velocity; LVOT = left ventricular outflow tract; RVOT = right ventricular outflow tract; TR = tricuspid regurgitation; Vmax = maximal velocity; VTI = velocity time integral; S = systolic; D = diastolic.

**NORMAL VALUES OF DIMENSION AND VOLUMES OF CARDIAC CHAMBERS.** As shown previously by others and us, the volumes and dimensions of the cardiac chambers were larger in men.[1,3,4,9] Furthermore, the LV dimensions and volumes were smaller and wall thicknesses significantly larger in the higher age groups. There was a significant, but not clinically meaningful, difference in LVEF by sex (difference 0.8%; $P = 0.006$). We found no significant difference for LVEF between age groups, and lower normal limits of 50.8% for women and 49.6% for men are well aligned to the recommendations,[9] even though they are somewhat lower than in the WASE (World Alliance of Societies of Echocardiography) study.[4] We present similar lengths in 4-chamber and 2-chamber views, indicating that the presented data have very limited foreshortening of images. The lower difference between sexes than previously observed by others[21,22] for 2D and 3D measurements of LVEF may be related to methodology. The finding of no age effect on LVEF may be explained by both end-diastolic and end-systolic LV volumes being lower with higher age.

Furthermore, indexing to height-cubed reduced the variation in LV volumes between sexes whereas indexing to BSA, height, or height-squared did not. LA ESV indexed to BSA or the different exponents of height were not different by age in women, but indexed LA volumes at end-diastole and pre-A were higher with higher age in both sexes. Thus, LA EF was significantly related to age, as previously shown by others.[23]

Importantly, compared with some previous studies and the current recommendations of the European

**TABLE 7 Mitral Annular Velocities by Pulsed-Wave Tissue Doppler According to Age and Sex**

| | Women, y | | | | Men, y | | | | *P* Value | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 20-39 (n = 64) | 40-59 (n = 357) | 60-79 (n = 355) | ≥80 (n = 12) | 20-39 (n = 49) | 40-59 (n = 284) | 60-79 (n = 279) | ≥80 (n = 12) | Age | Sex |
| Septal e′, cm/s | 11.6 ± 2.6 | 9.1 ± 2.2 | 6.9 ± 1.9 | 6.1 ± 1.9 | 11.4 ± 2.6 | 8.4 ± 2.1 | 6.7 ± 1.7 | 5.9 ± 1.7 | <0.001 | 0.03 |
| Lateral e′, cm/s | 16.2 ± 3.5 | 12.3 ± 2.8 | 8.9 ± 2.3 | 7.2 ± 1.7 | 16.6 ± 3.7 | 12.0 ± 3.2 | 9.0 ± 2.6 | 7.8 ± 1.6 | <0.001 | 0.621 |
| Septal S′, cm/s | 8.5 ± 1.4 | 7.9 ± 1.3 | 7.2 ± 1.4 | 6.3 ± 0.8 | 9.4 ± 1.5 | 8.3 ± 1.5 | 7.9 ± 1.4 | 7.4 ± 1.2 | <0.001 | <0.001 |
| Lateral S′, cm/s | 10.2 ± 2.2 | 9.4 ± 2.1 | 8.5 ± 2.1 | 7.8 ± 1.6 | 11.9 ± 2.1 | 10.0 ± 2.3 | 9.5 ± 2.3 | 8.8 ± 2.5 | <0.001 | <0.001 |
| Septal a′, cm/s | 9.1 ± 2.0 | 10.1 ± 1.9 | 10.6 ± 1.9 | 10.0 ± 2.6 | 9.8 ± 2.5 | 10.9 ± 2.2 | 11.0 ± 1.9 | 9.8 ± 1.6 | <0.001 | <0.001 |
| Lateral a′, cm/s | 9.0 ± 3.0 | 9.7 ± 2.2 | 10.8 ± 2.2 | 11.1 ± 3.8 | 8.8 ± 2.3 | 10.1 ± 2.4 | 11.2 ± 2.3 | 10.3 ± 3.1 | <0.001 | 0.04 |
| E/septal e′ ratio | 8.2 ± 1.8 | 8.8 ± 2.2 | 10.3 ± 2.7 | 11.3 ± 4.2 | 7.7 ± 1.8 | 8.6 ± 1.9 | 9.5 ± 2.3 | 9.3 ± 2.7 | <0.001 | <0.001 |
| E/lateral e′ ratio | 6.0 ± 1.9 | 6.5 ± 1.8 | 7.9 ± 2.3 | 9.2 ± 2.6 | 5.4 ± 2.0 | 6.1 ± 1.6 | 7.1 ± 2.1 | 7.1 ± 2.1 | <0.001 | <0.001 |
| E/e′ ratio[a] | 6.9 ± 1.6 | 7.4 ± 1.8 | 8.9 ± 2.1 | 10.1 ± 3.1 | 6.2 ± 1.4 | 7.0 ± 1.6 | 8.0 ± 2.0 | 7.9 ± 2.0 | <0.001 | <0.001 |

Values are mean ± SD. The presented Es are measured by pulsed-wave blood flow Doppler. [a]Average of septal and lateral e′.

a′ = peak mitral annular late diastolic velocity; e′ = peak mitral annular early diastolic velocity; S′ = peak mitral annular systolic velocity.

**TABLE 8 Mitral and Tricuspid Annular Velocities by Color Tissue Doppler According to Age and Sex**

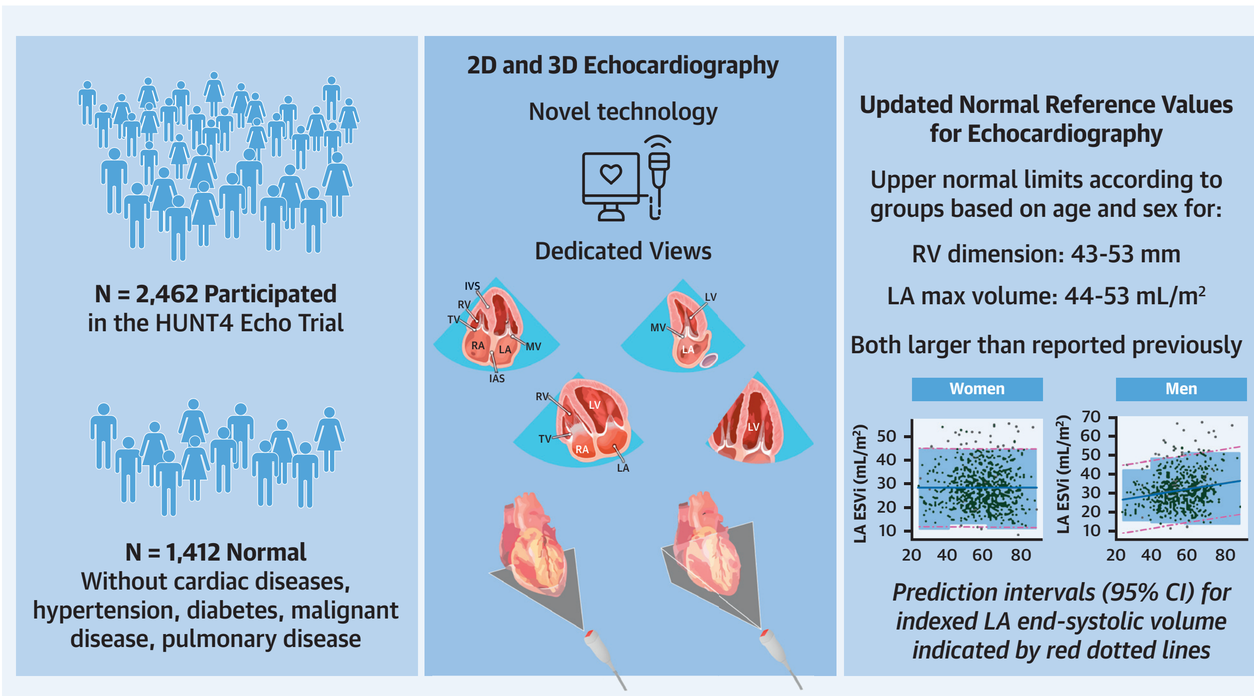
| | Women, y | | | | Men, y | | | | *P* Value | |
|---|---|---|---|---|---|---|---|---|---|---|
| Doppler Measure | 20-39 | 40-59 | 60-79 | ≥80 | 20-39 | 40-59 | 60-79 | ≥80 | Age | Sex |
| Mitral annular velocities | | | | | | | | | | |
| Anterior wall e′ | −12.6 ± 2.2 | −9.2 ± 2.4 | −6.2 ± 1.8 | −4.5 ± 1.7 | −12.3 ± 2.4 | −9.3 ± 2.4 | −6.4 ± 2.1 | −5.1 ± 1.6 | <0.001 | 0.478 |
| Anteroseptal wall e′ | −8.7 ± 1.7 | −6.9 ± 1.8 | −5.0 ± 1.5 | −3.7 ± 1.4 | −9.0 ± 1.9 | −6.8 ± 1.6 | −5.0 ± 1.5 | −3.7 ± 1.0 | <0.001 | 0.880 |
| Inferior wall e′ | −11.1 ± 2.2 | −8.5 ± 2.1 | −5.9 ± 1.8 | −5.1 ± 1.3 | −11.5 ± 2.3 | −8.3 ± 2.1 | −5.9 ± 2.0 | −4.7 ± 1.2 | <0.001 | 0.636 |
| Inferolateral wall e′ | −12.0 ± 2.1 | −9.4 ± 2.3 | −6.9 ± 2.1 | −4.6 ± 1.3 | −12.8 ± 2.0 | −9.3 ± 2.5 | −6.8 ± 2.3 | − 5.6 ± 1.7 | <0.001 | 0.907 |
| Lateral wall e′ | −12.4 ± 2.5 | −9.7 ± 2.3 | −6.9 ± 2.0 | −5.4 ± 1.3 | −13.0 ± 1.8 | −9.7 ± 2.5 | −7.0 ± 2.1 | −5.8 ± 1.9 | <0.001 | 0.517 |
| Septal wall e′ | −9.7 ± 1.8 | −7.5 ± 1.8 | −5.5 ± 1.5 | −4.6 ± 1.0 | −10.2 ± 2.2 | −7.1 ± 1.6 | −5.5 ± 1.5 | −4.6 ± 1.3 | <0.001 | 0.145 |
| Average e′, mean of 6 walls | −11.1 ± 1.5 | −8.5 ± 1.8 | −6.1 ± 1.5 | −4.6 ± 1.0 | −11.4 ± 1.8 | −8.4 ± 1.9 | −6.1 ± 1.5 | −4.9 ± 1.2 | <0.001 | 0.070 |
| Anterior wall a′ | −6.4 ± 1.8 | −7.1 ± 1.8 | −8.0 ± 1.8 | −8.1 ± 2.8 | −7.2 ± 1.8 | −8.1 ± 2.3 | −8.8 ± 1.9 | −8.0 ± 2.1 | <0.001 | <0.001 |
| Anteroseptal wall a′ | −4.8 ± 1.2 | −5.9 ± 1.5 | −6.6 ± 1.7 | −6.3 ± 1.8 | −5.9 ± 1.2 | −7.2 ± 1.4 | −7.8 ± 1.6 | −7.2 ± 1.7 | <0.001 | <0.001 |
| Inferior wall a′ | −7.1 ± 1.9 | −8.7 ± 1.5 | −9.1 ± 1.5 | −7.9 ± 1.4 | −8.0 ± 1.8 | −9.2 ± 2.2 | −9.7 ± 1.6 | −8.8 ± 1.7 | <0.001 | <0.001 |
| Inferolateral wall a′ | −5.9 ± 1.8 | −7.1 ± 2.0 | −8.3 ± 1.9 | −8.4 ± 2.7 | −6.2 ± 1.8 | −7.7 ± 2.5 | −9.0 ± 2.0 | −8.7 ± 2.7 | <0.001 | <0.001 |
| Lateral wall a′ | −6.1 ± 1.4 | −7.0 ± 2.1 | −8.2 ± 1.9 | −8.6 ± 2.6 | −6.1 ± 1.7 | −7.8 ± 2.0 | −8.9 ± 2.0 | −8.6 ± 2.3 | <0.001 | <0.001 |
| Septal wall a′ | −7.0 ± 1.5 | −7.9 ± 1.4 | −8.2 ± 1.4 | −7.4 ± 1.4 | −7.4 ± 1.4 | −8.8 ± 1.5 | −9.0 ± 1.4 | −8.1 ± 1.5 | <0.001 | <0.001 |
| Average a′, mean of 6 walls | −6.2 ± 1.3 | −7.3 ± 1.3 | −8.1 ± 1.3 | −7.5 ± 1.7 | −6.8 ± 1.2 | −8.2 ± 1.4 | −8.8 ± 1.3 | −8.2 ± 1.7 | <0.001 | <0.001 |
| Anterior wall S′ | 8.3 ± 2.1 | 7.1 ± 1.9 | 6.2 ± 1.7 | 5.7 ± 1.4 | 9.2 ± 2.0 | 7.8 ± 2.3 | 7.2 ± 2.1 | 5.8 ± 1.6 | <0.001 | <0.001 |
| Anteroseptal wall S′ | 6.2 ± 1.3 | 5.7 ± 1.2 | 5.0 ± 1.2 | 4.4 ± 1.1 | 7.1 ± 1.3 | 6.0 ± 1.4 | 5.5 ± 1.5 | 5.2 ± 1.0 | <0.001 | <0.001 |
| Inferior wall S′ | 7.4 ± 1.1 | 7.0 ± 1.4 | 6.2 ± 1.1 | 5.4 ± 0.6 | 8.7 ± 1.3 | 7.8 ± 1.3 | 7.2 ± 1.3 | 6.5 ± 1.2 | <0.001 | <0.001 |
| Inferolateral wall S′ | 7.2 ± 1.9 | 7.2 ± 1.7 | 6.8 ± 1.6 | 5.9 ± 1.5 | 9.0 ± 1.9 | 7.7 ± 2.5 | 7.4 ± 2.1 | 7.3 ± 3.1 | <0.001 | <0.001 |
| Lateral wall S′ | 7.8 ± 1.9 | 7.4 ± 1.6 | 6.8 ± 1.7 | 6.6 ± 1.1 | 9.3 ± 2.0 | 8.0 ± 2.2 | 7.7 ± 2.0 | 7.3 ± 2.6 | <0.001 | <0.001 |
| Septal wall S′ | 7.0 ± 1.0 | 6.5 ± 1.0 | 5.8 ± 1.1 | 5.3 ± 0.8 | 7.8 ± 1.2 | 7.0 ± 1.1 | 6.6 ± 1.1 | 6.5 ± 1.0 | <0.001 | <0.001 |
| Average S′, mean of 6 walls | 7.3 ± 1.2 | 6.8 ± 1.0 | 6.2 ± 1.1 | 5.5 ± 0.7 | 8.6 ± 1.3 | 7.5 ± 1.2 | 7.0 ± 1.3 | 6.4 ± 1.5 | <0.001 | <0.001 |
| Tricuspid annular velocities | | | | | | | | | | |
| Free wall e′ | −10.7 ± 2.0 | −9.1 ± 2.3 | −7.6 ± 1.9 | −7.3 ± 2.9 | −10.0 ± 2.3 | −8.7 ± 2.1 | −7.6 ± 2.4 | −7.0 ± 1.4 | <0.001 | 0.105 |
| Free wall a′ | −9.3 ± 2.6 | −10.7 ± 2.3 | −11.3 ± 2.2 | −11.5 ± 2.2 | −8.5 ± 2.7 | −10.1 ± 2.6 | −11.1 ± 2.3 | −11.4 ± 2.4 | <0.001 | 0.001 |
| Free wall S′ | 11.2 ± 1.6 | 10.8 ± 1.6 | 10.4 ± 2.1 | 10.3 ± 1.9 | 11.2 ± 1.8 | 11.1 ± 2.0 | 11.1 ± 1.9 | 12.0 ± 1.9 | 0.017 | <0.001 |

Values are mean ± SD.
Abbreviations as in Table 7.

Association of Cardiovascular Imaging and the American Society of Echocardiography, we measured larger LA volumes with upper normal limits for sex-based age groups (all ≥44 mL/m²).[1,9,10] The upper normal limits for the younger age groups are well aligned with the recent WASE Normal Values Study, suggesting an upper normal limit of 41 mL/m² (**Table 9**).[10] LA ESV indexed to BSA has been implemented as an important variable in the evaluation of diastolic dysfunction and increased filling pressures in the LV,[24] and has been shown to be a prognosticator for disease including stroke, heart failure, and AF.[25-27] By extrapolating the results to the recommended cutoff value of 34 mL/m²,[24] 27% of the healthy individuals in the present study had an enlarged LA volume. The need for revising the recommended cutoff for indexed LA ESV is also supported by others.[10,28-30] Importantly, neither indexing LA ESV to BSA nor to exponents of height removed the variation between sexes and age groups. A recent publication showed that indexing to height improved prediction of adverse events compared with indexing to BSA in obese individuals.[31] There is also an ongoing debate on how to best scale cardiac measures.[14] Because this was a cross-sectional study, we were not able to provide data on which indexing method best predicts future events. In evaluation of the model fits, we did not reveal significant differences between indexing by BSA or by exponents of height. Some of the differences between sexes related to different methods of indexing volumetric measurements may be explained by sex-specific differences in the distribution of body size.

**2D VS 3D MEASUREMENTS.** LV volumes by 3D measurements were 5% to 6% larger than 2D measurements, whereas there were no significant differences for LA volumes. These differences were less than previously reported.[32] We expect that the consistent results across 2D and 3D methods are mainly explained by more dedicated 2D recordings for the specific tasks, eg, dedicated views for assessment of the LA. It is well known that foreshortening of 2D recordings leads to underestimation of the measured volumes. As presented in **Table 2**, both length and

**CENTRAL ILLUSTRATION Study Overview**




**Eriksen-Volnes T, et al. J Am Coll Cardiol Img. 2023;16(12):1501-1515.**

Among 2,462 participants in the HUNT4 echocardiographic study, 1,412 fulfilled the criteria for the normal values study. Guideline-directed dedicated echocardiographic views were recorded for measurements of cardiac dimensions and left ventricular diastolic and systolic function. Updated normal values were provided. Left atrial volume indices and right ventricular dimensions were larger compared to previous studies. 2D = 2-dimensional; 3D = 3-dimensional; ESVi = end-systolic volume indexed to body surface area; IAS = interatrial septum; IVS = interventricular septum; LA = left atrium; LV = left ventricular; MV = mitral valve; RA = right atrial; RV = right ventricular; TV = tricuspidal valve.

area of the LA were consistent across 4-chamber and 2-chamber recordings, with a mean difference of only 1.2%. The importance of optimizing the views for the dedicated measurements is well supported by others.[9,13,32] We also present LA ESV for different 2D methods, such as MOD and area-length methods, and compared those with 3D methods. The recommended MOD and 3D methods were not significantly different, with $P = 0.28$.

The same methodologic aspects also relate to right-sided measurements.[12] The use of RV-focused views do, at least partly, explain the larger RV dimensions compared with previous studies.[9,12] Because testing of maximal oxygen consumption was part of the study, some selection bias toward a supranormal population may be present, but the high attendance rate indicates that it was less important than the use of the dedicated views.

Furthermore, some technologic aspects also may influence the 3D measurements. In general, 3D recordings have lower temporal and lateral resolutions compared with 2D, potentially influencing timing of end-diastole and end-systole as well as endocardial border detection. In addition, the 3D methods are model based, which may interfere with the geometry of the LV and LA present in the individual participants. These factors may influence the minor differences between 2D and 3D measurements of the LV and LA.

**DOPPLER MEASUREMENTS OF BLOOD FLOW AND TISSUE VELOCITIES.** Lower S′ and e′ with higher age is well known, reflecting impaired longitudinal LV function by age,[3,5,33,34] and highlight the high sensitivity for assessment of LV dysfunction.[35] The blood flow velocities were well aligned with previous studies,[3,36] consistently with less change of the methods and workflow over time. Lateral and septal e′ below 10 cm/s and 7 cm/s serve as potential markers for diastolic function,[24] and a significant proportion had lower normal limits of e′ below these cutoffs. Taking age into account may be of clinical importance, because the lower normal limits of e′ were

**TABLE 9 Cutoff Values for Normality**

| | Women, y | | | | Men, y | | | |
|---|---|---|---|---|---|---|---|---|
| | 20-39 | 40-59 | 60-79 | ≥80 | 20-39 | 40-59 | 60-79 | ≥80 |
| Left ventricle | | | | | | | | |
| IVS, end-diastole, mm | 9.3 | 10.0 | 11.0 | 10.2 | 10.5 | 11.3 | 12.1 | 12.5 |
| LV internal diameter, end-diastole, mm | 56.6 | 56.4 | 55.1 | 45.7 | 60.7 | 61.3 | 60.2 | 60.3 |
| LV posterior wall thickness, end-diastole, mm | 8.4 | 9.0 | 9.7 | 10.0 | 9.2 | 10.3 | 10.7 | 9.8 |
| LV outflow tract diameter, mm | 24.2 | 23.9 | 23.9 | 23.5 | 27.0 | 26.8 | 27.0 | 24.8 |
| LV EDVi, (MOD), mL/$m^2$ | 89.6 | 78.1 | 68.3 | 50.8 | 96.5 | 92.1 | 85.0 | 71.9 |
| LV EDVi, 3D, mL/$m^2$ | 86.6 | 81.7 | 71.5 | 64.0 | 97.1 | 91.3 | 84.3 | 76.6 |
| LV EDV indexed to height$^3$, (MOD), mL/$m^3$ | 33.5 | 30.1 | 26.7 | 20.1 | 33.8 | 32.3 | 30.6 | 26.4 |
| LV EDV indexed to height$^3$, 3D, mL/$m^3$ | 32.7 | 31.9 | 28.2 | 23.9 | 34.0 | 32.3 | 30.5 | 27.4 |
| LVEF ad modum Simpson, % | 51.4 | 51.7 | 49.8 | 56.1 | 46.5 | 49.4 | 50.4 | 49.3 |
| LVEF, 3D, % | 50.6 | 51.9 | 50.2 | 49.1 | 50.1 | 49.6 | 50.4 | 46.2 |
| Left atrium | | | | | | | | |
| LA ESV indexed to BSA, (MOD), mL/$m^2$ | 44.8 | 46.5 | 46.7 | 52.2 | 44.8 | 51.3 | 53.3 | NA |
| LA ESV indexed to BSA, 3D, mL/$m^2$ | 47.2 | 41.8 | 41.9 | 42.8 | 38.7 | 45.0 | 47.2 | 56.3 |
| LA ESV indexed to height$^3$, (MOD), mL/$m^3$ | 16.4 | 17.1 | 17.4 | 20.9 | 14.5 | 16.9 | 18.4 | NA |
| LA ESV indexed to height$^3$, (3D), mL/$m^3$ | 18.1 | 16.3 | 16.4 | 16.3 | 13.3 | 15.8 | 17.1 | NA |
| LA end-systolic area, 4-chamber view, $cm^2$ | 24.8 | 24.3 | 24.1 | 25.4 | 25.0 | 27.8 | 28.9 | NA |
| LA EF, 3D, % | 41.0 | 40.6 | 36.5 | 26.9 | 45.7 | 38.5 | 35.4 | 28.4 |
| Right ventricle | | | | | | | | |
| RV basal diameter, RV focused 4-chamber view, cm[a] | 4.6 | 4.4 | 4.3 | NA | NA | 5.3 | 5.1 | NA |
| RV mid diameter, RV focused 4-chamber view, cm | 3.5 | 3.3 | 3.1 | 3.2 | 3.4 | 3.9 | 3.7 | 3.8 |
| Right atrium | | | | | | | | |
| RA end-systolic area, RV focused 4-chamber view, $cm^2$[a] | 20.2 | 21.5 | 20.8 | NA | 28.2 | 27.7 | 28.4 | NA |
| RA ESVi, (MOD), mL/$m^2$[a] | 37.3 | 36.6 | 36.5 | NA | 52.7 | 47.5 | 48.7 | NA |
| Doppler measurements | | | | | | | | |
| Tricuspid regurgitation peak velocity, m/s | 2.73 | 2.72 | 2.76 | 2.63 | 2.73 | 2.83 | 2.84 | NA |
| E/e′ (average of septal and lateral e′) ratio | 10.1 | 10.9 | 13.1 | 16.1 | 9.0 | 10.1 | 12.0 | 11.8 |
| Septal e′, cm/s | 6.6 | 4.8 | 3.1 | 2.5 | 6.3 | 4.4 | 3.3 | 2.5 |
| Lateral e′, cm/s | 9.3 | 6.8 | 4.4 | 3.8 | 9.3 | 5.9 | 4.0 | 4.7 |

Values are mean + 1.96 SD or mean − 1.96 SD, unless otherwise indicated. [a]Cutoff values presented as 97.5th percentile.

EDVi = end-diastolic volume indexed to body surface area; ESVi = end-systolic volume indexed to body surface area; NA = not applicable because of a too low number of persons; other abbreviations as in Tables 2, 3, 6, and 7.

below the cutoffs for those aged ≥60 years. Compared with the NORRE and WASE studies, the present values of mitral annular septal and lateral e′ were generally well aligned. The present values were approximately 0.5 cm/s lower than presented in the NORRE and WASE studies, with highest values presented in the NORRE studies. Because age is a major determinant for mitral annular velocities, differences in distribution within the age groups may partly explain the minor differences between studies. In addition, the Doppler spectrum of pulsed-wave tissue Doppler recordings are wide compared with the size of the measurements. Therefore, small differences in gain settings and placement of the peak values may be another explanation.

**THE IMPORTANCE OF BLOOD PRESSURE AND BODY SIZE.** We found no large differences in LV volumes in the sensitivity analyses. However, interventricular septum thickness was smaller (difference 1 mm) and LA and RA ESVs indexed to BSA were somewhat larger in the sensitivity group compared with the overall groups. This highlights that in a general population free from cardiac diseases, the LA volume may not be a marker of cardiac risk as hypothesized earlier.[29]

**STUDY LIMITATIONS.** The main limitation is the population being mainly of Caucasian origin, which may reduce the generalizability to other races, but as shown by the WASE study the differences between races are quite small.[4] Furthermore, the effect by age presented is different between groups and not caused by ageing per se. Even though we have included a large population, we cannot exclude some selection bias toward a supranormal population in this study. Because no software for 3D assessment of the right-side chambers was available at our institution at the time of data collection, we did not record 3D volumes of the RA or RV. Even though we present highly feasible measurements of cardiac size and functional indices, the feasibility varies across the methods used (Supplemental Table 6).

## CONCLUSIONS

We present updated normal values for measures of left- and right-side ventricular and atrial size and function from a large healthy population with a wide age-span. Importantly, the upper normal limits for LA volumes and RV dimensions were higher than previously suggested, highlighting the importance of updated reference ranges according to refinement of technology and echocardiographic acquisitions. Furthermore, the small differences between 2D and 3D measurements also may be explained by more dedicated 2D recordings aligned to the axis of the respective chambers.

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**PERSPECTIVES**

**COMPETENCY IN MEDICAL KNOWLEDGE:** Overall, this study highlights the need for clinicians to be aware of how methodology may influence echocardiographic measurements before making clinical decisions. Indexing LV volumes to BSA takes less of the variation between sexes into account compared with indexing to height raised to the power of 3.

**TRANSLATIONAL OUTLOOK:** Updated normal reference values for echocardiography may improve care of individual patients. Implementing the prediction interval equations for normal values into future scanners may further improve the use of normal values in the everyday clinic.

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**KEY WORDS** cardiac imaging, left atrium, normal values, right atrium, epidemiology, population

**APPENDIX** For an expanded Methods section as well as supplemental tables, please see the online version of this paper.