

NORMAL ECHOCARDIOGRAPHIC MEASUREMENTS IN A KOREAN POPULATION STUDY: PART I. CARDIAC CHAMBER AND GREAT ARTERY EVALUATION

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BACKGROUND: Measurement of the cardiac chamber is essential, and current guidelines recommend measuring and reporting values for both sides of the cardiac chamber during echocardiographic evaluation. Normal echocardiographic reference values have been suggested previously, but detailed information about right-sided chambers and values according to gender was not included.

METHODS: This is a prospective multicenter (23 centers) study evaluating normal Korean adult subjects using comprehensive echocardiography. We included normal adult subjects (age; 20–79 years old) who had no significant cardiac disorders or illnesses,

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such as hypertension or diabetes, which could affect cardiac structure and function. We measured the cardiac chamber including both right and left ventricles as well as atria according to current echocardiography guidelines and compared values according to gender and age groups.

RESULTS: A total of 1003 subjects were evaluated and the mean age was 48 ± 16 years. Left ventricular (LV) dimensions increased, but LV volume decreased in older subjects. Right ventricular (RV) area decreased in women and older subjects, and the RV long-axis dimension showed a similar trend. Left atrial (LA) volume increased in men but there were no differences in LA volume index between men and women. The dimension of great arteries increased in men and older subjects.

CONCLUSION: Since there were considerable differences between men and women and in the different age groups, and the trends differed significantly between different echo variables, normal echocardiographic cutoff values should be differentially applied based on age and gender.

KEY WORDS: Echocardiography · Normal population · Reference value.

INTRODUCTION

Echocardiography has been referred to as the single most important study in patients with cardiovascular disorders, as it provides comprehensive information about cardiac function and hemodynamic parameters.¹⁾ Recently, there were improvements in echocardiographic techniques including higher resolution with harmonic imaging and better information about cardiac structure, function, and prognostic values became available.^{2,3)} Current echocardiographic guidelines recommend that physicians measure and provide detailed information on both right- and left-sided cardiac chambers when evaluating patients.^{4,5)} Although there are reports on normal echocardiographic data, reference values for cardiac structure and function may be influenced by physical characteristics of the target population.⁶⁻⁸⁾ Therefore, reference values from one population cannot be extrapolated to other populations.

Previously, normal echocardiographic reference values in Korea were defined in a multicenter prospective study.⁹⁾ Although reference values were provided according to age group, gender differences were not investigated. Furthermore, detailed information about right-sided cardiac chambers and tissue Doppler imaging for diastolic function was not provided.

In this regard, we performed the Normal echOcardiographic Measurements in KoreAn popuLation (NORMAL) study, which was a multicenter prospective study performed from January 2011 to March 2014 to establish normal reference values for echocardiography in a Korean population. We sought to provide two-dimensional (2D) and M-mode measurement values (Doppler and tissue Doppler variables will be reported in part II of the NORMAL study) for normal echocardiography, including both left and right-sided cardiac chambers and great arteries according to age and gender groups.

METHODS

STUDY POPULATIONS

The NORMAL study was a prospective nationwide multi-

center (23 centers) study evaluating normal Korean adult subjects using comprehensive echocardiography. We included normal adult subjects (age; 20–79 years old) who had no significant cardiac disorders or clinical illnesses that might affect cardiac structure and function, such as hypertension and diabetes. We also excluded subjects if a structural or functional abnormality on the cardiac valve or cardiac chamber was evident during echocardiographic examination. All study patients agreed to provide their information for research purposes and the study protocol was approved by the Institutional Review Board of each institute. Written informed consent was waived.

ECHOCARDIOGRAPHY

Echocardiographic images were acquired and measured at each institute. They were stored in DICOM format and electronically transferred to the Echocardiographic Core laboratory (ECL) in Samsung Medical Center. Final measurements and analysis were performed in ECL with a dedicated software package (EchoPAC, GE Medical Systems, Horten, Norway).

Echocardiographic measurements were performed according to the American Society of Echocardiography guidelines.^{5,10,11)} All echo variables were measured in three cardiac cycles and average values were taken. Briefly, M-mode echocardiography was performed on parasternal views. Left ventricular (LV) end-diastolic dimension (LVEDD), interventricular septal wall thickness (IVST), LV posterior wall thickness (LVPWT), and the dimension of the aortic root were measured at end-diastole. The LV end-systolic dimension (LVESD) and left atrial (LA) anteroposterior dimension were measured at end-systole. LVEDD and LVESD were indexed to body surface area (BSA). LV ejection fraction (LVEF) was calculated using linear method using following formula; $LVEF (\%) = (LVEDD^2 - LVESD^2) / LVEDD^2 \times 100 (\%)$. An M-mode echocardiogram of the right ventricular (RV) free wall was also obtained on a subcostal view to measure RV end-diastolic free wall thickness. Tricuspid annular plane systolic excursion (TAPSE) was measured by placing the M-mode cursor line along the movement of the tricuspid annu-

lus during an M-mode echocardiogram on an apical 4-chamber view.

LV dimensions (LVEDD and LVESD) and LV wall thickness (IVST and LVPWT) were also measured on 2D images using parasternal views. LV volumes and ejection fraction were measured using the biplane Simpson's method on apical 4-chamber and 2-chamber views. LV end-diastolic and end-systolic volume (LVEDV and LVESV) were measured and indexed to BSA. The LV long-axis dimension was also measured, and the sphericity index was calculated as the LV short-axis dimension (LVEDD) divided by the LV long-axis dimension. LV mass (LVM) was calculated using a linear method using both measurement values from M-mode and 2D images as follows: $LVM (gm) = 0.8 \times \{1.04 \times [(IVST + LVEDD + LVPWT)^3 - LVEDD^3]\} + 0.6 (gm)$. LVM was also indexed to BSA. Relative wall thickness (RWT) was calculated as follows: $RWT = 2 \times LVPWT / LVEDD$.

The basal and mid RV short-axis dimension and the RV long-axis dimension were measured in the RV-focused apical 4-chamber view at end-diastole (Fig. 1A and B). RV end-diastolic and end-systolic area (RVEDA and RVESA) were also measured in the RV-focused apical 4-chamber view (Fig. 1C and D), and RV fractional area change (RVFAC) was calculated as follows: $RVFAC (\%) = (RVEDA - RVESA) / RVEDA \times 100 (\%)$. Proximal and distal RV outflow tract dimensions were measured on the parasternal short-axis view.

The LA anteroposterior dimension was measured on para-

sternal views, and transverse and longitudinal dimensions were measured on an apical 4-chamber view at end-systole. LA volume was calculated using both the ellipsoid method and the area-length method and indexed to BSA. Right atrial (RA) transverse and longitudinal dimensions as well as RA area were measured on an apical 4-chamber view.

Images for aortic root measurement were acquired on a zoomed parasternal long-axis view and dimensions of the aortic annulus, the sinus of Valsalva, the sinotubular junction, and the proximal ascending aorta were measured at end-diastole using leading edge to leading edge techniques. The main pulmonary artery was measured at end-diastole on a parasternal short-axis view.

STATISTICAL ANALYSIS

Data are expressed as mean \pm standard deviation and 95% confidence intervals (CIs) are provided for continuous variables. The independent t-test was used to compare mean values between men and women, and a one-way analysis of variance test was performed to evaluate whether mean values differed based on age groups. Pearson's method was used to evaluate significant correlations among clinical and measurement variables. To evaluate the intra- and interobserver variability, 50 cases were randomly selected and intraclass correlation coefficients (ICC) were calculated. One researcher repeated measurements at least 2 weeks after the first measurements for intraobserver

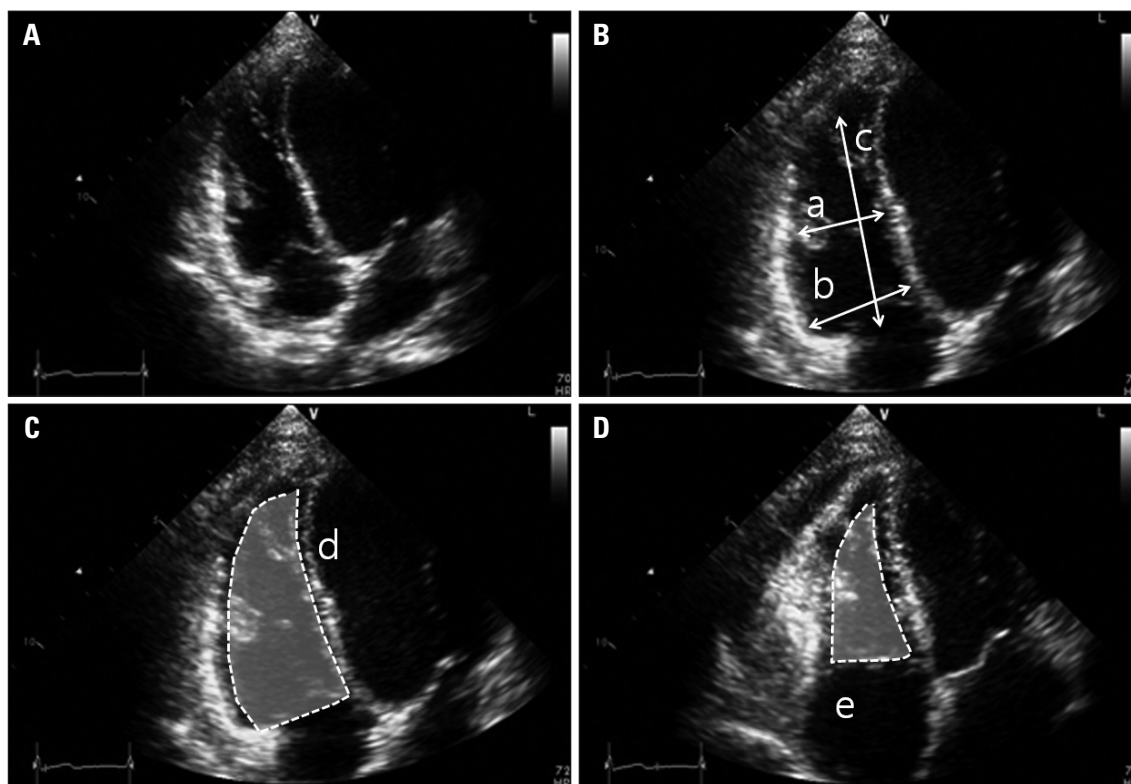


Fig. 1. Measurement of right ventricular (RV) dimension and RV fractional area change in focused RV view. After obtaining RV focused view (A), mid (a), basal (b), and longitudinal RV dimensions (c) are measured at end-diastolic period (B). In the same view, RV end-diastolic area (d) and RV end-systolic area (e) are measured and RV fractional area change are calculated as $(d - e) / d \times 100\%$ (C and D).

variability testing, and another researcher who was blinded to the first measurement value performed measurements to evaluate interobserver variability. p values < 0.05 were considered statistically significant. All statistical analyses were performed using SPSS Statistics version 21 (SPSS Inc., Chicago, IL, USA).

RESULTS

CLINICAL CHARACTERISTICS OF STUDY PATIENTS

A total of 1003 normal subjects from 23 centers were evaluated in the current study. Demographic and clinical data are provided in Table 1 according to gender and in Supplementary Table 1 according to gender and age. The mean age was 48 ± 16 years in both men and women. Physical findings such as weight, height, BSA, and body mass index were significantly higher in men compared to women ($p < 0.0001$ for all variables). Similarly, systolic and diastolic blood pressures in men were slightly higher than those in women, but all values were with-

in normal limits. There was no significant difference in heart rate between men and women. BSA decreased with age in both men and women. While older men had a lower body mass index than younger men, body mass index was increased in older women compared to younger women. Systolic blood pressure increased with age in both men and women, and this trend was stronger in women.

M-MODE ECHOCARDIOGRAPHIC DATA

M-mode variables according to gender groups and according to age and gender groups are presented in Table 2 and Supplementary Table 2, respectively. There were significant differences in M-mode variables between men and women, except in TAPSE. LVEDD was not significantly different according to age in men, though it increased with age in women. However, indexed LVEDD and LVESD were greater in women compared to men and indexed LVEDD was increased with age in both men and women. Likewise, indexed LVESD increased with age in women but no significant differences were noted according

Table 1. Demographic and clinical findings of study patients according to gender

| Variables | Men | | Women | | Total | | p |
|------------------|-----------------|-----------|-----------------|-----------|-----------------|-----------|------------|
| | Mean \pm SD | 95% CI | Mean \pm SD | 95% CI | Mean \pm SD | 95% CI | |
| Number | 487 | | 516 | | 1003 | | |
| Age (year) | 48 ± 16 | 17–79 | 48 ± 16 | 18–79 | 48 ± 16 | 18–79 | 0.9659 |
| Weight (kg) | 69 ± 9 | 50–87 | 56 ± 7 | 41–70 | 62 ± 11 | 41–83 | < 0.0001 |
| Height (cm) | 170 ± 7 | 157–184 | 158 ± 6 | 147–169 | 164 ± 9 | 147–181 | < 0.0001 |
| BSA (m^2) | 1.79 ± 0.14 | 1.51–2.07 | 1.55 ± 0.11 | 1.34–1.77 | 1.67 ± 0.17 | 1.33–2.01 | < 0.0001 |
| BMI (kg/m^2) | 23.7 ± 2.6 | 18.6–28.7 | 22.3 ± 2.8 | 16.9–27.8 | 23.0 ± 2.8 | 17.6–28.4 | < 0.0001 |
| SBP (mm Hg) | 123 ± 12 | 99–146 | 118 ± 13 | 93–142 | 120 ± 13 | 95–145 | < 0.0001 |
| DBP (mm Hg) | 75 ± 9 | 58–93 | 72 ± 10 | 53–91 | 73 ± 9 | 55–92 | < 0.0001 |
| Heart rate (bpm) | 68 ± 10 | 49–87 | 69 ± 9 | 51–86 | 68 ± 9 | 50–86 | 0.0635 |

BSA: body surface area, BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, SD: standard deviation, CI: confidence interval

Table 2. M-mode variables according to gender

| Variables | Men | | Women | | Total | | p |
|---|----------------|-----------|----------------|-----------|----------------|-----------|------------|
| | Mean \pm SD | 95% CI | Mean \pm SD | 95% CI | Mean \pm SD | 95% CI | |
| LVEDD (mm) | 50.5 ± 3.3 | 44.0–57.0 | 47.4 ± 3.3 | 41.0–53.9 | 48.9 ± 3.6 | 41.8–56.1 | < 0.0001 |
| LVESD (mm) | 30.9 ± 2.9 | 25.3–36.5 | 28.7 ± 2.8 | 23.3–34.1 | 29.8 ± 3 | 23.9–35.7 | < 0.0001 |
| LVEDD index (mm/m^2) | 28.3 ± 2.2 | 23.9–32.7 | 30.6 ± 2.5 | 25.7–35.5 | 29.5 ± 2.6 | 24.3–34.6 | < 0.0001 |
| LVESD index (mm/m^2) | 17.3 ± 1.7 | 13.9–20.7 | 18.5 ± 1.9 | 14.8–22.2 | 17.9 ± 1.9 | 14.2–21.6 | < 0.0001 |
| LVEF (%) by linear method | 62.4 ± 4.6 | 53.3–71.5 | 63.3 ± 4.3 | 54.8–71.8 | 62.9 ± 4.5 | 54.1–71.7 | 0.0023 |
| IVSWT (mm) | 8.2 ± 1.1 | 6.3–10.2 | 7.4 ± 0.9 | 5.7–9.1 | 7.8 ± 1 | 5.9–9.8 | < 0.0001 |
| LVPWT (mm) | 8.2 ± 0.9 | 6.5–9.9 | 7.4 ± 0.8 | 5.8–9.0 | 7.8 ± 0.9 | 6–9.6 | < 0.0001 |
| LA AP diameter (mm) | 36.1 ± 3.9 | 28.5–43.6 | 33.6 ± 4.0 | 25.7–41.5 | 34.8 ± 4.1 | 26.7–42.9 | < 0.0001 |
| Aortic root diameter (mm) | 32.2 ± 3.0 | 26.4–38.1 | 28.7 ± 2.8 | 23.2–34.3 | 30.4 ± 3.4 | 23.8–37.1 | < 0.0001 |
| RV end-diastolic free wall thickness (mm) | 4.2 ± 0.9 | 2.5–6.0 | 4.0 ± 0.8 | 2.4–5.6 | 4.1 ± 0.9 | 2.4–5.8 | < 0.0001 |
| TAPSE (mm) | 22.6 ± 3.2 | 16.3–29.0 | 22.3 ± 3.1 | 16.3–28.3 | 22.5 ± 3.1 | 16.3–28.6 | 0.0898 |

LVEDD: left ventricular end-diastolic dimension, LVESD: left ventricular end-systolic dimension, LVEF: left ventricular ejection fraction, IVSWT: interventricular septal wall thickness, LVPWT: left ventricular posterior wall thickness, LA: left atrium, AP: anteroposterior, RV: right ventricular, TAPSE: tricuspid annular plane systolic excursion, SD: standard deviation, CI: confidence interval

to age in men. LV wall thicknesses and LA anteroposterior dimension increased with age in both men and women. However, there was no significant change in RV end-diastolic free wall thickness according to age in both gender groups. TAPSE was significantly reduced only in elderly women (71 to 80 years old).

2D MEASUREMENT DATA ON CARDIAC CHAMBERS: VENTRICLES

Measurement values of the LV and RV using 2D echocardiography according to gender groups and according to age and gender groups are presented in Table 3 and Supplementary Table 3, respectively. Every variable regarding the dimension and wall thickness of both ventricles was significantly larger and thicker in men compared to women. Measurement values of LVEDD, LVESD and their indexed values showed similar trends compared with those from M-mode. The LVEDV and LVESV indices were also greater in men than in women. Interestingly, LVEF and the sphericity index, as well as RVFAC, were significantly higher in women. The LV short-axis dimension decreased with age in men and slightly increased in older women. However, the LV long-axis dimension was significantly decreased with age in both gender groups. Interestingly, LV volumes significantly decreased with age in both groups, which

was not observed in the mean values of LV short-axis dimensions. LV long-axis dimension was significantly correlated with height in both men and women ($r = 0.508, p < 0.0001$ in men and $r = 0.434, p < 0.0001$ in women). Interestingly, the LV long-axis dimension was more significantly correlated with LVEDV in both men and women ($r = 0.638, p < 0.0001$ in men and $r = 0.578, p < 0.0001$ in women) than the LV short-axis dimension was ($r = 0.528, p < 0.0001$ in men and $r = 0.511, p < 0.0001$ in women). Similar trends according to age and gender were noted in RV short-axis dimensions, long-axis dimensions, and RV areas in apical 4-chamber views.

2D MEASUREMENT DATA ON CARDIAC CHAMBERS: ATRIA

Measurement values of the LA and RA using 2D echocardiography according to gender groups and according to age and gender groups are presented in Table 4 and Supplementary Table 4, respectively. Every echo variable related to LA and RA size in men was significantly larger than those in women. However, the mean values of indexed LA volume measured using both ellipsoidal and area-length were not significantly different between men and women. Mean values of LA volume by the area-length method were significantly higher than those

Table 3. Measurement values of the left and right ventricles by 2D imaging according to gender

| Variables | Men | | Women | | Total | | p |
|--|-------------|-----------|-------------|-----------|-------------|-----------|----------|
| | Mean ± SD | 95% CI | Mean ± SD | 95% CI | Mean ± SD | 95% CI | |
| LVEDD (mm) | 49.1 ± 3.3 | 42.5–55.7 | 46.5 ± 3.2 | 40.2–52.7 | 47.7 ± 3.5 | 40.8–54.7 | < 0.0001 |
| LVESD (mm) | 30.5 ± 3.1 | 24.4–36.6 | 28.6 ± 3.0 | 22.8–34.5 | 29.5 ± 3.2 | 23.3–35.8 | < 0.0001 |
| LVEDD index (mm/m ²) | 27.5 ± 2.3 | 22.9–32.0 | 30.0 ± 2.4 | 25.3–34.6 | 28.8 ± 2.7 | 23.6–34.0 | < 0.0001 |
| LVESD index (mm/m ²) | 17.1 ± 1.9 | 13.4–20.7 | 18.5 ± 2.0 | 14.5–22.4 | 17.8 ± 2.1 | 13.7–21.8 | < 0.0001 |
| LVEF (%) by linear method | 61.3 ± 5.1 | 51.2–71.3 | 61.9 ± 5.5 | 51.1–72.7 | 61.6 ± 5.3 | 51.1–72.0 | 0.0634 |
| IVSWT (mm) | 8.1 ± 1.0 | 6.1–10.1 | 7.3 ± 0.9 | 5.5–9.1 | 7.7 ± 1.0 | 5.7–9.7 | < 0.0001 |
| LVPWT (mm) | 8.0 ± 0.9 | 6.2–9.9 | 7.3 ± 0.9 | 5.4–9.1 | 7.6 ± 1.0 | 5.7–9.6 | < 0.0001 |
| LVEDV (mL) | 113 ± 22 | 70–156 | 92 ± 16 | 59–124 | 102 ± 22 | 59–145 | < 0.0001 |
| LVESV (mL) | 43 ± 11 | 22–63 | 34 ± 8 | 17–50 | 38 ± 11 | 17–58 | < 0.0001 |
| LVEDV index (mL/m ²) | 63 ± 11 | 42–83 | 59 ± 9 | 40–77 | 61 ± 10 | 41–81 | < 0.0001 |
| LVESV index (mL/m ²) | 23.6 ± 5.2 | 13.4–33.9 | 21.6 ± 5.0 | 11.7–31.4 | 22.6 ± 5.2 | 12.3–32.8 | < 0.0001 |
| LVEF (%) by volumetric method | 62.6 ± 4.5 | 53.6–71.5 | 63.5 ± 4.8 | 54.1–72.9 | 63.1 ± 4.7 | 53.8–72.3 | 0.0014 |
| LV long-axis dimension (mm) | 88 ± 6 | 76–100 | 81 ± 6 | 70–92 | 84 ± 7 | 71–98 | < 0.0001 |
| Sphericity index | 0.56 ± 0.05 | 0.47–0.65 | 0.58 ± 0.05 | 0.48–0.68 | 0.57 ± 0.05 | 0.48–0.67 | < 0.0001 |
| RV end-diastolic area (cm ²) | 17.3 ± 3.3 | 10.9–23.8 | 14.3 ± 2.7 | 9.0–19.7 | 15.8 ± 3.4 | 9.2–22.4 | < 0.0001 |
| RV end-systolic area (cm ²) | 9.3 ± 2.2 | 5.0–13.6 | 7.4 ± 1.7 | 4.1–10.7 | 8.3 ± 2.2 | 4.1–12.6 | < 0.0001 |
| RVFAC (%) | 46 ± 6 | 34–59 | 48 ± 6 | 36–60 | 47 ± 6 | 35–60 | < 0.0001 |
| Basal RVD (mm) | 35.4 ± 3.7 | 28.1–42.8 | 32.6 ± 3.6 | 25.6–39.7 | 34.0 ± 3.9 | 26.3–41.7 | < 0.0001 |
| Mid RVD (mm) | 27.1 ± 3.7 | 19.8–34.4 | 24.7 ± 3.3 | 18.1–31.2 | 25.8 ± 3.7 | 18.5–33.1 | < 0.0001 |
| RV long-axis dimension (mm) | 70 ± 9 | 52–89 | 64 ± 9 | 46–82 | 67 ± 10 | 48–86 | < 0.0001 |
| Proximal RVOT dimension (mm) | 29.7 ± 4.3 | 21.3–38.1 | 27.0 ± 4.0 | 19.1–34.8 | 28.3 ± 4.4 | 19.7–36.9 | < 0.0001 |
| Distal RVOT dimension (mm) | 23.5 ± 3.1 | 17.4–29.6 | 22.2 ± 2.8 | 16.6–27.8 | 22.8 ± 3.0 | 16.9–28.8 | < 0.0001 |

LV: left ventricular, LVEDD: LV end-diastolic dimension, LVESD: LV end-systolic dimension, LVEF: LV ejection fraction, IVSWT: interventricular septal wall thickness, LVPWT: LV posterior wall thickness, LVEDV: LV end-diastolic volume, LVESV: LV end-systolic volume, RV: right ventricular, RVFAC: RV fractional area change, RVD: RV dimension, RVOT: RV outflow tract, 2D: two-dimensional, SD: standard deviation, CI: confidence interval

measured by the ellipsoid method. Echocardiographic variables related to LA size significantly increased with age only in women, and those variables were not significantly different according to age in men, except the LA anteroposterior dimension. However, the LA volume index increased with age in both men and women.

2D MEASUREMENT DATA ON GREAT VESSELS

Measurement values of the aortic root and the main pulmonary artery using 2D echocardiography according to gender groups and according to age and gender groups are presented

in Table 5 and Supplementary Table 5, respectively. Every echocardiographic variable regarding both the aortic root and the main pulmonary artery was greater in men than in women, and increased with age in both men and women.

LVM AND RWT

LVM, LVM index, and RWT calculated using both M-mode and 2D measurement values according to age and gender groups are presented in Table 6 and Supplementary Table 6, respectively. Both LVM and LVM index were significantly greater in men than in women. RWT was significantly greater in men com-

Table 4. Measurement values of the left and right atria by 2D imaging according to gender

| Variables | Men | | Women | | Total | | <i>p</i> |
|---|------------|-----------|------------|-----------|------------|-----------|----------|
| | Mean ± SD | 95% CI | Mean ± SD | 95% CI | Mean ± SD | 95% CI | |
| LA area (cm ²) at A4C | 16.3 ± 2.7 | 11.1–21.6 | 15.3 ± 2.7 | 9.9–20.6 | 15.8 ± 2.8 | 10.4–21.2 | < 0.0001 |
| LA area (cm ²) at A2C | 16.4 ± 2.6 | 11.3–21.6 | 15.1 ± 2.7 | 9.7–20.5 | 15.7 ± 2.8 | 10.3–21.2 | < 0.0001 |
| LA longitudinal dimension (cm) | 4.7 ± 0.5 | 3.8–5.6 | 4.6 ± 0.5 | 3.6–5.6 | 4.6 ± 0.5 | 3.7–5.6 | 0.0001 |
| LA transverse dimension (mm) | 38.7 ± 4.0 | 30.9–46.5 | 37.2 ± 3.9 | 29.6–44.8 | 37.9 ± 4.0 | 30.1–45.8 | < 0.0001 |
| LA AP dimension (mm) | 34.7 ± 4.2 | 26.5–43.0 | 32.5 ± 4.0 | 24.7–40.4 | 33.6 ± 4.3 | 25.3–41.9 | < 0.0001 |
| LA volume (mL) by EM | 33 ± 8 | 17–50 | 29 ± 8 | 14–45 | 31 ± 8 | 15–48 | < 0.0001 |
| LA volume index (mL/m ²) by EM | 18.7 ± 4.5 | 9.9–27.5 | 18.9 ± 5.0 | 9.2–28.7 | 18.8 ± 4.7 | 9.5–28.1 | 0.4217 |
| LA volume (mL) by ALM | 49 ± 11 | 27–70 | 43 ± 11 | 22–64 | 46 ± 11 | 24–68 | < 0.0001 |
| LA volume index (mL/m ²) by ALM | 27.2 ± 5.9 | 15.7–38.8 | 27.6 ± 6.7 | 14.5–40.8 | 27.5 ± 6.3 | 15.1–39.8 | 0.3241 |
| RA transverse dimension (mm) | 36.4 ± 4.1 | 28.4–44.4 | 33.2 ± 3.5 | 26.3–40.1 | 34.7 ± 4.1 | 26.7–42.8 | < 0.0001 |
| RA longitudinal dimension (mm) | 46.5 ± 4.6 | 37.5–55.5 | 43.9 ± 4.8 | 34.6–53.3 | 45.2 ± 4.9 | 35.7–54.7 | < 0.0001 |
| RA area (cm ²) | 14.2 ± 2.3 | 9.7–18.8 | 12.3 ± 2.2 | 8.0–16.7 | 13.3 ± 2.4 | 8.5–18.1 | < 0.0001 |

LA: left atrial, A4C: apical 4-chamber view, A2C: apical 2-chamber view, AP: anteroposterior, EM: ellipsoid method, ALM: area-length method, RA: right atrial, 2D: two-dimensional, SD: standard deviation, CI: confidence interval

Table 5. Measurements of the aortic root and main pulmonary artery by 2D imaging according to gender

| Variables | Men | | Women | | Total | | <i>p</i> |
|---|------------|-----------|------------|-----------|------------|-----------|----------|
| | Mean ± SD | 95% CI | Mean ± SD | 95% CI | Mean ± SD | 95% CI | |
| Aortic annulus (mm) | 21.3 ± 1.8 | 17.8–24.8 | 19.4 ± 1.6 | 16.3–22.6 | 20.3 ± 1.9 | 16.5–24.1 | < 0.0001 |
| Sinus of Valsalva (mm) | 33.5 ± 3.2 | 27.2–39.8 | 30.1 ± 3.0 | 24.2–36.0 | 31.8 ± 3.5 | 24.8–38.7 | < 0.0001 |
| ST junction (mm) | 27.3 ± 2.7 | 21.9–32.6 | 24.9 ± 2.7 | 19.6–30.2 | 26.0 ± 3.0 | 20.2–31.9 | < 0.0001 |
| Tubular portion of ascending aorta (mm) | 30.7 ± 3.7 | 23.5–38.0 | 29.1 ± 4.0 | 21.1–37.0 | 29.9 ± 4.0 | 22.1–37.6 | < 0.0001 |
| Main pulmonary artery (mm) | 23.5 ± 3.3 | 17.0–30.0 | 23.0 ± 3.1 | 16.8–29.1 | 23.2 ± 3.2 | 16.9–29.6 | 0.0086 |

ST: sinotubular, 2D: two-dimensional, SD: standard deviation, CI: confidence interval

Table 6. LVM and relative wall thickness according to gender

| Variables | Men | | Women | | Total | | <i>p</i> |
|-------------------------------------|-------------|-----------|-------------|-----------|-------------|-----------|----------|
| | Mean ± SD | 95% CI | Mean ± SD | 95% CI | Mean ± SD | 95% CI | |
| LVM (gm) by M-mode | 144 ± 28 | 90–199 | 114 ± 24 | 67–161 | 129 ± 30 | 70–187 | < 0.0001 |
| LVMi (gm/m ²) by M-mode | 80 ± 14 | 53–108 | 73 ± 15 | 45–102 | 77 ± 15 | 48–106 | < 0.0001 |
| LVM (gm) by 2D | 134 ± 25 | 85–184 | 107 ± 23 | 63–152 | 120 ± 28 | 66–174 | < 0.0001 |
| LVMi (gm/m ²) by 2D | 75 ± 13 | 49–100 | 69 ± 14 | 42–96 | 72 ± 14 | 45–99 | < 0.0001 |
| RWT by M-mode | 0.32 ± 0.04 | 0.26–0.39 | 0.31 ± 0.03 | 0.24–0.38 | 0.32 ± 0.04 | 0.25–0.39 | < 0.0001 |
| RWT by 2D | 0.33 ± 0.04 | 0.25–0.41 | 0.31 ± 0.04 | 0.23–0.39 | 0.32 ± 0.04 | 0.24–0.40 | < 0.0001 |

LVM: left ventricular mass, LVMi: LVM index, RWT: relative wall thickness, 2D: two-dimensional, SD: standard deviation, CI: confidence interval

pared to women as well. LVM index and RWT increased according to age in both men and women. Interestingly, the difference in RWT between men and women was more evident in young patients (age < 50 years).

INTRA- AND INTEROBSERVER VARIABILITY

ICCs for both intra- and interobserver variability testing are presented in Supplementary Table 7. For intraobserver variability, ICCs for echo variables were above 0.8, except that of the RV end-diastolic free wall thickness (ICC = 0.723, 95% CI = 0.535–0.843) and the RWT calculated from 2D measurement (ICC = 0.790, 95% CI = 0.639–0.883). For interobserver variability, ICCs of echocardiographic variables were above 0.8 except for RV end-diastolic free wall thickness (ICC = 0.521, 95% CI = 0.165–0.738), LVPWT (ICC = 0.712, 95% CI = 0.479–0.845), LVEF (ICC = 0.764, 95% CI = 0.372–0.898), and RVFAC (ICC = 0.611, 95% CI = 0.332–0.773).

DISCUSSION

This study provided normal reference measurement values of cardiac chambers and great arteries for comprehensive echocardiographic evaluation according to age and gender using data from the NORMAL study, which prospectively evaluated 1003 normal Korean patients from 23 nationwide centers. Briefly, most of cardiac chamber dimension and volume were greater in men compared to women and ventricular chamber size of both RV and LV were decrease according to age in both men and women. When indexed to BSA, LV volume indices were still larger in men compared to women, but indexed LV dimensions were usually greater in women and elderly populations. Interestingly, LA volumes were greater in men compared to women but, when indexed to BSA, difference according to sex was no longer evident. However, both LA volume and LA volume index increased with age in both men and women.

As previously noted, there were considerable differences in chamber size between men and women and according to age.⁽⁶⁻⁸⁾⁽¹²⁾ Although our current data were very similar with those from other populations, the effect of age on normal values showed slightly different trends in this study.⁽¹³⁻¹⁵⁾ For example, there were differential effects of age on LV short-axis dimension (LVEDD) between men and women, whereas the LV long-axis dimension was similarly affected by age in both men and women. These differences might be partly due to unique physical characteristics of the Korean population according to age and gender.⁽¹⁶⁾ The Korean economy has developed very quickly since 1960, and there are many differences in physical features and the incidence of metabolic syndrome between the young and elderly generations.⁽¹⁷⁾ In our data, younger subjects were taller than older subjects, and young men were heavier than elderly men, as expected. However, young ladies were lighter in weight than elderly women. Therefore, these physical characteristics might change when the young generation replaces those of middle age and the latter replace elderly subjects.

The effect of age on LV volume could not be offset by adjusting for BSA, as previously reported in other populations.⁽¹⁴⁾⁽¹⁵⁾ The effect of aging on LV volumes seems closely related with the LV long-axis dimension, considering that the LV long-axis dimension is more strongly correlated with LVEDV than the LV short-axis dimension. As there were only weak correlations between LV short- and long-axis dimensions, the greater effect of LV long-axis dimension on LV volume and its correlation with height might explain the trends of decreasing LV volumes along with age in both men and women.

As previously noted, RV size and function were very difficult to evaluate, especially in cases with a poor echo window.⁽¹⁸⁾ In our data, reproducibility was relatively low for several RV variables, such as RV free wall thickness and RVFAC. In this regard, when interpreting RV variables, meticulous care should be used to determine whether the measurement value was adequately acquired. Nevertheless, our data was consistent with prior studies and confirms that RV dimensions as well as RV area are significantly affected by age and gender.⁽¹⁴⁾⁽¹⁵⁾⁽¹⁹⁾⁽²⁰⁾

Gender differences in LA volume were significantly reduced when LA volume was adjusted with BSA, as described previously.⁽¹⁵⁾ In other words, LA volume might be more influenced by body size than gender. However, the effect of age on LA volume in a normal population was controversial and differs among populations.⁽¹⁴⁾⁽¹⁵⁾ Our data were similar to those from a Chinese population, in that the LA volume index significantly increased with age in both men and women. However, European data did not show any difference in LA volume, even after adjustment for BSA.⁽¹⁵⁾

Kou et al.⁽¹⁵⁾ suggested that normal range of the LA volume index, which stands as 16–34 mL/m² in the current guidelines, was slightly low. Our study supports this assertion. In addition, LA volume as measured by the area-length method was significantly larger than the LA volume measured by Simpson's method or the ellipsoid method. Therefore, when LA volume or volume index is reported, the exact method should be clarified.

Effects of age and gender on the great arteries were consistent with previous studies, and the size of the aortic root and the main pulmonary artery as well as the proximal and distal RV outflow tract dimension increased with age in both men and women.⁽¹⁴⁾ LVM index and RWT were also significantly affected by age in both men and women. Interestingly, RWT in younger women (age < 50 years) was significantly lower than RWT in men, but these became similar after the age of 50. This might be consistent with findings that cardiovascular risks of postmenopausal women exceeded the risks of men of the same age.⁽²¹⁾⁽²²⁾

Several limitations of this study should be acknowledged. First, we included only normal Korean subjects in the NORMAL study, and our data might not be applicable to other populations. Second, our NORMAL study did not include three-dimensional (3D) echocardiography data and we could not provide reference values for 3D echocardiography. The next

limitation was that patients with significant disease, such as hypertension and diabetes, were excluded based on past medical histories obtained from the study subjects, and results of blood sampling and/or other clinical tests were not obtained. Therefore, patients with preclinical hypertension or subclinical coronary artery disease might be included in the current study. However, their effects on the structure of the heart are unlikely to be significant.

In conclusion, we provided normal reference values for echocardiographic measurements of the cardiac chambers and great arteries from the NORMAL study. As these values change considerably with age and gender, these should be considered when evaluating cardiac function and structure by echocardiography. Since physical characteristics of the Korean population change continuously, a new study for echocardiographic reference values, including 3D data, may be needed in the future.

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Supplementary Table 1. Demographic and clinical findings according to age and gender

| Age groups | Men (mean ± SD) | | | | | Women (mean ± SD) | | | | | p* | | |
|--------------------------|-----------------|-------------|-------------|-------------|-------------|-------------------|----------|-------------|------------|-------------|-------------|-------------|----------|
| | 21-30 | 31-40 | 41-50 | 51-60 | 61-70 | 71-80 | 21-30 | 31-40 | 41-50 | 51-60 | | 61-70 | 71-80 |
| Number | 87 | 88 | 88 | 94 | 89 | 41 | 87 | 86 | 98 | 112 | 87 | 46 | |
| Age (year) | 26 ± 3 | 36 ± 3 | 46 ± 3 | 55 ± 3 | 66 ± 3 | 74 ± 2 | < 0.0001 | 25 ± 3 | 36 ± 3 | 46 ± 3 | 55 ± 3 | 74 ± 2 | < 0.0001 |
| Weight (kg) | 70 ± 10 | 74 ± 11 | 71 ± 8 | 68 ± 8 | 65 ± 8 | 61 ± 7 | < 0.0001 | 54 ± 8 | 55 ± 7 | 56 ± 7 | 57 ± 7 | 55 ± 8 | 0.2046 |
| Height (cm) | 174 ± 6 | 174 ± 6 | 172 ± 6 | 169 ± 5 | 166 ± 6 | 163 ± 7 | < 0.0001 | 162 ± 5 | 160 ± 4 | 159 ± 5 | 157 ± 5 | 154 ± 5 | < 0.0001 |
| BSA (m ²) | 1.83 ± 0.14 | 1.88 ± 0.14 | 1.83 ± 0.13 | 1.78 ± 0.12 | 1.72 ± 0.11 | 1.65 ± 0.12 | < 0.0001 | 1.56 ± 0.12 | 1.56 ± 0.1 | 1.57 ± 0.11 | 1.56 ± 0.10 | 1.52 ± 0.11 | 0.1036 |
| BMI (kg/m ²) | 22.9 ± 2.7 | 24.3 ± 2.9 | 24.0 ± 2.4 | 23.8 ± 2.4 | 23.6 ± 2.3 | 22.9 ± 2.1 | 0.0029 | 20.7 ± 2.9 | 21.6 ± 2.5 | 22.3 ± 2.2 | 23.2 ± 2.7 | 23.1 ± 2.9 | < 0.0001 |
| SBP (mm Hg) | 120 ± 10 | 123 ± 10 | 123 ± 12 | 123 ± 12 | 123 ± 14 | 128 ± 14 | 0.0469 | 111 ± 10 | 112 ± 12 | 117 ± 12 | 121 ± 13 | 124 ± 10 | < 0.0001 |
| DBP (mm Hg) | 74 ± 8 | 77 ± 8 | 76 ± 9 | 74 ± 10 | 75 ± 9 | 75 ± 10 | 0.3003 | 68 ± 8 | 68 ± 10 | 73 ± 11 | 74 ± 9 | 72 ± 10 | < 0.0001 |
| Heart rate (bpm) | 69 ± 9 | 69 ± 11 | 67 ± 8 | 66 ± 10 | 67 ± 9 | 68 ± 11 | 0.1835 | 71 ± 9 | 70 ± 9 | 71 ± 9 | 67 ± 8 | 70 ± 8 | < 0.0001 |

*p value from analysis of variance test in each gender. BSA: body surface area, BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, SD: standard deviation

Supplementary Table 2. M-mode variables according to age and gender

| Age groups | Men (mean ± SD) | | | | | Women (mean ± SD) | | | | | p* | | | |
|---|-----------------|------------|------------|------------|------------|-------------------|----------|------------|------------|------------|------------|------------|------------|----------|
| | 21-30 | 31-40 | 41-50 | 51-60 | 61-70 | 71-80 | 21-30 | 31-40 | 41-50 | 51-60 | | 61-70 | 71-80 | |
| IVEDD (mm) | 50.3 ± 3.4 | 50.9 ± 3.5 | 50.9 ± 3.2 | 51.0 ± 3.2 | 49.8 ± 3.2 | 49.8 ± 3.3 | 0.0519 | 46.0 ± 3.1 | 46.7 ± 2.8 | 47.5 ± 3.4 | 48.1 ± 3.3 | 48.5 ± 3.1 | 47.6 ± 3.3 | < 0.0001 |
| IVESD (mm) | 31.4 ± 2.6 | 31.7 ± 3.0 | 31.4 ± 2.9 | 30.8 ± 2.9 | 30.0 ± 2.8 | 29.5 ± 2.2 | < 0.0001 | 28.4 ± 2.4 | 28.7 ± 2.5 | 29.0 ± 2.7 | 29.0 ± 3.0 | 28.7 ± 3.0 | 27.9 ± 2.9 | 0.1740 |
| IVEDD index (mm/m ²) | 27.5 ± 2.0 | 27.1 ± 1.8 | 28.0 ± 2.1 | 28.8 ± 2.3 | 29.0 ± 2.1 | 30.2 ± 2.3 | < 0.0001 | 29.5 ± 2.2 | 29.9 ± 2.0 | 30.4 ± 2.3 | 31.0 ± 2.5 | 31.6 ± 2.5 | 31.5 ± 2.8 | < 0.0001 |
| IVESD index (mm/m ²) | 17.2 ± 1.6 | 16.9 ± 1.6 | 17.2 ± 1.8 | 17.4 ± 1.9 | 17.5 ± 1.6 | 17.9 ± 1.7 | 0.0251 | 18.2 ± 1.7 | 18.4 ± 1.6 | 18.6 ± 1.8 | 18.7 ± 2.1 | 18.7 ± 2.0 | 18.5 ± 2.2 | 0.5652 |
| IVEF (%) by linear method | 60.8 ± 4.1 | 61.2 ± 4.4 | 61.9 ± 4.6 | 63.5 ± 4.9 | 63.5 ± 4.5 | 64.6 ± 4.3 | < 0.0001 | 61.8 ± 3.9 | 62.1 ± 4.1 | 62.7 ± 3.9 | 63.6 ± 4.4 | 65.0 ± 4.3 | 65.6 ± 4.3 | < 0.0001 |
| IVSWT (mm) | 8.1 ± 0.9 | 8.1 ± 1.0 | 8.1 ± 1.0 | 8.3 ± 1.1 | 8.5 ± 1.0 | 8.5 ± 0.8 | 0.0058 | 6.9 ± 0.6 | 7.1 ± 0.8 | 7.3 ± 0.8 | 7.6 ± 0.8 | 8.0 ± 0.9 | 8.1 ± 0.8 | < 0.0001 |
| IYPWT (mm) | 8.0 ± 0.8 | 8.1 ± 0.9 | 8.0 ± 0.9 | 8.2 ± 0.8 | 8.5 ± 0.8 | 8.5 ± 0.8 | 0.0004 | 6.8 ± 0.6 | 7.0 ± 0.7 | 7.3 ± 0.7 | 7.5 ± 0.8 | 7.9 ± 0.7 | 8.1 ± 0.6 | < 0.0001 |
| LA AP diameter (mm) | 33.6 ± 3.7 | 35.6 ± 3.7 | 35.7 ± 3.3 | 37.2 ± 3.5 | 37.6 ± 3.9 | 37.1 ± 3.8 | < 0.0001 | 30.6 ± 2.8 | 31.6 ± 3.2 | 33.2 ± 3.4 | 34.5 ± 3.1 | 36.0 ± 4.0 | 37.5 ± 4.2 | < 0.0001 |
| Aortic root diameter (mm) | 30.5 ± 2.2 | 31.3 ± 2.6 | 32.3 ± 3.1 | 32.9 ± 2.7 | 33.6 ± 3.1 | 33.3 ± 3.1 | < 0.0001 | 26.3 ± 2.0 | 27.4 ± 2.1 | 28.8 ± 2.3 | 29.5 ± 2.6 | 30.2 ± 2.6 | 31.2 ± 3.0 | < 0.0001 |
| RV end-diastolic free wall thickness (mm) | 4.1 ± 0.9 | 4.3 ± 0.8 | 4.2 ± 0.9 | 4.2 ± 1.0 | 4.4 ± 0.9 | 4.2 ± 0.7 | 0.4648 | 3.8 ± 0.8 | 3.9 ± 0.8 | 4.1 ± 0.8 | 4.0 ± 0.8 | 4.0 ± 0.8 | 4.2 ± 0.9 | 0.0664 |
| TAPSE (mm) | 22.8 ± 3.2 | 22.6 ± 3.2 | 22.6 ± 3.5 | 22.8 ± 3.1 | 22.7 ± 3.3 | 22.2 ± 2.9 | 0.9666 | 22.0 ± 2.4 | 22.2 ± 3.0 | 23.0 ± 2.9 | 22.7 ± 3.3 | 22.0 ± 3.1 | 21.2 ± 3.5 | 0.0098 |

*p value from analysis of variance test in each gender. IVEDD: left ventricular end-diastolic dimension, IVESD: left ventricular end-systolic dimension, IVEF: left ventricular ejection fraction, IVSWT: interventricular septal wall thickness, IYPWT: left ventricular posterior wall thickness, LA: left atrium, AP: anteroposterior, RV: right ventricular, TAPSE: tricuspid annular plane systolic excursion, SD: standard deviation

Supplementary Table 3. Measurement values of left and right ventricle by 2D imaging according to age and gender

| Age groups | Men (mean ± SD) | | | | | p* | Women (mean ± SD) | | | | | p* | | |
|--|-----------------|-------------|-------------|-------------|-------------|-------------|-------------------|-------------|-------------|-------------|-------------|-------------|-------------|---------|
| | 21-30 | 31-40 | 41-50 | 51-60 | 61-70 | | 71-80 | 21-30 | 31-40 | 41-50 | 51-60 | | 61-70 | 71-80 |
| IVEDD (mm) | 49.6 ± 3.4 | 49.6 ± 3.3 | 49.4 ± 3.4 | 49.0 ± 3.2 | 48.3 ± 3.6 | 48.4 ± 2.8 | 0.0617 | 45.9 ± 2.8 | 46.0 ± 2.9 | 46.4 ± 2.9 | 46.9 ± 3.6 | 47.1 ± 3.3 | 46.2 ± 3.4 | 0.0358 |
| IVESD (mm) | 31.5 ± 2.9 | 31.1 ± 2.9 | 31.1 ± 2.7 | 30.3 ± 3.0 | 29.3 ± 3.7 | 29.1 ± 2.1 | <0.0001 | 28.7 ± 2.8 | 29.0 ± 2.6 | 28.8 ± 2.9 | 28.5 ± 3.5 | 28.4 ± 2.9 | 28.0 ± 3.0 | 0.4919 |
| IVEDD index (mm/m ²) | 27.2 ± 2.3 | 26.4 ± 2.0 | 27.1 ± 2.3 | 27.7 ± 2.3 | 28.1 ± 2.1 | 29.4 ± 2.1 | <0.0001 | 29.5 ± 2.2 | 29.4 ± 1.8 | 29.7 ± 2.1 | 30.2 ± 2.7 | 30.7 ± 2.5 | 30.5 ± 2.7 | 0.0004 |
| IVESD index (mm/m ²) | 17.3 ± 1.9 | 16.6 ± 1.6 | 17.1 ± 1.8 | 17.1 ± 2.0 | 17.0 ± 2.1 | 17.7 ± 1.7 | 0.0465 | 18.4 ± 2.0 | 18.6 ± 1.8 | 18.5 ± 1.9 | 18.4 ± 2.3 | 18.5 ± 2.0 | 18.5 ± 2.3 | 0.9951 |
| IVEF (%) by linear method | 59.4 ± 4.9 | 60.5 ± 4.5 | 60.2 ± 4.7 | 61.6 ± 4.9 | 63.3 ± 5.5 | 63.7 ± 5.0 | <0.0001 | 60.7 ± 5.0 | 60.2 ± 5.1 | 61.3 ± 5.3 | 62.9 ± 6.0 | 63.5 ± 5.3 | 63.2 ± 5.2 | <0.0001 |
| IVSWT (mm) | 8.0 ± 1.0 | 8.0 ± 1.0 | 7.9 ± 1.0 | 8.3 ± 1.1 | 8.3 ± 0.9 | 8.2 ± 1.1 | 0.0370 | 6.7 ± 0.7 | 6.9 ± 0.8 | 7.1 ± 0.7 | 7.5 ± 0.8 | 7.8 ± 0.8 | 8.0 ± 0.9 | <0.0001 |
| IVPWT (mm) | 7.8 ± 1.0 | 7.9 ± 0.8 | 8.0 ± 1.0 | 8.2 ± 0.8 | 8.2 ± 0.8 | 8.3 ± 1.1 | 0.0048 | 6.7 ± 0.7 | 6.8 ± 0.9 | 7.1 ± 0.7 | 7.4 ± 0.9 | 7.7 ± 0.9 | 8.0 ± 1.0 | <0.0001 |
| IVEDV (mL) | 124 ± 21 | 124 ± 23 | 113 ± 19 | 110 ± 17 | 101 ± 20 | 100 ± 16 | <0.0001 | 96 ± 16 | 95 ± 14 | 93 ± 17 | 91 ± 17 | 88 ± 16 | 82 ± 15 | <0.0001 |
| IVESV (mL) | 48 ± 10 | 48 ± 10 | 43 ± 10 | 41 ± 9 | 36 ± 9 | 36 ± 7 | <0.0001 | 36 ± 9 | 35 ± 7 | 34 ± 8 | 34 ± 9 | 32 ± 8 | 29 ± 7 | <0.0001 |
| IVEDV index (mL/m ²) | 67 ± 10 | 66 ± 11 | 62 ± 10 | 62 ± 10 | 58 ± 11 | 61 ± 9 | <0.0001 | 61 ± 9 | 60 ± 8 | 59 ± 10 | 59 ± 10 | 57 ± 9 | 54 ± 10 | 0.0009 |
| IVESV index (mL/m ²) | 26.0 ± 4.8 | 25.4 ± 4.9 | 23.7 ± 5.1 | 22.8 ± 5.3 | 21.1 ± 5.1 | 22.1 ± 4.0 | <0.0001 | 23.2 ± 5.0 | 22.4 ± 4.2 | 21.5 ± 4.9 | 21.6 ± 5.5 | 20.6 ± 4.4 | 19.1 ± 5.1 | 0.0001 |
| IVEF (%) by volumetric method | 61.5 ± 4.4 | 61.4 ± 3.7 | 62.0 ± 4.6 | 63.3 ± 4.8 | 64.0 ± 4.9 | 63.4 ± 4.2 | 0.0002 | 62.3 ± 4.8 | 63.0 ± 4.7 | 64 ± 4.1 | 63.4 ± 5.0 | 63.9 ± 4.9 | 65.2 ± 5.3 | 0.0205 |
| IV long-axis dimension (mm) | 91 ± 6 | 91 ± 6 | 88 ± 5 | 88 ± 5 | 84 ± 5 | 83 ± 4 | <0.0001 | 84 ± 6 | 82 ± 5 | 82 ± 5 | 80 ± 5 | 78 ± 5 | 77 ± 5 | <0.0001 |
| Sphericity index | 0.55 ± 0.05 | 0.55 ± 0.04 | 0.56 ± 0.04 | 0.56 ± 0.04 | 0.58 ± 0.04 | 0.58 ± 0.04 | <0.0001 | 0.55 ± 0.04 | 0.56 ± 0.04 | 0.57 ± 0.04 | 0.59 ± 0.05 | 0.60 ± 0.04 | 0.60 ± 0.05 | <0.0001 |
| RV end-diastolic area (cm ²) | 18.5 ± 3.4 | 18.4 ± 3.5 | 16.9 ± 3.0 | 17.1 ± 3.0 | 16.3 ± 3.1 | 16.2 ± 3.1 | <0.0001 | 15.7 ± 3.0 | 14.3 ± 2.7 | 14 ± 2.4 | 13.8 ± 2.5 | 14.4 ± 2.9 | 13.8 ± 2.4 | <0.0001 |
| RV end-systolic area (cm ²) | 10.1 ± 2.0 | 10.1 ± 2.4 | 9.0 ± 2.1 | 9.0 ± 2.0 | 8.8 ± 2.1 | 8.7 ± 2.1 | <0.0001 | 8.1 ± 1.6 | 7.4 ± 1.7 | 7.2 ± 1.6 | 7.2 ± 1.6 | 7.4 ± 1.9 | 7.4 ± 1.6 | 0.0074 |
| RVFAC (%) | 46 ± 6 | 46 ± 5 | 47 ± 8 | 48 ± 7 | 46 ± 6 | 46 ± 7 | 0.2337 | 48 ± 7 | 48 ± 6 | 49 ± 5 | 48 ± 6 | 49 ± 7 | 47 ± 7 | 0.2763 |
| Basal RVD (mm) | 36.1 ± 3.9 | 36.0 ± 3.6 | 35.0 ± 3.3 | 35.6 ± 3.4 | 34.7 ± 4.4 | 35.0 ± 3.8 | 0.0583 | 32.7 ± 3.5 | 32.4 ± 3.5 | 32.2 ± 3.9 | 32.7 ± 3.1 | 33.3 ± 3.9 | 32.6 ± 3.6 | 0.4121 |
| Mid RVD (mm) | 27.7 ± 3.6 | 28.3 ± 3.8 | 27.2 ± 3.8 | 26.5 ± 3.5 | 26.2 ± 3.8 | 26.3 ± 3.2 | 0.0008 | 25.5 ± 3.4 | 24.6 ± 3.0 | 24.2 ± 3.3 | 24.3 ± 3.2 | 24.8 ± 3.4 | 24.9 ± 4.0 | 0.0894 |
| RV long-axis dimension (mm) | 73 ± 9 | 72 ± 10 | 70 ± 8 | 69 ± 10 | 67 ± 9 | 67 ± 9 | 0.0002 | 67 ± 10 | 64 ± 9 | 64 ± 8 | 63 ± 9 | 63 ± 9 | 61 ± 8 | 0.0142 |
| Proximal RVOT dimension (mm) | 28.0 ± 4.2 | 28.9 ± 3.9 | 29.2 ± 4.5 | 31.1 ± 4.0 | 30.6 ± 3.7 | 31.0 ± 5.0 | <0.0001 | 24.6 ± 4.0 | 26.5 ± 3.4 | 27.1 ± 3.6 | 27.6 ± 3.7 | 28.3 ± 4.4 | 28.1 ± 3.7 | <0.0001 |
| Distal RVOT dimension (mm) | 22.3 ± 2.7 | 23.8 ± 3.2 | 23.3 ± 3.1 | 23.4 ± 3.1 | 24.2 ± 2.8 | 25.2 ± 3.5 | <0.0001 | 21.1 ± 2.4 | 21.1 ± 2.2 | 21.6 ± 2.6 | 22.9 ± 2.9 | 23.5 ± 2.9 | 23.4 ± 2.9 | <0.0001 |

*p value from analysis of variance test in each gender. IV: left ventricular, IVEDD: IV end-diastolic dimension, IVESD: IV end-systolic dimension, IVEF: IV ejection fraction, IVSWT: interventricular septal wall thickness, IVPWT: IV posterior wall thickness, IVEDV: IV end-diastolic volume, IVESV: IV end-systolic volume, RV: right ventricular, RVFAC: RV fractional area change, RVD: RV dimension, RVOT: RV outflow tract, 2D: two-dimensional, SD: standard deviation

Supplementary Table 4. Measurement values of left and right atrium by 2D imaging according to age and gender

| Age groups | Men (mean ± SD) | | | | | Women (mean ± SD) | | | | | p* | | | |
|---|-----------------|------------|------------|------------|------------|-------------------|----------|------------|------------|------------|------------|------------|------------|----------|
| | 21-30 | 31-40 | 41-50 | 51-60 | 61-70 | 71-80 | 21-30 | 31-40 | 41-50 | 51-60 | | 61-70 | 71-80 | |
| LA area (cm ²) at A4C | 16.3 ± 2.5 | 16.4 ± 2.9 | 16.2 ± 2.5 | 16.6 ± 3.1 | 16.3 ± 2.6 | 16.1 ± 2.7 | 0.9468 | 14.2 ± 2.1 | 14.5 ± 2.5 | 15.1 ± 2.8 | 15.6 ± 2.4 | 15.9 ± 2.8 | 16.8 ± 3.4 | < 0.0001 |
| LA area (cm ²) at A2C | 15.9 ± 2.4 | 15.9 ± 2.7 | 16.5 ± 2.5 | 17.1 ± 2.8 | 16.7 ± 2.7 | 16.5 ± 2.6 | 0.0161 | 13.4 ± 2.3 | 14.4 ± 2.0 | 14.9 ± 2.8 | 15.4 ± 2.7 | 16.4 ± 2.6 | 16.5 ± 3.0 | < 0.0001 |
| LA longitudinal dimension (cm) | 4.6 ± 0.4 | 4.7 ± 0.5 | 4.7 ± 0.4 | 4.8 ± 0.5 | 4.7 ± 0.5 | 4.7 ± 0.4 | 0.0982 | 4.3 ± 0.5 | 4.5 ± 0.5 | 4.6 ± 0.5 | 4.7 ± 0.5 | 4.8 ± 0.5 | 4.8 ± 0.5 | < 0.0001 |
| LA transverse dimension (mm) | 38.9 ± 3.6 | 38.3 ± 4.1 | 38.8 ± 3.9 | 38.8 ± 4.2 | 38.8 ± 4.0 | 38.5 ± 4.1 | 0.9071 | 36.5 ± 3.4 | 36.8 ± 4.0 | 36.7 ± 3.8 | 37.5 ± 4.0 | 37.7 ± 3.9 | 38.7 ± 4.1 | 0.0186 |
| LA AP dimension (mm) | 33.1 ± 4.2 | 34.7 ± 4.5 | 34.2 ± 3.7 | 35.6 ± 3.7 | 35.5 ± 4.5 | 35.8 ± 4.3 | 0.0002 | 30.2 ± 3.0 | 31.2 ± 3.5 | 32.2 ± 3.8 | 33.3 ± 3.7 | 34.2 ± 4.1 | 35.1 ± 4.5 | < 0.0001 |
| LA volume (mL) by EM | 48 ± 10 | 48 ± 11 | 48 ± 10 | 51 ± 12 | 50 ± 11 | 48 ± 11 | 0.4943 | 38 ± 8 | 40 ± 8 | 42 ± 11 | 44 ± 10 | 47 ± 11 | 49 ± 15 | < 0.0001 |
| LA volume index (mL/m ²) by EM | 26.3 ± 4.9 | 25.3 ± 5.4 | 26.5 ± 4.9 | 28.5 ± 6.8 | 28.8 ± 6.1 | 28.9 ± 6.2 | < 0.0001 | 24.4 ± 4.9 | 25.6 ± 4.9 | 27.1 ± 6.9 | 28.3 ± 6.7 | 30.2 ± 6.1 | 32.4 ± 8.6 | < 0.0001 |
| LA volume (mL) by ALM | 31 ± 7 | 33 ± 8 | 33 ± 7 | 35 ± 9 | 34 ± 9 | 35 ± 9 | 0.0213 | 25 ± 6 | 27 ± 6 | 29 ± 8 | 31 ± 7 | 33 ± 9 | 35 ± 10 | < 0.0001 |
| LA volume index (mL/m ²) by ALM | 16.9 ± 3.5 | 17.3 ± 4.0 | 18.1 ± 3.7 | 19.8 ± 4.9 | 19.9 ± 4.7 | 21.0 ± 5.0 | < 0.0001 | 15.8 ± 3.4 | 17.3 ± 3.7 | 18.2 ± 4.5 | 19.7 ± 4.6 | 21.2 ± 5.2 | 22.9 ± 5.8 | < 0.0001 |
| RA transverse dimension (mm) | 36.9 ± 4.1 | 37.3 ± 3.7 | 36.5 ± 4.4 | 36.0 ± 4.1 | 35.4 ± 3.9 | 36.2 ± 4.2 | 0.0302 | 33.4 ± 3.2 | 33.3 ± 3.3 | 33.0 ± 3.9 | 33.3 ± 3.8 | 33.5 ± 3.4 | 32.1 ± 3.1 | 0.3165 |
| RA longitudinal dimension (mm) | 45.4 ± 4.3 | 46.8 ± 5.0 | 46.1 ± 4.7 | 47.2 ± 4.6 | 46.9 ± 4.4 | 46.8 ± 4.5 | 0.1451 | 41.6 ± 3.9 | 42.7 ± 4.7 | 43.8 ± 4.4 | 45.0 ± 4.4 | 45.4 ± 5.2 | 45.5 ± 5.2 | < 0.0001 |
| RA area (cm ²) | 14.1 ± 2.3 | 14.7 ± 2.5 | 14.0 ± 2.1 | 14.4 ± 2.3 | 13.9 ± 2.3 | 14.4 ± 2.3 | 0.1889 | 11.6 ± 1.9 | 12.0 ± 2.1 | 12.2 ± 2.3 | 12.7 ± 2.2 | 13.0 ± 2.4 | 12.6 ± 2.0 | 0.0006 |

*p value from analysis of variance test in each gender. LA: left atrial, A4C: apical 4-chamber view, A2C: apical 2-chamber view, AP: anteroposterior, EM: ellipsoid method, ALM: area-length method, RA: right atrial, 2D: two-dimensional, SD: standard deviation

Supplementary Table 5. Measurement values of aortic root and main pulmonary artery by 2D imaging according to age and gender

| Age groups | Men (mean ± SD) | | | | | Women (mean ± SD) | | | | | p* | | | |
|---|-----------------|------------|------------|------------|------------|-------------------|----------|------------|------------|------------|------------|------------|------------|----------|
| | 21-30 | 31-40 | 41-50 | 51-60 | 61-70 | 71-80 | 21-30 | 31-40 | 41-50 | 51-60 | | 61-70 | 71-80 | |
| Aortic annulus (mm) | 21.3 ± 1.8 | 21.4 ± 1.9 | 21.5 ± 2.1 | 21.3 ± 1.7 | 20.9 ± 1.5 | 21.4 ± 1.8 | 0.4085 | 18.9 ± 1.5 | 19.1 ± 1.8 | 19.3 ± 1.5 | 19.5 ± 1.5 | 20.1 ± 1.5 | 19.5 ± 1.8 | 0.0001 |
| Sinus of Valsalva (mm) | 31.2 ± 3.0 | 32.7 ± 2.6 | 33.7 ± 3.2 | 34.0 ± 2.9 | 35.1 ± 3.1 | 35.0 ± 3.1 | < 0.0001 | 27.8 ± 2.4 | 28.7 ± 2.4 | 29.9 ± 2.5 | 30.7 ± 2.7 | 32.0 ± 2.6 | 32.4 ± 2.8 | < 0.0001 |
| ST junction (mm) | 24.9 ± 2.3 | 26.9 ± 2.0 | 27.5 ± 2.6 | 27.9 ± 2.5 | 28.5 ± 2.8 | 28.3 ± 2.6 | < 0.0001 | 22.7 ± 2.2 | 23.8 ± 2.4 | 24.8 ± 2.3 | 25.7 ± 2.5 | 26.4 ± 2.4 | 26.5 ± 2.7 | < 0.0001 |
| Tubular portion of ascending aorta (mm) | 27.0 ± 2.3 | 29.6 ± 3.0 | 30.5 ± 2.9 | 31.6 ± 2.7 | 33.6 ± 3.3 | 33.5 ± 4.0 | < 0.0001 | 25.0 ± 2.1 | 26.2 ± 2.5 | 29.0 ± 2.9 | 30.6 ± 3.4 | 32.3 ± 3.1 | 32.6 ± 3.9 | < 0.0001 |
| Main pulmonary artery (mm) | 22.4 ± 3.4 | 23.5 ± 3.0 | 23.3 ± 3.2 | 23.0 ± 3.0 | 24.5 ± 3.5 | 25.5 ± 3.2 | < 0.0001 | 21.4 ± 2.6 | 22.2 ± 2.8 | 22.6 ± 2.7 | 23.2 ± 2.9 | 24.4 ± 3.5 | 24.6 ± 3.2 | < 0.0001 |

*p value from analysis of variance test in each gender. ST: sinotubular, 2D: two-dimensional, SD: standard deviation

Supplementary Table 6. LVM and relative wall thickness according to age and gender

| Age groups | Men (mean ± SD) | | | | | | Women (mean ± SD) | | | | | | p* |
|-------------------------------------|-----------------|-------------|-------------|-------------|-------------|-------------|-------------------|-------------|-------------|-------------|-------------|-------------|----------|
| | 21-30 | 31-40 | 41-50 | 51-60 | 61-70 | 71-80 | 21-30 | 31-40 | 41-50 | 51-60 | 61-70 | 71-80 | |
| LVM (gm) by M-mode | 139 ± 27 | 144 ± 31 | 143 ± 29 | 147 ± 27 | 147 ± 26 | 147 ± 24 | 97 ± 17 | 104 ± 20 | 111 ± 22 | 120 ± 23 | 129 ± 23 | 128 ± 21 | < 0.0001 |
| LVMl (gm/m ³) by M-mode | 76 ± 12 | 76 ± 13 | 78 ± 14 | 83 ± 15 | 85 ± 14 | 89 ± 13 | 62 ± 9 | 66 ± 11 | 71 ± 13 | 77 ± 14 | 84 ± 14 | 84 ± 12 | < 0.0001 |
| LVM (gm) by 2D | 133 ± 27 | 134 ± 26 | 133 ± 27 | 137 ± 23 | 134 ± 24 | 135 ± 25 | 95 ± 17 | 98 ± 20 | 104 ± 19 | 112 ± 23 | 119 ± 23 | 121 ± 24 | < 0.0001 |
| LVMl (gm/m ³) by 2D | 72 ± 12 | 71 ± 12 | 73 ± 14 | 77 ± 12 | 78 ± 13 | 82 ± 14 | 61 ± 10 | 62 ± 10 | 67 ± 11 | 72 ± 14 | 77 ± 14 | 79 ± 15 | < 0.0001 |
| RWT by M-mode | 0.32 ± 0.03 | 0.32 ± 0.03 | 0.32 ± 0.03 | 0.32 ± 0.04 | 0.34 ± 0.04 | 0.34 ± 0.04 | 0.30 ± 0.03 | 0.30 ± 0.03 | 0.31 ± 0.03 | 0.31 ± 0.03 | 0.33 ± 0.03 | 0.34 ± 0.04 | < 0.0001 |
| RWT by 2D | 0.32 ± 0.04 | 0.32 ± 0.03 | 0.32 ± 0.04 | 0.34 ± 0.04 | 0.34 ± 0.04 | 0.35 ± 0.05 | 0.29 ± 0.03 | 0.30 ± 0.04 | 0.31 ± 0.03 | 0.32 ± 0.04 | 0.33 ± 0.04 | 0.35 ± 0.04 | < 0.0001 |

*p value from analysis of variance test in each gender. LVM: left ventricular mass, LVMl: LVM index, RWT: relative wall thickness, 2D: two-dimensional, SD: standard deviation

Supplementary Table 7. Intra- and interobserver variability data

| | Intraobserver variability | | Interobserver variability | |
|---|---------------------------|-------------|---------------------------|-------------|
| | ICC | 95% CI | ICC | 95% CI |
| M-mode measurements | | | | |
| LVEDD (mm) | 0.990 | 0.982–0.995 | 0.981 | 0.964–0.990 |
| LVEDS (mm) | 0.983 | 0.955–0.993 | 0.938 | 0.675–0.978 |
| IVSWT (mm) | 0.970 | 0.944–0.984 | 0.906 | 0.831–0.949 |
| LVPWT (mm) | 0.958 | 0.922–0.978 | 0.866 | 0.758–0.927 |
| LA AP diameter (mm) | 0.986 | 0.974–0.993 | 0.956 | 0.901–0.978 |
| Aortic root diameter (mm) | 0.970 | 0.945–0.984 | 0.968 | 0.938–0.984 |
| RV end-diastolic free wall thickness (mm) | 0.723 | 0.535–0.843 | 0.521 | 0.165–0.738 |
| TAPSE (mm) | 0.931 | 0.875–0.963 | 0.913 | 0.841–0.953 |
| 2D measurements | | | | |
| Ventricles | | | | |
| LVEDD (mm) | 0.934 | 0.879–0.965 | 0.940 | 0.889–0.968 |
| LVEDS (mm) | 0.954 | 0.914–0.975 | 0.921 | 0.850–0.958 |
| IVSWT (mm) | 0.922 | 0.840–0.960 | 0.860 | 0.740–0.925 |
| LVPWT (mm) | 0.884 | 0.792–0.937 | 0.712 | 0.479–0.845 |
| LVEDV (mL) | 0.973 | 0.915–0.989 | 0.958 | 0.911–0.979 |
| LVESV (mL) | 0.948 | 0.851–0.977 | 0.901 | 0.631–0.962 |
| LVEDV index (mL/m ²) | 0.945 | 0.862–0.975 | 0.838 | 0.715–0.911 |
| LVESV index (mL/m ²) | 0.914 | 0.789–0.960 | 0.824 | 0.669–0.906 |
| LVEF (%) | 0.807 | 0.655–0.895 | 0.764 | 0.372–0.898 |
| LV long-axis dimension (mm) | 0.954 | 0.915–0.975 | 0.866 | 0.606–0.943 |
| Sphericity index | 0.926 | 0.865–0.960 | 0.873 | 0.707–0.940 |
| RV end-diastolic area (cm ²) | 0.957 | 0.921–0.977 | 0.884 | 0.791–0.937 |
| RV end-systolic area (cm ²) | 0.964 | 0.934–0.981 | 0.883 | 0.790–0.937 |
| RVFAC (%) | 0.804 | 0.661–0.891 | 0.611 | 0.371–0.774 |
| Basal RVD (mm) | 0.875 | 0.777–0.932 | 0.897 | 0.806–0.946 |
| Mid RVD (mm) | 0.930 | 0.870–0.963 | 0.823 | 0.665–0.907 |
| RV long-axis dimension (mm) | 0.962 | 0.925–0.981 | 0.891 | 0.772–0.945 |
| Proximal RVOT dimension (mm) | 0.979 | 0.961–0.989 | 0.959 | 0.925–0.978 |
| Distal RVOT dimension (mm) | 0.927 | 0.868–0.961 | 0.878 | 0.781–0.933 |
| Atrium | | | | |
| LA area (cm ²) at A4C | 0.936 | 0.882–0.966 | 0.889 | 0.798–0.940 |
| LA area (cm ²) at A2C | 0.955 | 0.917–0.976 | 0.896 | 0.806–0.945 |
| LA longitudinal dimension (cm) | 0.886 | 0.795–0.938 | 0.832 | 0.698–0.909 |
| LA transverse dimension (mm) | 0.969 | 0.942–0.983 | 0.911 | 0.839–0.952 |
| LA AP dimension (mm) | 0.958 | 0.923–0.978 | 0.870 | 0.506–0.951 |
| LA volume (mL) by EM | 0.966 | 0.937–0.982 | 0.932 | 0.870–0.964 |
| LA volume index (mL/m ²) by EM | 0.966 | 0.937–0.982 | 0.924 | 0.854–0.960 |
| LA volume (mL) by ALM | 0.972 | 0.948–0.985 | 0.913 | 0.727–0.964 |
| LA volume index (mL/m ²) by ALM | 0.963 | 0.932–0.980 | 0.899 | 0.689–0.958 |
| RA transverse dimension (mm) | 0.907 | 0.832–0.949 | 0.863 | 0.673–0.936 |
| RA longitudinal dimension (mm) | 0.938 | 0.886–0.967 | 0.908 | 0.834–0.951 |
| RA area (cm ²) | 0.940 | 0.890–0.968 | 0.932 | 0.874–0.963 |
| Great vessels | | | | |
| Aortic annulus (mm) | 0.902 | 0.823–0.947 | 0.866 | 0.761–0.927 |
| Sinus of Valsalva (mm) | 0.969 | 0.942–0.983 | 0.961 | 0.922–0.980 |
| ST junction (mm) | 0.944 | 0.897–0.970 | 0.871 | 0.724–0.936 |

Supplementary Table 7. Intra- and interobserver variability data (continued)

| | Intraobserver variability | | Interobserver variability | |
|---|---------------------------|-------------|---------------------------|-------------|
| | ICC | 95% CI | ICC | 95% CI |
| Tubular portion of ascending aorta (mm) | 0.979 | 0.960–0.989 | 0.972 | 0.948–0.985 |
| Main pulmonary artery (mm) | 0.941 | 0.891–0.968 | 0.883 | 0.790–0.937 |
| LVM and RWT | | | | |
| LVM (gm) by M-mode | 0.992 | 0.986–0.996 | 0.962 | 0.930–0.980 |
| LVMI (gm/m ²) by M-mode | 0.987 | 0.976–0.993 | 0.939 | 0.889–0.967 |
| LVM (gm) by 2D | 0.975 | 0.939–0.988 | 0.936 | 0.859–0.969 |
| LVMI (gm/m ²) by 2D | 0.954 | 0.896–0.978 | 0.884 | 0.753–0.942 |
| RWT by M-mode | 0.930 | 0.872–0.962 | 0.787 | 0.624–0.883 |
| RWT by 2D | 0.790 | 0.639–0.883 | 0.600 | 0.332–0.773 |

ICC: intraclass correlation coefficient, LV: left ventricular, LVEDD: LV end-diastolic dimension, LVESD: LV end-systolic dimension, IVSWT: interventricular septal wall thickness, LVPWT: LV posterior wall thickness, LA: left atrial, AP: anteroposterior, TAPSE: tricuspid annular plane systolic excursion, LVEDV: LV end-diastolic volume, LVESV: LV end-systolic volume, LVEF: LV ejection fraction, RV: right ventricular, RVFAC: RV fractional area change, RVD: RV dimension, RVOT: RV outflow tract, A4C: apical 4-chamber view, A2C: apical 2-chamber view, EM: ellipsoid method, ALM: area length method, RA: right atrial, ST: sinotubular, LVM: LV mass, RWT: relative wall thickness, LVMI: LVM index, 2D: two-dimensional, CI: confidence interval