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Normal Echocardiographic Measurements in a Korean Population Study: Part II. Doppler and Tissue Doppler Imaging

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Background: Hemodynamic and functional evaluation with Doppler and tissue Doppler study as a part of comprehensive echocardiography is essential but normal reference values have never been reported from Korean normal population especially according to age and sex.

Methods: Using Normal echOcaRdiographic Measurements in a KoreAn popuLation study subjects, we obtained normal reference values for Doppler and tissue Doppler echocardiography including tricuspid annular velocities according to current guidelines and compared values according to gender and age groups.

Results: Mitral early diastolic (E) and late diastolic (A) velocity as well as E/A ratio were significantly higher in women compared to those in men. Conversely, mitral peak systolic and late diastolic annular velocity in both septal and lateral mitral annulus were significantly lower in women compared to those in men. However, there were no significant differences in both septal and lateral mitral early diastolic annular (e') velocity between men and women. In both men and women, mitral E velocity and its deceleration time as well as both E/A and E/e' ratio considerably increased with age. There were no significant differences in tricuspid inflow velocities and tricuspid lateral annular velocities between men and women except e' velocity, which was significantly higher in women compared to that in men. However, changes in both tricuspid inflow and lateral annular velocities according to age were similar to those in mitral velocities.

Conclusion: Since there were significant differences in Doppler and tissue Doppler echocardiographic variables between men and women and changes according to age were even more considerable in both gender groups, normal Doppler echocardiographic values should be differentially applied based on age and sex.

KEY WORDS: Transthoracic echocardiography · Doppler · Tissue Doppler · Normal population · Reference value.

Introduction

As Doppler and tissue Doppler images were able to provide important hemodynamic information in various cardiovascular disorders noninvasively, echocardiography has been widely adopted as a noninvasive tool of choice for clinical and hemodynamic evaluation of patients with heart failure.[1)2)] However, there have been only few studies which evaluated normal echocardiographic reference values of Doppler and tissue Doppler imaging (TDI) variables according to age and sex in a large number of normal subjects and no such data are available from Korean population yet.[3-6)]

Previous study about normal echocardiographic reference values did not include variables from TDI and reference values specific to sex were not provided.[7)] In this regard, we sought to provide normal reference values for variables from Doppler and TDI according to sex and age groups using the Normal echOcaRdiographic Measurements in a KoreAn popuLation (NORMAL) study.[8)]

Methods

Study populations

Inclusion and exclusion criteria of the NORMAL study were presented in the part I of the current study.[8)] Briefly, this was a prospective nationwide multicenter (23 centers) study evaluating normal Korean 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 purposes of the research 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. Like previous report, images were stored in digital image communication in medicine format and transferred to the Echocardiographic Core Laboratory (ECL) in Samsung Medical Center.[8)] Final measurements and analysis were performed in ECL with a dedicated software package (EchoPAC, GE Medical Systems, Horten, Norway). All echocardiographic measurements were performed according to the American Society of Echocardiography guidelines.[1)] Briefly, on the apical 4-chamber view, mitral inflow velocities were obtained using pulsed-wave (PW) Doppler imaging with a 1–3 mm sample volume placed between the mitral leaflet tips during diastole. Early diastolic (E) velocity, late diastolic (A) velocity, E to A ratio (E/A), and mitral E wave deceleration time (DT). Continuous-wave Doppler imaging for the measurement of isovolumic relaxation time (IVRT) were performed by placing the sample volume in the left ventricular outflow tract (LVOT) to simultaneously display the end of aortic ejection and the onset of mitral inflow. Tricuspid inflow velocity was obtained using PW Doppler with sample volume placed between the tips of tricuspid valve leaflet on apical 4-chamber view. Mitral annular velocities were obtained at the lateral and septal mitral annulus from the apical 4-chamber view using TDI. Tricuspid lateral annular velocities were also obtained at lateral annulus of tricuspid valve from the apical 4-chamber view. Peak systolic (s'), early diastolic annular (e') velocity and late diastolic annular (a') velocity of each annulus were measured.

LVOT flow velocity was measured at apical long-axis view or anteriorly angulated 4-chamber view using PW Doppler with sample volume positioned on the left ventricular side of the aortic valve just proximal to the region of flow acceleration. Right ventricular outflow tract (RVOT) flow velocity was also measured on parasternal short-axis view at aortic valve level placing sample volume just below pulmonary valve. Peak velocity and velocity-time integral (VTI) of both ventricular outflow velocities were obtained.

Spectral Doppler signal of pulmonary venous flow was obtained in the apical 4-chamber view placing a 2–3 mm sample volume placed 0.5 cm into the pulmonary vein for optimal recording of the spectral waveforms. Pulmonary vein systolic (PVS) and diastolic (PVD) velocities as well as pulmonary vein reversal flow velocity during atrial contraction (PVAr) were measured. Every conventional and tissue Doppler parameter was measured in 3 consecutive beats, and averaged.

Statistical analysis

Mean ± SD and 95% confidence intervals (CIs) for continuous variables are presented. Independent t-test was used for the comparison of mean values between men and women and a one-way analysis of variance test was performed to evaluate whether mean values differed according to age groups. To evaluate the intra- and interobserver variability, we randomly selected 50 cases and calculated intraclass correlation coefficients (ICC). To determine intraobserver measurement variability, one researcher repeated measurements at least 2 weeks after the first measurements, and another researcher who did not have information about the measurement value repeated measurements to evaluate interobserver variability. We considered p values < 0.05 as statistically significant. All statistical analyses were performed using SPSS statistics version 21 (SPSS Inc., Chicago, IL, USA).

Results

Variables from mitral inflow and annular velocities

A total of 1003 normal subjects from 23 centers were evaluated in the current study. Demographic and clinical data are provided in previous report.[8] M-mode variables according to gender groups and according to age and gender groups are presented in Table 1 and Supplementary Table 1, respectively. Mitral E and A velocity were significantly higher in women compared to men. Mitral E/A ratio was also greater in women compared to men. DT of mitral E velocity was longer in men compared to women. Mitral A velocity and DT of E velocity increased and mitral E velocity and E/A ratio decreased with age in both men and women. IVRT was slightly longer in men compared to women and increased with age. There were no significant differences in mitral septal and lateral e' velocities between men and women. However, both septal and lateral s' and a' velocities were significantly higher in men compared to wom-

Table 1. Mitral inflow and annular velocities and pulmonary venous flow velocities according to gender

Variables	Men		Women		Total		p value
	Mean ± SD	95% CI	Mean ± SD	95% CI	Mean ± SD	95% CI	
Mitral E (m/sec)	0.66 ± 0.14	0.38–0.95	0.73 ± 0.17	0.39–1.07	0.70 ± 0.16	0.38–1.02	< 0.0001
Mitral A (m/sec)	0.59 ± 0.17	0.26–0.91	0.62 ± 0.17	0.28–0.96	0.60 ± 0.17	0.27–0.94	0.0029
Mitral E/A ratio	1.2 ± 0.4	0.4–2.1	1.3 ± 0.5	0.2–2.4	1.3 ± 0.5	0.3–2.2	0.0255
DT of mitral E (msec)	212 ± 40	133–290	207 ± 37	134–280	209 ± 39	133–285	0.0354
IVRT (msec)	90 ± 16	57–122	87 ± 17	53–120	88 ± 17	55–121	0.0108
Septal s' (cm/sec)	8.1 ± 1.4	5.3–10.9	7.8 ± 1.3	5.1–10.4	7.9 ± 1.4	5.2–10.7	0.0001
Septal e' (cm/sec)	9.2 ± 2.6	4.2–14.2	9.3 ± 3.1	3.3–15.3	9.3 ± 2.8	3.7–14.8	0.4347
Septal a' (cm/sec)	9.2 ± 1.7	5.8–12.6	8.5 ± 1.8	5.0–12.0	8.8 ± 1.8	5.3–12.4	< 0.0001
Lateral s' (cm/sec)	10.2 ± 2.5	5.3–15.0	9.6 ± 2.3	5.0–14.1	9.9 ± 2.4	5.1–14.6	0.0001
Lateral e' (cm/sec)	12.3 ± 3.5	5.4–19.2	12.6 ± 3.8	5.1–20.0	12.4 ± 3.7	5.2–19.6	0.2386
Lateral a' (cm/sec)	9.4 ± 2.3	4.9–13.9	9.0 ± 2.2	4.6–13.3	9.2 ± 2.3	4.7–13.6	0.0032
E/e' ratio (septal)	7.6 ± 2.1	3.5–11.7	8.4 ± 2.5	3.4–13.4	8.0 ± 2.4	3.4–12.7	< 0.0001
E/e' ratio (lateral)	5.7 ± 1.8	2.2–9.3	6.2 ± 1.8	2.6–9.8	6.0 ± 1.8	2.4–9.6	0.0001
PVS (cm/sec)	52 ± 12	28–77	55 ± 12	30–79	54 ± 12	29–78	0.0083
PVD (cm/sec)	46 ± 12	23–69	46 ± 11	25–67	46 ± 11	24–68	0.6368
PVAr (cm/sec)	26 ± 6	14–38	26 ± 5	15–36	26 ± 6	15–37	0.4066

E: early diastolic inflow velocity, A: late diastolic inflow velocity, DT: deceleration time, IVRT: isovolumic relaxation time, s': systolic annular velocity, e': early diastolic annular velocity, a': late diastolic annular velocity, PVS: pulmonary venous systolic velocity, PVD: pulmonary venous diastolic velocity, PVAr: pulmonary venous reversal flow velocity during atrial contraction, CI: confidence interval en. The s' and e' velocities decreased and a' velocity increased with age in both sex groups and the changes according to ages were greater in women compared to men. E/e' ratio calculated from the e' values of both septal and lateral annulus were significantly higher in women compared to men. E/e' ratio increased with age in both men and women.

Variables from pulmonary vein flow velocities

Measurement values of pulmonary vein flow Doppler variables according to gender groups and according to age and gender groups are also presented in Table 1 and Supplementary Table 1, respectively. PVS was significantly higher in women compared to men. However, there were no significant differences in PVD and PVAr between men and women. PVS and PVAr increased with age in both gender groups. However, PVD decreased according to age in both men and women.

Variables from tricuspid inflow and annular velocities

Measurement values of the tricuspid inflow and annular velocity according to gender groups and according to age and gender groups are presented in Table 2 and Supplementary Table 2, respectively. There were no significant differences in tricuspid E and A velocities, E/A ratio and DT of tricuspid E velocity between men and women. Like mitral inflow velocities, tricuspid E velocity decreased and A velocity increased with age in both men and women. Thus tricuspid E/A ratio decreased according to age. DT of tricuspid E velocity also increased according to age in both sex. Tricuspid e' velocity was greater in women compared to men. However, there were no significant difference in tricuspid lateral s' and a' velocity between men and women. However, tricuspid lateral s' and e' velocities decreased and a' velocity increased with age in both sexes.

Variables from left and right ventricular outflow flow velocities

Measurement values of LVOT and RVOT flow velocities according to gender groups and according to age and gender groups are presented in Table 3 and Supplementary Table 3, respectively. LVOT peak systolic flow velocity and LVOT VTI value were higher in women compared with men. However, there were no significant differences in RVOT peak flow velocity between men and women and RVOT VTI was slightly greater in women compared to men. LVOT peak flow velocities and LVOT VTI increased with age in both men and women. However, RVOT peak flow velocity showed decreasing trends according to age in both men and women. And RVOT VTI showed decreasing trends only in men and there were no significant changes according to age in women.

Intra- and interobserver variability

ICCs for both intra- and interobserver variability testing are presented in Supplementary Table 4. For both intraobserver variability, ICCs for echo variables were above 0.9, except that of the DT of mitral E velocity (ICC = 0.896, 95% CI = 0.812–0.944), IVRT (ICC = 0.855, 95% CI = 0.684–0.929), and DT of tricuspid E velocity (ICC = 0.879, 95% CI = 0.779–0.936). For interobserver variability, ICCs of echocardiographic vari-

Table 2. Measurement values of the tricuspid inflow and annular velocity according to gender

Variables	Men		Women		Total		*p* value
	Mean ± SD	95% CI	Mean ± SD	95% CI	Mean ± SD	95% CI	
Tricuspid E (m/sec)	0.48 ± 0.11	0.27–0.69	0.49 ± 0.11	0.27–0.71	0.48 ± 0.11	0.27–0.70	0.1031
Tricuspid A (m/sec)	0.34 ± 0.09	0.15–0.52	0.35 ± 0.10	0.14–0.55	0.34 ± 0.10	0.15–0.54	0.2682
Tricuspid E/A ratio	1.5 ± 0.5	0.6–2.4	1.5 ± 0.5	0.6–2.5	1.5 ± 0.5	0.6–2.4	0.5200
DT of tricuspid E (msec)	227 ± 52	125–330	226 ± 48	131–320	226 ± 50	128–325	0.6251
Tricuspid lateral s' (cm/sec)	12.3 ± 2.3	7.8–16.9	12.3 ± 2.1	8.2–16.3	12.3 ± 2.2	8.0–16.6	0.5836
Tricuspid lateral e' (cm/sec)	10.9 ± 3.0	5.0–16.9	11.9 ± 3.5	5.0–18.8	11.4 ± 3.3	4.9–17.9	< 0.0001
Tricuspid lateral a' (cm/sec)	12.4 ± 3.5	5.5–19.3	12.9 ± 3.7	5.7–20.0	12.6 ± 3.6	5.6–19.7	0.0533

E: early diastolic inflow velocity, A: late diastolic inflow velocity, DT: deceleration time, s': systolic annular velocity, e': early diastolic annular velocity, a': late diastolic annular velocity, CI: confidence interval

Table 3. Measurement values of LVOT and RVOT flow velocity according to gender

Variables	Men		Women		Total		*p* value
	Mean ± SD	95% CI	Mean ± SD	95% CI	Mean ± SD	95% CI	
LVOT peak velocity (cm/sec)	96 ± 15	66–126	99 ± 16	67–131	97 ± 16	66–129	0.0119
LVOT VTI (cm)	20.0 ± 3.3	13.5–26.6	21.5 ± 3.7	14.2–28.8	20.8 ± 3.6	13.7–27.9	< 0.0001
RVOT peak velocity (cm/sec)	76 ± 15	47–104	76 ± 13	51–101	76 ± 14	49–102	0.5891
RVOT VTI (cm)	17.2 ± 3.1	11.2–23.2	17.7 ± 3.0	11.8–23.6	17.4 ± 3.0	11.5–23.4	0.0070

LVOT: left ventricular outflow tract, VTI: velocity-time integral, RVOT: right ventricular outflow tract, CI: confidence interval ables were above 0.8 except for IVRT (ICC = 0.898, 95% CI = 0.815–0.944), and DT of tricuspid E velocity (ICC = 0.832, 95% CI = 0.698–0.910).

Discussion

This study provided normal reference measurement values of Doppler and TDI variables for comprehensive echocardiographic evaluation according to age and gender using data from the NORMAL study. Briefly, there were statistically significant differences between men and women in most of the Doppler and TDI variables. But the differences according to gender did not seem to be clinically important. Interestingly, changes of the variables according to the age were more considerable compared with those according to gender.

As the prevalence and incidence of heart failure with preserved ejection fraction increased with age, evaluation of diastolic function and filling pressure in the elderly subject is more important.[9] Although current echocardiographic guideline suggested normal value of Doppler and TDI variables according to the age, diagnostic algorithm for the grading of diastolic dysfunction did not consider normal reference values of these variables according to age for routine echocardiographic evaluation.[10] Actually if we apply the diagnostic scheme to elderly women of current study subjects more than half of them would be classified as having diastolic dysfunction grade I or II. Therefore, consideration of the age factor, when evaluating diastolic function especially in elderly female subject is needed to avoid unnecessary sophisticated cardiac evaluation for asymptomatic normal subjects.

In this regard, mitral inflow and annular velocities, which are representative variables for diastolic functions and filling pressure, changed according to ages suggesting trends of more diastolic dysfunction and increased filling pressure in the elderly subjects. That is to say, A velocity and E/e' ratio increased whereas E velocity, E/A ratio, and e' velocity decreased with ages in both men and women. These results were well consistent with previous studies from European and Japanese population and confirms that age reference values should be taken into account when evaluating diastolic function or filling pressures according to those variables.[3)4)] Interestingly, those changes seemed to be more significant in women compared to men and these trends were very similar to the results from the studies from Japan, which evaluated normal echocardiographic values for Japanese subjects.[4] As suggested in the previous studies, these findings might partially explain why elderly women have relatively higher incidence of heart failure with preserved ejection fraction and higher filling pressure and why there were higher cardiovascular mortality in elderly female. However, in other studies evaluating European populations which evaluated the reference values according to age groups of 20–40, 40–60, and more than 60 years old, those trends of more significant changes according to age especially in the elderly female was not noted.[5)11)]

Although mean values of both septal and lateral e' velocities were not significantly different between men and women, values according to the age groups were significantly different between the gender groups. And there were considerable differences in septal and lateral mitral annular velocities and every TDI variables measured from mitral and tricuspid lateral annulus were greater compared with the values from septal annulus, which was consistent with previous reports.[12] The absolute value as well as relative value of each annular velocity might be useful for differentiating normal subjects from those with constrictive pericarditis or restrictive cardiomyopathy.[13] Lower velocities of s' and e' and higher value of a' were observed especially female older subjects. This again might explain why women are susceptible for heart failure with preserved ejection fraction.

Although clinical implication of pulmonary venous and tricuspid inflow velocities are often regarded as less important compared with those of mitral valves, variables from those flow velocities might be useful for differential diagnosis of constrictive pericarditis from restrictive cardiomyopathy and estimating filling pressures of both ventricles.[14] For pulmonary venous flow variables, PVS and PVAr increased and PVD decreased according to age in both men and women, which findings were consistent with previous reports in that healthy older subjects had higher PVS, PVAr, and lower PVD compared with younger subjects.[15] And these results were also consistent with the prior study from healthy Korean population.[7] However, higher PVS value in men compared to women in our study was not consistently observed in the previous studies.[4)11)]

Likewise, no significant differences were found between men and women for the tricuspid inflow velocities and its DT. Interestingly, the tricuspid inflow velocities and its DT showed significant differences according to age group, which were similar to those of mitral inflows. And the mean values of the variables were very similar to the previous study for Korean population.[7]

There are several limitations to be acknowledged for this study. First, we included only normal Korean subjects in the NORMAL study and there might be considerable differences in clinical and demographic characteristics as we discussed in the prior reports.[8] Thus our data might not be applicable to other populations. Second, we did not evaluate myocardial velocity using TDI or speckle tracking techniques. Lastly, as acknowledged in the previous report, patients with significant 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.[8] Therefore, patients with subclinical hypertension or coronary artery disease might be included in the current study. However, their effects on the variables of the current study are unlikely to be significant.

In conclusion, we provided normal values for Doppler and TDI variables for comprehensive echocardiography including right-sided heart from the NORMAL study. As there were significant changes among different age groups, normal reference values according to age should be used for Doppler and TDI variables.

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Supplementary Table 1. Measurement values of mitral inflow and annular velocities and pulmonary venous flow velocities according to age and gender

Age groups	Men (mean ± SD)						*p* value*	Women (mean ± SD)						*p* value*
	21–30	31–40	41–50	51–60	61–70	71–80		21–30	31–40	41–50	51–60	61–70	71–80	
Mitral E (m/sec)	0.74 ± 0.12	0.70 ± 0.13	0.67 ± 0.14	0.63 ± 0.13	0.60 ± 0.14	0.61 ± 0.16	< 0.0001	0.88 ± 0.16	0.80 ± 0.13	0.75 ± 0.14	0.69 ± 0.17	0.64 ± 0.14	0.59 ± 0.15	< 0.0001
Mitral A (m/sec)	0.45 ± 0.09	0.50 ± 0.10	0.53 ± 0.11	0.62 ± 0.13	0.74 ± 0.14	0.76 ± 0.19	< 0.0001	0.47 ± 0.11	0.51 ± 0.11	0.59 ± 0.13	0.65 ± 0.14	0.76 ± 0.16	0.82 ± 0.15	< 0.0001
Mitral E/A ratio	1.7 ± 0.4	1.4 ± 0.4	1.3 ± 0.4	1.1 ± 0.2	0.8 ± 0.2	0.9 ± 0.3	< 0.0001	2.0 ± 0.6	1.6 ± 0.4	1.3 ± 0.3	1.1 ± 0.3	0.9 ± 0.2	0.7 ± 0.2	< 0.0001
DT of mitral E (msec)	196 ± 35	205 ± 35	207 ± 36	212 ± 37	230 ± 47	231 ± 41	< 0.0001	194 ± 27	194 ± 29	200 ± 32	207 ± 40	225 ± 37	233 ± 43	< 0.0001
IVRT (msec)	84 ± 15	85 ± 12	90 ± 17	93 ± 16	94 ± 17	95 ± 20	< 0.0001	76 ± 11	81 ± 13	85 ± 14	91 ± 15	94 ± 20	96 ± 20	< 0.0001
Medial s' (cm/sec)	8.6 ± 1.4	8.5 ± 1.4	8.0 ± 1.3	8.1 ± 1.5	7.5 ± 1.4	7.7 ± 1.4	< 0.0001	8.5 ± 1.3	8.2 ± 1.3	8.0 ± 1.3	7.3 ± 1.3	7.2 ± 1.1	7.0 ± 1.2	< 0.0001
Medial e' (cm/sec)	11.9 ± 2.0	10.5 ± 1.9	9.4 ± 2.1	8.3 ± 1.8	7.0 ± 1.7	7.3 ± 2.0	< 0.0001	12.9 ± 2.1	11.3 ± 1.9	9.7 ± 2.0	8.1 ± 2.1	6.9 ± 1.9	5.6 ± 1.5	< 0.0001
Medial a' (cm/sec)	8.4 ± 1.9	8.5 ± 1.4	8.8 ± 1.5	9.6 ± 1.5	9.9 ± 1.4	10.5 ± 2.2	< 0.0001	7.2 ± 1.6	7.9 ± 1.4	8.5 ± 1.8	8.8 ± 1.5	9.4 ± 1.6	9.6 ± 1.7	< 0.0001
Lateral s' (cm/sec)	11.5 ± 2.6	11.0 ± 2.2	9.8 ± 2.6	9.7 ± 2.3	9.1 ± 1.9	9.4 ± 2.4	< 0.0001	11.1 ± 2.0	10.6 ± 2.4	9.9 ± 2.3	8.8 ± 2.1	8.4 ± 1.7	8.3 ± 1.7	< 0.0001
Lateral e' (cm/sec)	15.9 ± 3.3	14.0 ± 2.4	12.5 ± 2.9	11.2 ± 2.1	9.6 ± 2.4	9.0 ± 3.0	< 0.0001	17.2 ± 2.5	15.5 ± 2.1	13.0 ± 2.1	11.0 ± 2.4	9.3 ± 2.4	7.7 ± 1.8	< 0.0001
Lateral a' (cm/sec)	8.6 ± 2.5	8.3 ± 1.6	8.9 ± 2.1	10.0 ± 2.2	10.4 ± 1.9	10.9 ± 2.6	< 0.0001	7.1 ± 1.6	8.1 ± 1.8	9.2 ± 1.9	9.5 ± 1.8	10.1 ± 2.4	10.2 ± 2.4	< 0.0001
E/e' ratio (septal)	6.3 ± 1.4	6.8 ± 1.4	7.4 ± 2.1	7.9 ± 1.9	8.9 ± 2.2	8.7 ± 2.4	< 0.0001	6.9 ± 1.5	7.2 ± 1.5	7.9 ± 1.9	8.9 ± 2.4	9.8 ± 2.8	11.1 ± 3.2	< 0.0001
E/e' ratio (lateral)	4.9 ± 1.4	5.1 ± 1.2	5.6 ± 1.5	5.8 ± 1.5	6.5 ± 1.9	7.4 ± 2.7	< 0.0001	5.2 ± 1.1	5.2 ± 1.1	5.8 ± 1.2	6.5 ± 1.9	7.2 ± 2.0	7.9 ± 2.4	< 0.0001
PVS (cm/sec)	47 ± 12	49 ± 10	50 ± 11	55 ± 12	58 ± 13	61 ± 11	< 0.0001	51 ± 10	51 ± 10	53 ± 12	55 ± 13	56 ± 12	65 ± 15	< 0.0001
PVD (cm/sec)	53 ± 13	50 ± 9	47 ± 12	44 ± 11	41 ± 8	40 ± 12	< 0.0001	54 ± 11	50 ± 10	46 ± 9	43 ± 10	40 ± 10	39 ± 8	< 0.0001
PVAr (cm/sec)	23 ± 6	24 ± 5	25 ± 5	27 ± 5	30 ± 6	29 ± 5	< 0.0001	23 ± 6	25 ± 4	26 ± 6	26 ± 5	27 ± 5	29 ± 5	< 0.0001

**p* value from analysis of variance test in each sex. E: early diastolic inflow velocity, A: late diastolic inflow velocity, DT: deceleration time, IVRT: isovolumic relaxation time, s': systolic annular velocity, e': early diastolic annular velocity, a': late diastolic annular velocity, PVS: pulmonary venous systolic velocity, PVD: pulmonary venous diastolic velocity, PVAr: pulmonary venous reversal flow during atrial contraction

Supplementary Table 2. Measurement values of the tricuspid inflow and annular velocity according to age and gender

Age groups	Men (mean ± SD)						p value*	Women (mean ± SD)						p value*
	21–30	31–40	41–50	51–60	61–70	71–80		21–30	31–40	41–50	51–60	61–70	71–80	
Tricuspid E (m/sec)	0.54 ± 0.10	0.51 ± 0.11	0.48 ± 0.10	0.45 ± 0.11	0.44 ± 0.09	0.44 ± 0.10	< 0.0001	0.57 ± 0.10	0.53 ± 0.10	0.50 ± 0.11	0.45 ± 0.08	0.45 ± 0.09	0.42 ± 0.11	< 0.0001
Tricuspid A (m/sec)	0.30 ± 0.07	0.32 ± 0.09	0.32 ± 0.09	0.34 ± 0.08	0.38 ± 0.09	0.40 ± 0.13	< 0.0001	0.31 ± 0.08	0.32 ± 0.09	0.33 ± 0.09	0.34 ± 0.10	0.38 ± 0.12	0.43 ± 0.12	< 0.0001
Tricuspid E/A ratio	1.9 ± 0.5	1.7 ± 0.5	1.5 ± 0.4	1.4 ± 0.4	1.2 ± 0.3	1.2 ± 0.4	< 0.0001	1.9 ± 0.5	1.8 ± 0.4	1.6 ± 0.4	1.4 ± 0.4	1.3 ± 0.3	1.0 ± 0.3	< 0.0001
DT of tricuspid E (msec)	222 ± 50	222 ± 49	209 ± 42	235 ± 53	242 ± 54	240 ± 66	0.0005	213 ± 41	221 ± 40	218 ± 44	235 ± 53	231 ± 54	240 ± 52	0.0030
Tricuspid lateral s' (cm/sec)	13.1 ± 2.5	12.7 ± 2.2	11.8 ± 2.0	12.1 ± 1.9	12.1 ± 2.4	12.2 ± 2.9	0.0055	12.8 ± 1.9	12.6 ± 1.8	12.3 ± 2.0	12.0 ± 1.9	12.0 ± 2.5	11.6 ± 2.3	0.0035
Tricuspid lateral e' (cm/sec)	13.3 ± 2.8	12.2 ± 2.8	10.8 ± 2.7	10.1 ± 2.5	9.0 ± 2.3	9.5 ± 2.7	< 0.0001	15.6 ± 3.2	13.7 ± 2.8	12.0 ± 2.9	10.5 ± 2.3	9.6 ± 2.4	8.8 ± 2.5	< 0.0001
Tricuspid lateral a' (cm/sec)	10.1 ± 2.7	11.5 ± 2.7	11.4 ± 3.1	13.3 ± 3.2	14.5 ± 3.4	14.5 ± 3.8	< 0.0001	9.6 ± 2.8	11.3 ± 2.9	13.3 ± 3.4	14.1 ± 3.2	14.5 ± 3.4	15.0 ± 3.3	< 0.0001

*p value from analysis of variance test in each sex. E: early diastolic inflow velocity, A: late diastolic inflow velocity, DT: deceleration time, s': systolic annular velocity, e': early diastolic annular velocity, a': late diastolic annular velocity

Supplementary Table 3. Measurement values of LVOT and RVOT velocity according to age and gender

Age groups	Men (mean ± SD)						p value*	Women (mean ± SD)						p value*
	21–30	31–40	41–50	51–60	61–70	71–80		21–30	31–40	41–50	51–60	61–70	71–80	
LVOT peak velocity (cm/sec)	95 ± 14	93 ± 15	94 ± 14	97 ± 15	99 ± 17	99 ± 17	0.0326	93 ± 14	95 ± 15	100 ± 16	98 ± 17	104 ± 17	103 ± 15	0.0001
LVOT VTI (cm)	19.2 ± 3.0	19.0 ± 2.7	19.6 ± 3.2	20.5 ± 3.1	21.2 ± 3.6	21.3 ± 4.4	< 0.0001	20.2 ± 3.1	20.5 ± 3.4	21.5 ± 3.6	21.9 ± 4.1	22.7 ± 3.8	22.3 ± 3.6	< 0.0001
RVOT peak velocity (cm/sec)	79 ± 13	77 ± 14	72 ± 13	75 ± 16	74 ± 16	74 ± 13	0.0239	76 ± 12	79 ± 12	78 ± 13	74 ± 12	75 ± 13	75 ± 13	0.0378
RVOT VTI (cm)	18.1 ± 2.9	17.3 ± 2.7	16.7 ± 3.0	17.1 ± 3.2	16.9 ± 3.4	16.6 ± 2.9	0.0248	17.8 ± 2.8	18.1 ± 3.1	18.0 ± 2.5	17.3 ± 3.0	17.6 ± 3.0	17.2 ± 3.8	0.3148

*p value from analysis of variance test in each sex. LVOT: left ventricular outflow tract, VTI: velocity-time integral, RVOT: right ventricular outflow tract

Supplementary Table 4. Intra- and interobserver variability data

Variables	Intraobserver variability		Interobserver variability	
	ICC	95% CI	ICC	95% CI
Mitral inflow and annular velocity				
Mitral E (m/sec)	0.984	0.969–0.991	0.982	0.872–0.994
Mitral A (m/sec)	0.991	0.983–0.995	0.983	0.969–0.991
Mitral E/A ratio	0.978	0.959–0.988	0.989	0.976–0.995
DT of mitral E (msec)	0.896	0.812–0.944	0.918	0.808–0.961
IVRT (msec)	0.855	0.684–0.929	0.898	0.815–0.944
Septal s' (cm/sec)	0.974	0.952–0.986	0.957	0.919–0.977
Septal e' (cm/sec)	0.984	0.971–0.992	0.978	0.903–0.992
Septal a' (cm/sec)	0.975	0.953–0.987	0.946	0.848–0.976
Lateral s' (cm/sec)	0.966	0.937–0.982	0.939	0.889–0.967
Lateral e' (cm/sec)	0.983	0.969–0.991	0.968	0.940–0.983
Lateral a' (cm/sec)	0.986	0.974–0.993	0.936	0.869–0.967
E/e' ratio (septal)	0.960	0.924–0.979	0.971	0.945–0.984
E/e' ratio (lateral)	0.961	0.927–0.979	0.871	0.761–0.931
Pulmonary venous flow velocity				
PVS (cm/sec)	0.981	0.964–0.990	0.972	0.946–0.985
PVD (cm/sec)	0.992	0.985–0.996	0.966	0.931–0.983
PVAr (cm/sec)	0.911	0.835–0.952	0.912	0.832–0.954
Tricuspid inflow and annular velocity				
Tricuspid E (m/sec)	0.971	0.943–0.985	0.958	0.912–0.979
Tricuspid A (m/sec)	0.966	0.935–0.982	0.943	0.862–0.974
Tricuspid E/A ratio	0.938	0.880–0.968	0.919	0.849–0.957
DT of tricuspid E (msec)	0.879	0.779–0.936	0.832	0.698–0.910
Tricuspid lateral s' (cm/sec)	0.992	0.984–0.996	0.965	0.935–0.981
Tricuspid lateral e' (cm/sec)	0.974	0.952–0.986	0.971	0.936–0.986
Tricuspid lateral a' (cm/sec)	0.973	0.951–0.986	0.943	0.861–0.973
LVOT and RVOT flow velocity				
LVOT peak velocity (cm/sec)	0.992	0.986–0.996	0.974	0.952–0.986
LVOT VTI (cm)	0.984	0.969–0.991	0.966	0.881–0.986
RVOT peak velocity (cm/sec)	0.992	0.984–0.996	0.985	0.972–0.992
RVOT VTI (cm)	0.969	0.943–0.984	0.957	0.829–0.983

ICC: intraclass correlation coefficient, E: early diastolic inflow velocity, A: late diastolic inflow velocity, DT: deceleration time, IVRT: isovolumic relaxation time, s': systolic annular velocity, e': early diastolic annular velocity, a': late diastolic annular velocity, PVS: pulmonary venous systolic velocity, PVD: pulmonary venous diastolic velocity, PVAr: pulmonary venous reversal flow during atrial contraction, LVOT: left ventricular outflow tract, RVOT: right ventricular outflow tract, VTI: velocity-time integral, CI: confidence interval