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ORIGINAL PAPER

Normal reference values for mitral annular plane systolic excursion by motion-mode and speckle tracking echocardiography: a prospective, multicentre, population-based study

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Aims

Mitral annular plane systolic excursion (MAPSE) is a simple and reliable index for evaluating left ventricular (LV) systolic function, particularly in patients with poor image quality; however, the lack of reference values limits its widespread use. This study aimed to establish the normal ranges for MAPSE measured using motion-mode (M-mode) and two-dimensional speckle tracking echocardiography (2D-STE) and to explore its principal determinants.

Methods and results

This multicentre, prospective, cross-sectional study included 1952 healthy participants [840 men (43%); age range, 18–80 years] from 55 centres. MAPSE was measured using M-mode echocardiography and 2D-STE. The results showed that women had a higher MAPSE than men and MAPSE decreased with age. The age- and sex-specific reference values for MAPSE were established for these two methods. Multiple linear regression analyses revealed that MAPSE on M-mode echocardiography correlated with age and MAPSE on 2D-STE with age, blood pressure (BP), heart rate, and LV volume. Moreover, MAPSE measured by 2D-STE correlated more strongly with global longitudinal strain compared with that measured using M-mode echocardiography.

Conclusion

Normal MAPSE reference values were established based on age and sex. BP, heart rate, and LV volume are potential factors that influence MAPSE and should be considered in clinical practice. Normal values are useful for evaluating LV longitudinal systolic function, especially in patients with poor image quality, and may further facilitate the use of MAPSE in routine assessments.

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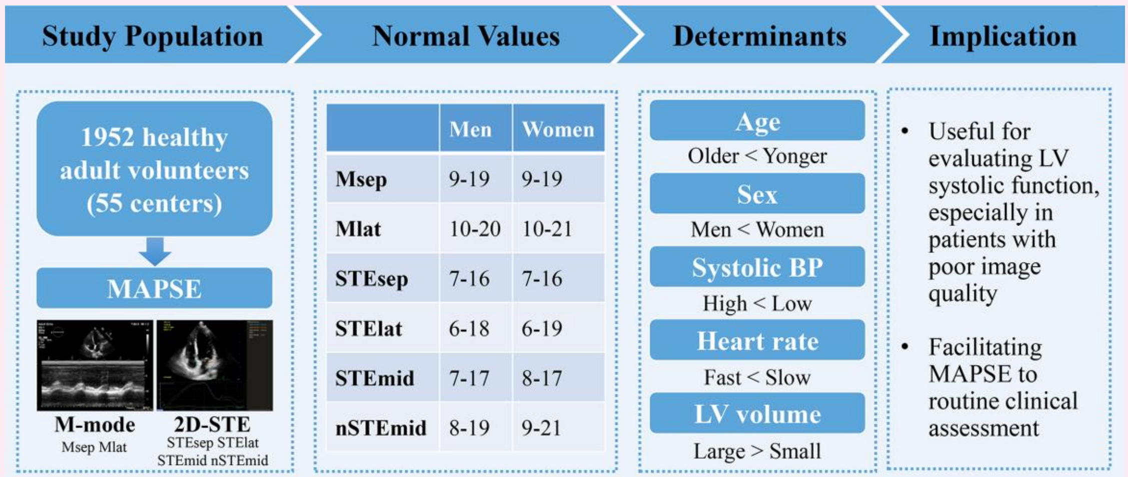
Graphical Abstract



Normal reference values for mitral annular plane systolic excursion by motion-mode and speckle tracking echocardiography. 2D-STE, two-dimensional speckle tracking echocardiography; other abbreviations as per *Tables 1* and *2*.

Keywords mitral annulus displacement • ventricular function • normal values • speckle tracking • echocardiography

Introduction

The assessment of left ventricular (LV) systolic function plays a key role in the diagnosis, management, and prognosis of cardiac diseases.[1] Determination of LV ejection fraction (LVEF) using two-dimensional (2D) or three-dimensional methods and global longitudinal strain (GLS) using speckle tracking echocardiography (STE) is recommended for evaluating LV systolic function.[2,3] However, both methods require tracing of the LV endocardium, which is highly dependent on an adequate visualization of the LV myocardium. Therefore, an approach that does not rely on image quality is desirable for assessing LV systolic function.

Mitral annular plane systolic excursion (MAPSE) quantitatively reflects LV longitudinal systolic function because the longitudinal movement of the mitral valve annulus plays a leading role in LV pumping, whereas the apex is relatively stationary.[4] Moreover, MAPSE is independent of image quality since its measurement only requires visualization of the mitral annulus without delineation of the LV endocardial boundary.[5] Therefore, the 2015 Chamber Quantification Guidelines from the American Society of Echocardiography (ASE) and the European Association of Cardiovascular Imaging (EACVI) recommend the use of MAPSE as a substitute parameter when LVEF or GLS cannot be detected accurately owing to suboptimal delineation or tracking in patients with poor image quality.[3] Moreover, a 2020 consensus recommendation from the Heart Failure Association of the European Society of Cardiology stated that MAPSE could be used as an alternative index for evaluating LV systolic function in patients with heart failure with preserved ejection fraction.[6]

Currently, MAPSE is determined primarily using motion-mode (M-mode) echocardiography as this method is more readily implemented. However, M-mode echocardiography is angle dependent and has limited accuracy. Another technique, two-dimensional speckle tracking echocardiography (2D-STE), can track the mitral annulus and measure MAPSE automatically without angle dependence.[7] Previous studies have verified the accuracy, convenience, and high reproducibility of 2D-STE for measuring MAPSE to assess LV systolic function.[8,9] However, the lack of large, multicentre, population-based normal reference values for MAPSE using both M-mode echocardiography and 2D-STE has impeded efforts towards its wider implementation in routine clinical practice. In addition, the principal determinants of MAPSE have not yet been investigated thoroughly. Therefore, we aimed to establish the normal reference values for MAPSE measured using M-mode echocardiography and 2D-STE and to explore the primary determinants of MAPSE in a large prospective multicentre study. This may facilitate its implementation in routine clinical assessment for the detection of LV systolic dysfunction.

Methods

Study population

This was a nationwide, multicentre, prospective, observational, cross-sectional study of healthy adults in China, conducted from January 2021 to January 2022. The study was designed initially to enrol 2400 normal healthy adult volunteers with an even distribution of age and sex. Specifically, we aimed to include at least 400 participants in each age group (18–29, 30–39, 40–49, 50–59, 60–69, and ≥70 years, with $n = 200$ men). The sample size was determined according to the guidelines of the Clinical and Laboratory Standards Institute,[10] in which the minimum number of patients was 120 in each group. The sample size was adjusted based on an assumptive 30% exclusion rate. The principal investigators, Professors W.-D.R. and C.-Y.M., invited echocardiographic laboratories accredited by the Chinese Society of Ultrasound in Medicine from regionally representative tertiary hospitals in all provinces and municipalities throughout China to participate in the study. Ultimately, 55 echocardiographic laboratories participated in this study.

Healthy individuals were identified from check-ups at medical examination centres. The inclusion criteria were as follows: age ≥ 18 years; no history or clinical evidence of cardiac, cardiovascular, lung, or kidney disease; and no abnormal findings on physical examination, biochemical examination, electrocardiography, or echocardiography. The exclusion criteria were as follows: hypertension [blood pressure (BP) > 140/80 mmHg] or receiving medication for hypertension; body mass index > 30 kg/m^2; total cholesterol ≥ 6.2 mmol/L, triglyceride ≥ 2.3 mmol/L, or high-density lipoprotein cholesterol < 1.0 mmol/L; endocrine diseases, such as diabetes mellitus (fasting blood glucose ≥ 7.0 mmol/L), thyroid disease, pheochromocytoma, adrenal insufficiency, and hyperaldosteronism; anaemia; abnormal liver function; connective tissue diseases, such as rheumatoid arthritis, vasculitis, systemic lupus erythematosus, dermatomyositis, and scleroderma; malignancy; current pregnancy or lactation; professional sport activity; and a history of alcoholism. Moreover, patients with mitral annulus calcification were excluded.

All participants provided written informed consent. This study conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was registered with the North American Clinical Trials Network (registration ID: NCT04399447).

Echocardiographic image acquisition

To ensure standardization and uniformity of image acquisition and clinical data records, each participating laboratory designated a supervisory physician who was intensively trained in advance at the core laboratories. The image acquisition and quantitative assessments were performed following a standardized protocol created by two core laboratories (First Hospital and Shengjing Hospital of China Medical University) as per the ASE recommendations.[3,11] Each participating laboratory regularly transmitted the collected demographic information and the recorded raw digital images in Digital Imaging and Communications in Medicine using network discs to the core laboratories for central analyses. Two senior experts from the core laboratories (L.S. from Shengjing Hospital of China Medical University and S.-W.L. from First Hospital of China Medical University) performed quality control checks by reviewing each echocardiographic image. The final measurements and statistical analyses were performed at the core laboratories. All echocardiographic images were acquired and assessed by experienced cardiologists who were blinded to the clinical data.

The echocardiographic examinations were performed using an EPIQ7C imaging system (Philips Healthcare, Andover, MA, USA) equipped with an S5-1 transducer (1–5 MHz). Standard 2D images were recorded during normal respiration using optimal technical setting parameters and a frame rate of at least 50 fps. The presence of LV foreshortening in the apical view was avoided. At least three cardiac cycles were recorded for each view. LV end-diastolic volume (EDV), end-systolic volume (ESV), and EF were measured using the biplane Simpson method. LV diastolic function was assessed according to the ASE recommendations.[12]

Using M-mode echocardiography in the apical four-chamber view, sampling lines were placed in the septal and lateral mitral annuli to measure the corresponding MAPSE (Msep and Mlat, respectively). MAPSE was also measured at the core laboratories using 2D-STE with the commercially available software QLAB (version 13.0; Philips Healthcare, Andover, MA, USA). After entering the tissue motion in the mitral annular displacement mode, three anatomical landmark points on the septal and lateral mitral annuli and the LV apical myocardium were selected in an automatically located diastolic frame in the apical four-chamber view. The software then tracked the three selected points frame-by-frame. The displacement of the septal and lateral mitral annuli from the LV base to the apex was calculated throughout the cardiac cycle, and the displacement–time curves were plotted (*Figure 1*). The maximal MAPSE in the septal and lateral mitral annuli (STEsep and STElat), and at the midpoint between the two (STEmid), was automatically displayed. STEmid was normalized by calculating the ratio of STEmid to the LV long-axis length at end-diastole (nSTEmid). The average values of the three measurements were used for further analysis.

LV GLS was measured from the apical two-, four-, and three-chamber views using an automated method with the QLAB AutoStrain LV package. The endocardial borders were corrected manually if necessary, and LV GLS was not used for further data analysis if, even after a manual adjustment, the participant had inadequate tracking of more than one segment in at least one apical view. For simplicity, the absolute values of GLS were used for data interpretation.

Statistical analyses

Age groups were compared using an analysis of variance. A *post hoc* analysis (Bonferroni test) was performed to analyse intergroup differences. Bivariate correlations were presented as Pearson's coefficients (*r*). Simple and multiple

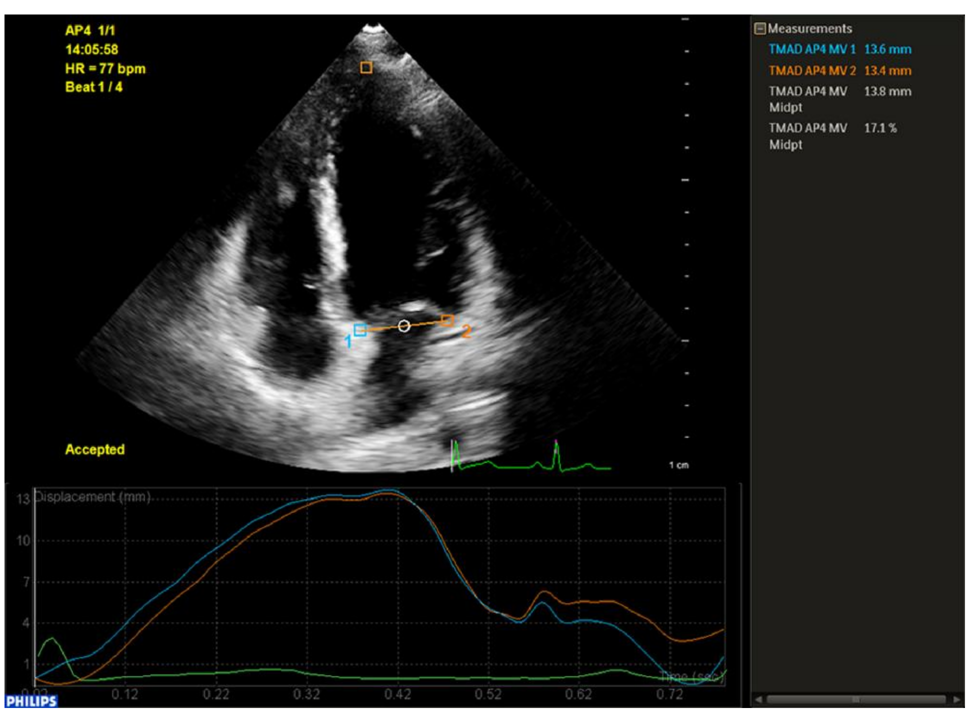


Figure 1 Representative image for measuring MAPSE using 2D-STE.

Table 1 Baseline demographic characteristics of the study population

Parameters	Total ($n = 1952$)	Men ($n = 840$)	Women ($n = 1112$)	*P*-value (men vs. women)
Age (years)	45 ± 15	45 ± 15	44 ± 14	0.30
Height (cm)	166 ± 8	172 ± 6	161 ± 5	<0.001
Weight (kg)	62 ± 10	69 ± 9	57 ± 7	<0.001
BSA (m^2)	1.69 ± 0.17	1.82 ± 0.14	1.59 ± 0.11	<0.001
Body mass index (kg/m^2)	22.5 ± 2.5	23.2 ± 2.4	22.0 ± 2.4	<0.001
Systolic BP (mmHg)	118 ± 10	121 ± 9	116 ± 10	<0.001
Diastolic BP (mmHg)	75 ± 7	76 ± 7	74 ± 7	<0.001
Heart rate (bpm)	73 ± 9	73 ± 9	73 ± 9	0.23
Waistline (cm)	79 ± 9	83 ± 9	76 ± 8	<0.001

Values shown are means ± standard deviation.
BP, blood pressure; BSA, body surface area.

Table 2 MAPSE according to sex

Parameters	Total ($n = 1952$)	Men ($n = 840$)	Women ($n = 1112$)	*P*-value (men vs. women)
Msep (mm)				
Mean ± SD	14.0 ± 2.5	14.0 ± 2.5	14.0 ± 2.5	0.94
95% CI	9–19	9–19	9–19	
Mlat (mm)				
Mean ± SD	15.5 ± 2.8	15.2 ± 2.6	15.7 ± 2.8	<0.001
95% CI	10–21	10–20	10–21	
STEsep (mm)				
Mean ± SD	11.5 ± 2.3	11.3 ± 2.3	11.6 ± 2.3	0.004
95% CI	7–16	7–16	7–16	
STElat (mm)				
Mean ± SD	12.4 ± 3.2	12.1 ± 3.1	12.6 ± 3.2	0.001
95% CI	6–19	6–18	6–19	
STEmid (mm)				
Mean ± SD	12.2 ± 2.5	12.0 ± 2.4	12.4 ± 2.5	0.001
95% CI	7–17	7–17	8–17	
nSTEmid (%)				
Mean ± SD	14.5 ± 3.1	13.8 ± 2.8	15.0 ± 3.2	<0.001
95% CI	8–21	8–19	9–21	

CI, confidence interval; MAPSE, mitral annular plane systolic excursion; Msep and Mlat, septal and lateral MAPSE by M-mode echocardiography; STEsep, STElat, and STEmid, septal, lateral, and midpoint MAPSE measured by 2D-STE; nSTEmid, normalized STEmid by LV long-axis length at end-diastole; SD, standard deviation.

linear regressions were used to explore the determinants of MAPSE; parameters with *P*-values < 0.05 in the simple analysis were included in the multiple regression model. The degree of collinearity was reflected by the variance inflation factor, with a factor > 5 indicating severe collinearity. The normal range for MAPSE was defined as the range that included 95% of the normal population, and the values at the 2.5th and 97.5th percentiles were defined as the lower and upper limits of normality, respectively. The same observer repeated the measurements at different time points with an interval of at least 3 months to evaluate intra-observer reproducibility, and a second independent observer repeated the measurements twice to assess the inter-observer reproducibility. Intra- and inter-observer reproducibility was evaluated by calculating the coefficient of variation (CV) based on re-evaluation of the same image in a subset of 50 randomly selected participants. A *P*-value of <0.05 was considered to be statistically significant. All statistical analyses were performed using SPSS software (version 26.0; IBM Corp., Armonk, NY, USA) and R version 4.1.2.

Results

Population characteristics

A total of 1952 healthy participants [age groups: 18–29 years, $n = 339$ (17.4%); 30–39 years, $n = 458$ (23.5%); 40–49 years, $n = 424$ (21.7%); 50–59 years, $n = 366$ (18.8%); 60–70 years, $n = 230$ (11.8%); and ≥70 years, $n = 135$ (6.9%)] from 55 participating institutions were included in this study. Among them were 840 men (43%) with a mean age of 45 ± 15 years (range, 18–80 years) and 1112 women (57%) with a mean age of 44 ± 14 years (range, 18–79 years).

Table 1 shows the baseline demographic characteristics of the study population. Men exhibited significantly greater heights, weights, body surface areas (BSAs), body mass indexes, systolic and diastolic BPs, and waist circumferences than those of women. However, neither age nor heart rate differed significantly between the two sexes. LV EDV, ESV, and end-diastolic and end-systolic diameters were significantly higher in men, whereas women had higher LV end-diastolic and end-systolic diameters indexed to BSAs. Women also had higher LVEF than men. Moreover, left atrial volume index, mitral *E*, *e*′, average *E*/*e*′, and *E*/*A* values were higher in women than in men (see Supplementary data online, *Table S1*).

Establishment of normal reference values for MAPSE

The normal ranges of each MAPSE parameter stratified by sex are shown in *Table 2*. Compared with men, Mlat measured using M-mode echocardiography and each MAPSE parameter measured using 2D-STE were higher in women.

The normal ranges of each MAPSE parameter stratified by age are presented in *Table 3*. Msep decreased gradually with age in both sexes and was negatively correlated with age in both men (*r*, −0.12; $P < 0.001$) and women (*r*, −0.21; $P < 0.001$; *Figure 2*). Moreover, each MAPSE parameter measured by 2D-STE decreased gradually with age in both sexes and was correlated negatively with age in men (*r*, −0.11 to −0.25; all $P < 0.05$) and women (*r*, −0.17 to −0.33; all $P < 0.05$; *Figure 2*).

Determinants of MAPSE

The correlation heat map showed that MAPSE measured using M-mode echocardiography may be related to age, BSA, and LV EDV (*Figure 3*), and the multiple linear regression analysis revealed that Msep and Mlat were independently correlated with age (*Table 4*).

The correlation heat map showed that MAPSE measured using 2D-STE may be related to age, BSA, body mass index, waist circumference, systolic BP, heart rate, LV EDV, and LV EDV indexed to BSA (*Figure 3*). The multiple linear regression analysis revealed that STEsep, STElat, and STEmid were independently correlated with age, systolic BP, heart rate, and LV EDV, whereas nSTEmid was independently correlated with age, systolic BP, and heart rate (*Table 4*). Waist circumference and LV EDV indexed to BSA were excluded from multiple linear regression models because of their strong collinearity. The

Table 3 MAPSE according to age decades

Parameters	18–29 years ($n = 339$)	30–39 years ($n = 458$)	40–49 years ($n = 424$)	50–59 years ($n = 366$)	60–69 years ($n = 230$)	≥70 years ($n = 135$)	*P*-value
Men (*n*)	159	186	157	163	103	72	
Msep (mm)							
Mean ± SD	14.3 ± 2.5	14.5 ± 2.3	13.9 ± 2.4	13.7 ± 2.7	13.8 ± 2.4	$13.4 \pm 2.2^{\ddagger}$	0.005
95% CI	9–19	10–19	9–19	8–19	9–19	9–18	
Mlat (mm)							
Mean ± SD	15.2 ± 2.7	15.7 ± 2.5	15.3 ± 2.5	14.9 ± 2.7	15.3 ± 2.8	14.9 ± 2.6	0.09
95% CI	10–20	11–21	10–20	10–20	10–21	10–20	
STEsep (mm)							
Mean ± SD	12.0 ± 2.3	11.9 ± 2.3	$11.1 \pm 2.1^{*,\ddagger}$	$11.0 \pm 2.2^{*,\ddagger}$	$10.6 \pm 2.2^{*,\ddagger}$	$10.1 \pm 2.4^{*,\ddagger,\S}$	<0.001
95% CI	7–17	7–16	7–15	7–15	6–15	5–15	
STElat (mm)							
Mean ± SD	12.5 ± 3.0	12.7 ± 3.4	$11.6 \pm 3.1^{\ddagger}$	12.1 ± 3.0	11.9 ± 3.0	$11.2 \pm 3.2^{*,\ddagger}$	0.001
95% CI	7–18	6–19	6–18	6–18	6–18	5–17	
STEmid (mm)							
Mean ± SD	12.6 ± 2.3	12.6 ± 2.6	$11.7 \pm 2.2^{*,\ddagger}$	12.0 ± 2.4	$11.4 \pm 2.4^{*,\ddagger}$	$10.9 \pm 2.4^{*,\ddagger,\#}$	<0.001
95% CI	8–17	8–18	7–16	7–17	7–16	6–16	
nSTEmid (%)							
Mean ± SD	14.2 ± 2.5	14.1 ± 2.9	13.6 ± 2.6	13.5 ± 2.8	13.6 ± 3.1	13.2 ± 2.9	0.03
95% CI	9–19	8–20	9–19	8–19	8–20	8–19	
Women (*n*)	180	272	267	203	127	63	
Msep (mm)							
Mean ± SD	14.5 ± 2.4	14.5 ± 2.5	14.2 ± 2.8	$13.6 \pm 2.3^{*,\ddagger}$	$13.2 \pm 2.3^{*,\ddagger,\S}$	$12.8 \pm 2.1^{*,\ddagger,\S}$	<0.001
95% CI	10–19	10–19	9–20	9–18	9–18	9–17	
Mlat (mm)							
Mean ± SD	16.0 ± 2.7	16.1 ± 2.8	15.9 ± 2.9	15.4 ± 2.8	15.2 ± 2.8	14.9 ± 2.4	0.002
95% CI	11–21	11–22	10–22	10–21	10–21	10–20	
STEsep (mm)							
Mean ± SD	12.2 ± 2.2	12.4 ± 2.1	11.9 ± 2.2	$11.0 \pm 2.3^{*,\ddagger,\S}$	$10.4 \pm 2.1^{*,\ddagger,\S}$	$9.8 \pm 2.5^{*,\ddagger,\S,\#}$	<0.001
95% CI	8–17	8–17	8–16	6–16	6–15	5–15	
STElat (mm)							
Mean ± SD	13.0 ± 3.3	13.1 ± 2.9	12.8 ± 3.1	$12.1 \pm 3.1^{\ddagger}$	$11.8 \pm 3.3^{*,\ddagger}$	$11.1 \pm 3.2^{*,\ddagger,\S}$	<0.001
95% CI	7–19	7–19	7–19	6–18	5–18	5–17	
STEmid (mm)							
Mean ± SD	12.7 ± 2.6	13.0 ± 2.4	12.7 ± 2.5	$12.0 \pm 2.5^{\ddagger}$	$11.5 \pm 2.5^{*,\ddagger,\S}$	$10.7 \pm 2.4^{*,\ddagger,\S,\#}$	<0.001
95% CI	8–18	8–18	8–18	7–17	7–16	6–15	
nSTEmid (%)							
Mean ± SD	15.2 ± 3.0	15.7 ± 3.0	15.3 ± 3.1	$14.4 \pm 3.4^{\ddagger}$	$14.0 \pm 3.1^{*,\ddagger,\S}$	$13.6 \pm 3.0^{*,\ddagger,\S}$	<0.001
95% CI	9–21	10–22	9–21	8–21	8–20	8–19	

P-value, differences among age groups. $^{*}P < 0.05$ vs. 18–29 years. $^{\ddagger}P < 0.05$ vs. 30–39 years. $^{\S}P < 0.05$ vs. 40–49 years. $^{\#}P < 0.05$ vs. 50–59 years. Abbreviations as per *Table 2*.

restricted cubic spline analysis showed that each MAPSE parameter measured using 2D-STE was negatively associated with systolic BP and heart rate after adjusting for potential confounders (see Supplementary data online, *Figure S1*). Participants with optimal BP (<120/80 mmHg) had a higher MAPSE measured by 2D-STE than those with non-optimal BP (≥120/80 and <140/90 mmHg; $P < 0.05$; see Supplementary data online, *Figure S2*).

Correlation of MAPSE and LV GLS

LV GLS using all three apical views with optimal image quality was obtained in 1683 participants (86.2%). LV GLS was positively correlated with Msep ($r = 0.08$; $P = 0.002$), Mlat ($r = 0.15$; $P < 0.001$), STEsep ($r = 0.31$; $P < 0.001$), STElat ($r = 0.30$; $P < 0.001$), STEmid ($r = 0.35$; $P < 0.001$), and nSTEmid ($r = 0.38$; $P < 0.001$; see Supplementary data online, *Figure S3*). Of these, nSTEmid showed the highest correlation with GLS.

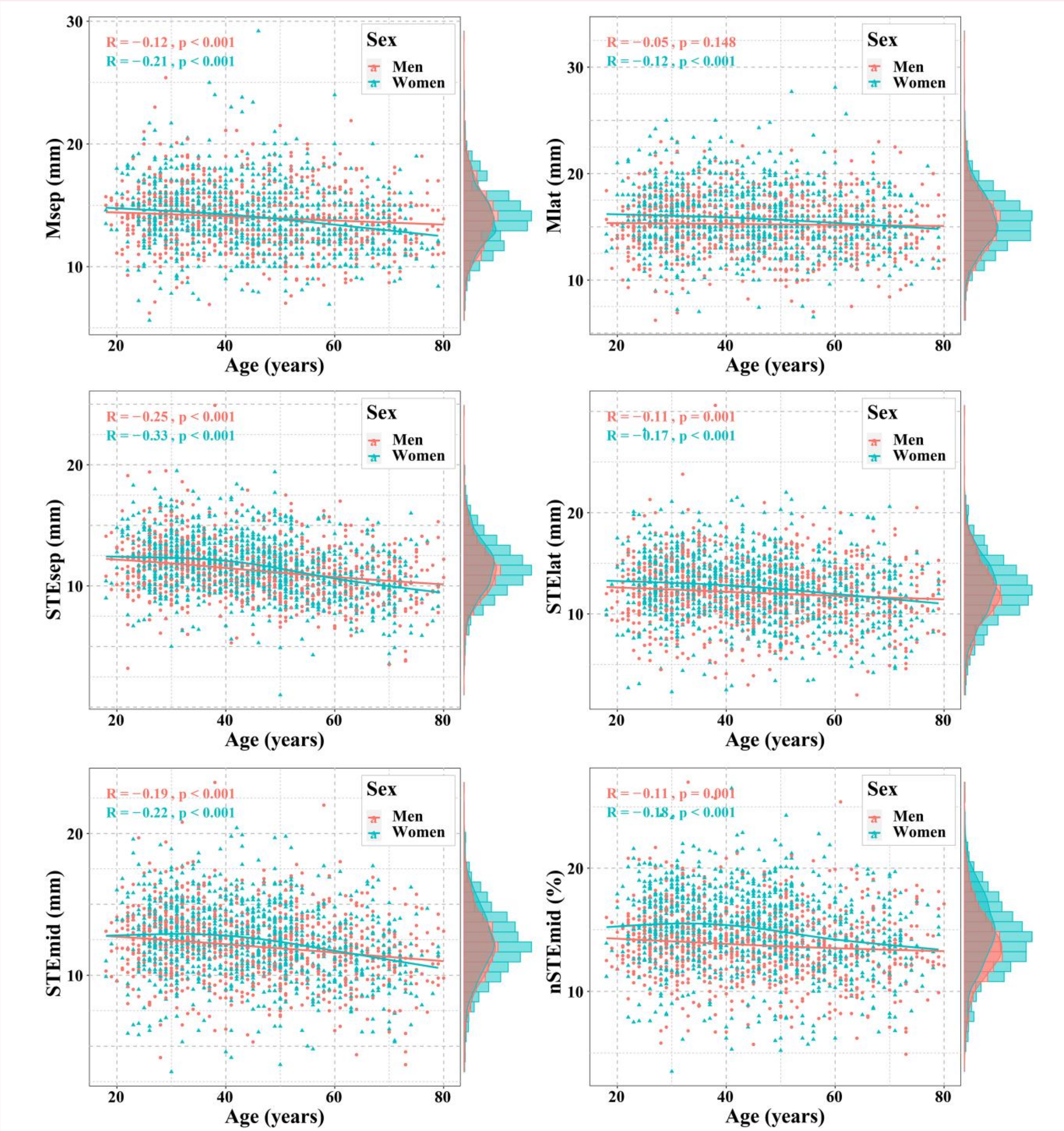


Figure 2 Scatter plot showing the correlations between MAPSE and age stratified by sex.

Measurement reproducibility

Both M-mode echocardiography and 2D-STE demonstrated high intra- and inter-observer reproducibility for MAPSE measurements (see Supplementary data online, *Table S2*). The intra-observer CVs for Msep, Mlat, STEsep, STElat, STEmid, and nSTEmid were 4.3, 7.9, 6.8, 8.5, 5.2, and 5.6%, respectively. The inter-observer CVs for Msep, Mlat, STEsep, STElat, STEmid, and nSTEmid were 6.4, 8.5, 7.2, 9.4, 9.4, and 9.8%, respectively.

Discussion

The present study revealed three significant findings. First, the universal normal values of MAPSE measured using M-mode echocardiography and 2D-STE were established using a large, multicentre, nationwide, prospective, observational, and cross-sectional study with a wide age range. Second, women had marginally higher MAPSE values than men, and older individuals tended to have lower MAPSE values than younger individuals, underscoring the importance of contextualizing age and sex when using normal MAPSE values. Third, MAPSE on M-mode echocardiography correlated with age and sex, and MAPSE on 2D-STE correlated with age, sex, BP, heart rate, and LV volume. Normal values are useful for evaluating LV systolic function, especially in patients with poor image quality, and may further facilitate the use of MAPSE for routine clinical assessments. These principal determinants should be considered when assessing LV systolic function using MAPSE in individual patients.

MAPSE has proved to be a useful index for evaluating LV global systolic function.[5] The mitral annular plane moves towards the apex in the longitudinal direction, primarily from the contraction of the (sub-endocardial and sub-epicardial) longitudinal fibres of the LV wall during systole, while the position of the apex is relatively stationary. Thus, MAPSE can reflect the capacity of the LV global longitudinal shortening deformation (contraction). LV GLS is another excellent marker of the myocardial longitudinal function, which has been proved to be a sensitive index for evaluating slight myocardial abnormalities, especially in early disease stages.[3] However, similar to LVEF, optimal image quality is essential for the correct determination of GLS. In contrast, MAPSE measurement requires only visualization of the mitral annulus, which is possible in virtually all patients, without a delineation of the LV endocardial boundary. Thus, MAPSE has the inherent advantages of convenience, high reproducibility, and image quality independence. Therefore, MAPSE can be used as a simple and robust complementary index to GLS for evaluating LV subclinical systolic dysfunction, especially in patients with poor image quality. Moreover, MAPSE plays a significant role in the assessment of disease severity, differential diagnosis, risk stratification, and prognostic prediction for most cardiac diseases (heart failure, ischaemic heart disease, valvulopathy, and cardiomyopathies; see Supplementary data online, *Table S3*).

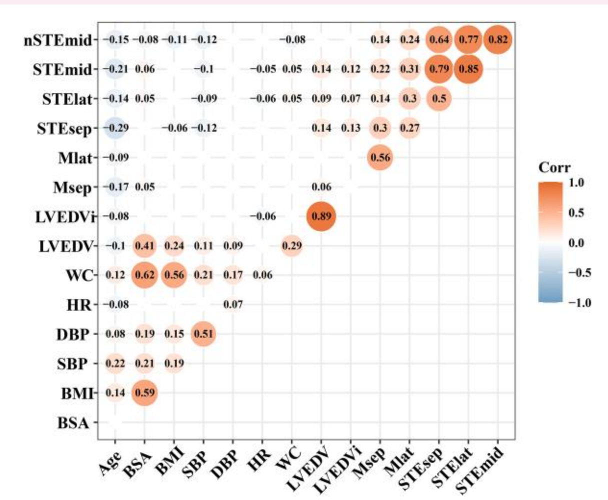


Figure 3 Correlation map showing the relationships between MAPSE and clinical characteristics. The red and blue bubbles, respectively, represent the positive and negative correlations, and the size and colour intensities of the bubbles represent the magnitude of correlation coefficients. Only the correlation with $P < 0.05$ is shown. BSA, body surface area; BMI, body mass index; DBP, diastolic blood pressure; HR, heart rate; SBP, systolic blood pressure; WC, waist circumferences; other abbreviations as per *Tables 2* and *4*.

Table 5 Advantages and disadvantages of MAPSE measured by M-mode and speckle tracking echocardiography

Technique	M-mode echocardiography	Speckle tracking echocardiography
Advantages		
	Less dependent on imaging quality	Less dependent on imaging quality
	Good reproducibility	Good reproducibility
	Easy to apply	Good correlation with GLS
	Less vendor or software dependent	Less angle dependent
		Able to measure MAPSE of the midpoint of the mitral annulus
Disadvantages		
	Angle dependent	Vendor and software dependent
	Unable to measure MAPSE of the midpoint of the mitral annulus	

GLS, global longitudinal strain.

Table 4 Multivariable analysis for determining MAPSE

Variables	M-mode echocardiography		Speckle tracking echocardiography			
	Msep	Mlat	STEsep	STElat	STEmid	nSTEmid
Age	−0.03 (<0.001)	−0.02 (<0.001)	−0.04 (<0.001)	−0.03 (<0.001)	−0.03 (<0.001)	−0.03 (<0.001)
BSA	0.52 (0.15)	0.19 (0.64)	0.22 (0.58)	0.93 (0.10)	0.66 (0.13)	−0.56 (0.31)
Body mass index	—	—	−0.05 (0.06)	−0.02 (0.53)	−0.04 (0.15)	−0.07 (0.06)
Systolic BP	—	—	−0.02 (0.004)	−0.03 (0.001)	−0.02 (0.001)	−0.02 (0.006)
Heart rate	—	—	−0.01 (0.05)	−0.02 (0.007)	−0.02 (0.01)	−0.02 (0.02)
LV EDV	0.004 (0.20)	0.004 (0.25)	0.02 (<0.001)	0.01 (0.007)	0.02 (<0.001)	−0.004 (0.29)

Values shown are partial regression coefficients (*P*-value).
EDV, end-diastolic volume; LV, left ventricular; other abbreviations as per *Tables 1* and *2*.

However, the implementation of MAPSE in routine clinical practice has been limited owing to the scarcity of direct large population-based normative data. In the HUNT study including 1266 healthy individuals, Støylen *et al.*[13] provided normal reference values for mean MAPSE and MAPSE normalized to LV length measured using M-mode echocardiography. However, mean MAPSE was obtained by calculating the average values of MAPSE in the two, four, and six points of mitral annuli using different apical views, and MAPSE values calculated directly at the mitral annulus site were not provided. To capitalize on the simplicity and feasibility of M-mode echocardiography, the present study established direct normal ranges for MAPSE in the septal and lateral mitral annuli. Additionally, considering the advantages and disadvantages of both M-mode echocardiography and 2D-STE, this study further established the normal range of MAPSE measured using 2D-STE. This will provide a more comprehensive reference cut-off value of MAPSE for clinical applications.

MAPSE measurement techniques

Current techniques for measuring MAPSE include M-mode echocardiography, tissue Doppler imaging, and 2D-STE.[14,15] Among these techniques, tissue Doppler imaging has been rarely used because of its angle dependence and relatively poor stability, which does not reflect the actual mitral annulus displacement. Although M-mode echocardiography is also subject to the angle between the ultrasound beam and the direction of motion of the mitral annulus, it is more readily implemented in daily clinical practice. In contrast, 2D-STE is angle independent and can accurately measure MAPSE.[7,16] Moreover, 2D-STE can obtain MAPSE at the midpoint of the mitral annulus, which represents the mean level of MAPSE and better reflects LV global longitudinal function. Our findings also confirmed that in contrast to Msep and Mlat, MAPSE measured using 2D-STE showed a greater coefficient of correlation with GLS, indicating that 2D-STE-based MAPSE may more sensitively reflect LV longitudinal function. Therefore, MAPSE measured using M-mode echocardiography or 2D-STE has both advantages and disadvantages (*Table 5*), and physicians can choose different measurement techniques to evaluate LV systolic function according to the situation by selecting the corresponding normal reference values and considering the principal determinants.

Correlation between MAPSE and GLS

We found a significant positive correlation between MAPSE and GLS ($r = 0.08–0.38$), and nSTEmid had the highest correlation with GLS. This indicates that as MAPSE values increase, there is a tendency for a corresponding increase in GLS values. Our review of the relevant literature demonstrated that similar results have been reported. Chiu *et al.*[16] reported a correlation coefficient of 0.61 in haemodialysis patients, and Wenzelburger *et al.*[17] reported a correlation coefficient of 0.43 in patients with heart failure with preserved ejection fraction. Notably, the reported correlation coefficients varied across different studies, which may be primarily attributed to factors such as differences in study populations. In particular, the range of MAPSE and GLS is narrow in the healthy population, while the range tends to be relatively wider in pathological conditions, which may lead to higher correlation coefficients. Furthermore, the software used for measuring GLS and the analysis of different MAPSE parameters may contribute to the observed differences in correlation coefficients.

Age- and sex-related differences in MAPSE

Our results revealed a marginal yet significant effect of sex on MAPSE, with higher MAPSE values in women than in men. Conversely, Støylen *et al.*[13] found that MAPSE measured by M-mode echocardiography was independent of sex. This discrepancy may be related to differences in race and ethnicity. Additionally, our research was based on MAPSE using M-mode echocardiography and 2D-STE, whereas their study used mean MAPSE in the four and six points of mitral annuli using M-mode echocardiography; this difference may have contributed to the inconsistency between results. Our results are also comparable with the findings of the WASE study, which demonstrated that men had relatively lower LVEF and GLS (absolute values) than women.[18] The potential mechanism may be related to hormones, which generate sex differences in cardiac contractility; however, the detailed mechanism remains to be elucidated.[19] Our results also showed that older individuals tend to have lower MAPSE values independent of sex, consistent with prior reports that illustrate stepwise reductions of GLS with advancing age.[20] The reduction in LV function may be the result of age-related myocardial apoptosis compounded by the increased fibrosis associated with ageing.[21]

Primary determinants of MAPSE for 2D-STE

We found that MAPSE measured using 2D-STE was inversely correlated with BP and heart rate in addition to age and sex, suggesting that BP and heart rate should be considered when detecting LV systolic dysfunction using MAPSE. This may also reflect the sensitivity of MAPSE measured using 2D-STE for evaluating slight changes in myocardial function from another perspective. Moreover, our results showed that STEsep, STElat, and STEmid were associated significantly and independently with LV volume. In other words, healthy participants with relatively larger LV volumes may have larger STEsep, STElat, and STEmid values than those with normal LV volumes, which may interfere with the accurate assessment of LV function. Moreover, nSTEmid was independent of LV size. Therefore, nSTEmid may be a more reliable index than the other MAPSE parameters in clinical practice, given that it has a relatively better correlation with GLS and fewer determinants, and may make the comparisons between individuals more objective.

Limitations

The major limitation of this study was the unequal distribution of participants despite attempts to recruit a proportional population, with balanced sex and age groups, as per the initial study design. Unfortunately, men and older individuals had more risk factors and were, therefore, more likely to be excluded, causing the unequal distribution. This was consistent with previous studies and the real clinical setting.[19]

Mitral valve annulus calcification may affect the measurement value of MAPSE; therefore, we excluded these patients to ensure the accuracy of the normal reference values. Thus, our findings may not apply to patients with mitral valve calcification. Moreover, professional sport activities have been shown to be associated with morphological and metabolic changes and physiologic remodelling in the heart.[22] Thus, we excluded individuals involved in professional sports to avoid any associated influences on MAPSE, which may have limited the generalizability of the results.

Moreover, while sonomicrometry is regarded as the gold standard for MAPSE measurement, it is invasive and, therefore, not applicable to this study. As a result, we could not compare our results with measurements based on the gold standard method. Additionally, because the study was based on measurements obtained using a software solution from a single vendor, the direct implementation of the reference range for MAPSE assessed using different software should be performed with caution.

Additionally, this study only included Chinese participants. Previous studies have shown subtle differences in subclinical myocardial functions across racial and ethnic groups with greater LV systolic myocardial strain among Chinese Americans.[23] Therefore, further research is needed to validate whether the reference range can be extrapolated to other racial and ethnic groups.

Notably, the narrow measurement range of MAPSE may increase the likelihood of errors when applying these reference values to a wide range of cardiac diseases in routine clinical practice. Therefore, physicians should consider clinical information when using MAPSE in their daily practice, aiming to minimize the potential errors to the greatest extent possible.

Conclusion

Normal reference values of MAPSE measured using M-mode echocardiography and 2D-STE were established according to age and sex. Blood pressure, heart rate, and LV volume are potential factors that influence MAPSE and should be considered in clinical practice. The normal values are useful for evaluating LV global systolic function, especially in patients whose LV GLS or EF cannot be measured accurately because of poor image quality, and may further facilitate the use of MAPSE in routine clinical assessments.

Supplementary data

Supplementary data are available at *European Heart Journal - Cardiovascular Imaging* online.

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Data availability

The data underlying this article will be shared upon reasonable request from the corresponding authors.

Appendix

The following hospitals (investigators) participated in this study: The First Hospital of Dalian Medical University (Tao Cong); Suining Central Hospital (Xiao-Yong Luo); Fengning Manchu Autonomous County Hospital (Dong-Sheng Zhao); Handan First Hospital (Shao-Bo Wang); The People's Hospital of Qinghai Province (Hai-Xia Sun); The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China (Dong-Mei Yang); Affiliated Hospital of Liaoning University of Traditional Chinese Medicine (Lin-Wei Hong); Urumqi Friendship Hospital (Bao-Ling Wang); Chengdu First People's Hospital (Xin-Yun Chen); The Affiliated Hospital of Inner Mongolia Medical University (Xiao-Shan Zhang); The First Affiliated Hospital of Jinzhou Medical University (Yu-Hong Li); The People's Hospital of Leshan (Ying Liu); The Second People's Hospital of Chengdu (Yun Shi); The People's Hospital of Chongzuo (Mei Li); The Second Hospital, Cheeloo College of Medicine, Shandong University (Yong-Mei Wang); The Affiliated Hospital of Southwest Medical University (Ji-Zhu Xia); The Affiliated Hospital of Youjiang Medical University for Nationalities (Cheng-Cai Chen); The Fourth Hospital of Hebei Medical University (Xiao-Hong Gong); The Second Affiliated Hospital of Shenyang Medical College (Wei Sun); Xingtai Third Hospital (Hong-Bing Peng); Shijiazhuang People's Hospital (Xiao-Qing Yang); Dandong Central Hospital (Xin Jin); Baicheng Central Hospital (Fan Zhang); Nanchong Central Hospital, The Second Clinical Medical College of North Sichuan Medical College (University) (Yan-Hua Li); The Third People's Hospital of Chengdu (Feng Xiong); Hunan Provincial People's Hospital, The First Affiliated Hospital of Hunan Normal University (Xiang-Dang Long); The Second Affiliated Hospital of Guangzhou University of Chinese Medicine (Peng-Tao Sun); Nanyang Second General Hospital (Xu-Meng Ding); Jiujiang University Affiliated Hospital (Xue-Hua Xiao); The First Affiliated Hospital of Hainan Medical College (En-Hai Zheng); Benxi Central Hospital (Xing-Bin Wang); Guang'an People's Hospital (Fang Yi); Guangxi International Zhuang Medicine Hospital (Min-Hua Chen); The First Affiliated Hospital of Xi'an Jiaotong University (Wen Wen); Yulin First People's Hospital (Hong-Xia Yin); Hospital of Chengdu University of Traditional Chinese Medicine (Yan Zhang); The Second Affiliated Hospital of Xi'an Jiaotong University (Qi Zhou); and Central Hospital Affiliated to Shenyang Medical College (Tong Zang).

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