Reference Values of Left and Right Atrial Volumes and Phasic Function based on A Large Sample of Healthy Chinese Adults: A Cardiovascular Magnetic Resonance Study

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Abstract

The left and right atrial (LA and RA) volumes and function are tightly linked to the morbidity and mortality of multiple cardiovascular diseases. We aimed to establish cardiovascular magnetic resonance (CMR) reference values for LA and RA volumes and phasic function based on a large sample of healthy Chinese adults. 408 validated healthy Chinese adults (54% men; aged 21–70 years) were included. The atrial volumes: maximum, minimum, and pre-atrial contraction ($V_{\max}$, $V_{\min}$, and V_{pac}); atrial phasic emptying fractions: total, passive, and booster (EF total, EF passive, and EF booster); atrial phasic emptying volumes: total, passive, and active (TEV, PEV, and AEV); and atrial expansion index (EI) were measured. Normal reference values were calculated and were stratified by sex (men and women) and age decades. The absolute LA and RA volumes and the indexed RA volumes were all greater in men. Women demonstrated higher LAEF total, LAEF booster, LAEI, RAEF total, RAEF passive, RAEF booster, and RAEI, while men had greater RATEV and RAAEV. Aging was positively correlated with the absolute and indexed LA and RA volumes, except for LA $V_{\max}$. LA and RA reservoir and conduit function including EF total, EI, EF passive, and PEV increased with age, while the atrial booster function (EF booster and AEV) decreased. We systematically provide age- and sex-specific CMR reference values for LA, RA volumes and phasic function based on a large sample of healthy Chinese adults with a wide age range. Both age and sex are closely associated with atrial volumes and function.

Introduction

The left and right atrium (LA and RA) play an integral role in modulating ventricular filling with its reservoir, conduit, and booster pump function [1–3]. It has been established that atrial volumes and function are closely related to the morbidity and mortality of multiple cardiovascular diseases, such as atrial fibrillation recurrence [4, 5], hypertrophic cardiomyopathy [6], heart failure [7], acute myocardial infarction [8], pulmonary hypertension [9], and congenital heart diseases [10]. Compared with traditional echocardiography, cardiovascular magnetic resonance (CMR) is well recognized as the “gold standard” method for assessing atrial structure and function, with higher accuracy and reproducibility [11–13].

Normal reference values are essential to differentiate between normal and pathological cardiovascular conditions. Evidence is available that there are significant racial differences in atrial size and function [14, 15], emphasizing the necessity of the establishment of ethnic-specific normal values for atrial structure and function. Although a few studies have reported normal reference values of LA and RA volumes and function for Chinese adults [16, 17], their provided parameters are less comprehensive and are based on limited sample size. In addition, age-related normal values have not been well provided in the Chinese population. Therefore, the present study aimed to systematically establish age- and sex-specific CMR reference values for LA, RA volumes and phasic function based on a large sample of healthy Chinese adults free of hypertension, diabetes, and obesity, and further investigate their associations with age and sex.

Materials And Methods

Study population

Our study population came from the local medical imaging and health screening institution, which aimed at the early detection of various diseases through systemic examinations, with cardiovascular disease screening being one of the key items. The main screening items included (1) baseline characteristics: age, sex, height, weight, exercise intensity, occupation, personal and family history, etc. (2) physical examination and electrocardiogram. (3) laboratory and biochemical tests: routine blood, urine, stool tests, and fasting blood glucose, insulin, lipid tests, and sex hormone tests, and thyroid, liver, kidney function tests, etc. (4) imaging examination: CMR, echocardiography, chest X-ray film or chest CT, magnetic resonance examination of brain, spine, and abdomen. All the examinations for individuals were completed within the same day and the diagnosis was performed by physicians with more than ten years' experience. The authors were authorized full access to all the subject information.

A total of 1,164 consecutive Chinese adults completed the above full-body screening package from January 1, 2013, to June 1, 2020, in the local health screening institution. From this pool of population, subjects who met the following exclusion criteria were excluded: (1) subjects with chief complaint or cardiovascular symptoms, abnormal electrocardiogram, abnormal findings of hypertrophic cardiomyopathy (defined as end-diastolic left ventricular (LV) wall thickness ≥ 15 mm in any left ventricular segment [18]), congenital heart diseases, valvular heart diseases (defined as observed dephasing jet), cardiac tumor, or known diseases may affect cardiac morphology and function, such as anemia, hyperthyroidism, gout, and major brain, lung, liver, and kidney diseases detected by comprehensive health screening; (2) subjects with hypertension (defined as blood pressure $\geq 140/90$ mmHg or use of antihypertensive medication according to the seventh Joint National Committee recommendation [19]), diabetes (defined as fasting blood glucose (FBG) ≥ 126 mg/dl or history of hypoglycemic medication), or obesity (defined as body mass index (BMI) ≥ 28 kg/m² for the Chinese populations [20]); (3) subjects with unqualified images affecting the assessment of atrial volumes, such as artifacts and incomplete or suboptimal presentation of LA contours in the 2- or 4-chamber views. The present study was approved by the local institutional review board and the requirement for subject consent was waived by the Chinese Ethics Committee (reference number: ChiECRCT20190198).

CMR protocol

CMR studies were performed on 1.5T magnetic resonance scanners (Signa HDxt, General Electric Medical Systems, Waukesha, WI, and Magnetom Essenza, Siemens, Erlangen, Germany) with 16-channel phased-array surface coil. Balanced steady-state free precession (SSFP) with breath-hold were used to acquire images in the supine position, comprising a stack of contiguous parallel short-axis slices covering the whole left and right ventricle from base to apex. Moreover, three long-axis slice (two-, three- and four-chamber views) images were also acquired. All the individuals were examined under a sinus rhythm.

The parameters of sequence for Signa HDxt, General Electric Medical Systems are as follows: repetition time = 4 ms, echo time = 1.75 ms, flip angle = 60°, field of view = 310 mm × 310 mm, matrix size = 224 ×

224. The scanning parameters for Magnetom Essenza, Siemens are as follows: repetition time = 4.38 ms, echo time = 1.37 ms, flip angle = 60°, field of view = 275 mm × 340 mm, matrix size = 224 × 256.

Volumetric analysis

Volumetric analysis was performed using commercial software (cvi42® version 5.12.1, Circle Cardiovascular Imaging, Canada). All the basic information about subjects (including age, sex, etc.) was hidden during image analysis. LA endocardial contours were manually traced in the 2- and 4-chamber views excluding pulmonary veins and the LA appendage. RA endocardial contours were tracked in the 4-chamber view, only. LA volumes and RA volumes were calculated using the previously validated biplane area-length and the single plane area-length method, respectively [21]. The maximum volume ($V_{\max}$), pre-atrial contraction volume (V_{pac}), and minimum volume ($V_{\min}$) for both LA and RA were assessed at ventricular end-systole, at ventricular diastole before atrial contraction, and at late ventricular diastole after atrial contraction, respectively (Fig. 1).

Phasic atrial emptying fraction (EF), emptying volume (EV), and expansion index (EI) were calculated to characterize reservoir, conduit, and booster pump phases of the atrial function [15, 22]:

Reservoir function:

- Total emptying fraction (EF total) = $V_{\max} - V_{\min} / V_{\max} \times 100$
- Total emptying volume (TEV) = $V_{\max} - V_{\min}$
- Expansion index (EI) = $\text{TEV} / V_{\min}$

Conduit function:

- Passive emptying fraction (EF passive) = $V_{\max} - V_{\text{pac}} / V_{\max} \times 100$
- Passive emptying volume (PEV) = $V_{\max} - V_{\text{pac}}$

Booster function:

- Booster emptying fraction (EF booster) = $V_{\text{pac}} - V_{\min} / V_{\text{pac}} \times 100$
- Active emptying volume (AEV) = $V_{\text{pac}} - V_{\min}$

All atrial volumes were indexed to body surface area (BSA). BSA was calculated using the Mosteller formula: $\text{BSA (m}^2\text{)} = (\text{height (cm)} \cdot \text{weight (kg)} / 3600)^{1/2}$.

Statistical analysis

All statistical analyses were performed using SPSS (version 26.0, IBM SPSS Inc, Chicago, IL, USA) and GraphPad Prism (version 8.0.2, La Jolla, CA). Normally distributed continuous variables are presented as mean ± standard deviation (SD) and non-normally distributed variables are expressed as median (interquartile range). Sex differences in demographic characteristics, atrial volumes, and phasic function parameters were compared using Student's *t*-test, or Mann-Whitney-U test where appropriate. The

subjects were stratified by sex (men and women) and age decade (21–30, 31–40, 41–50, 51–60, 61–70 years). The associations of atrial volumes and phasic function parameters with age were investigated using simple linear regression analysis. Intra- and inter-observer reproducibility were assessed in 30 randomly selected subjects using intraclass correlation coefficients (ICC) and Bland-Altman analyses. Differences were regarded as statistically significant at $p < 0.05$. All p values were two-sided.

Results

Demographic characteristics of subjects

In the total population of 1,164 subjects, 756 subjects were excluded, leaving 408 validated healthy Chinese adults (220 men, 44.4 ± 12.1 years). The baseline characteristics of the study population are shown in Table 1.

Table 1
Baseline characteristics of all the subjects and stratified according to gender

	Total (n = 408)	Men(n = 220)	Women (n = 188)	p-value
Age (years)	44.4 ± 12.1	43.5 ± 11.5	45.3 ± 12.8	0.128
BMI (kg/m ²)	23.3 ± 2.7	24.2 ± 2.4	22.3 ± 2.8	< 0.001
BSA (m ²)	1.72 ± 0.18	1.83 ± 0.15	1.59 ± 0.13	< 0.001
SBP (mmHg)	114.9 ± 13.5	118.2 ± 11.7	111.1 ± 14.5	< 0.001
DBP (mmHg)	70.8 ± 9.8	73.3 ± 9.6	67.7 ± 9.1	< 0.001
Heart rate (bpm)	65.6 ± 8.8	64.3 ± 8.6	67.1 ± 8.9	0.001
FBG (mmol/L)	5.26 ± 0.51	5.34 ± 0.50	5.17 ± 0.51	0.001
TC (mmol/L)	4.96 ± 0.88	5.00 ± 0.81	4.93 ± 0.95	0.419
TG (mmol/L)	1.11 (0.79–1.62)	1.31 (0.96–1.86)	0.90 (0.74–1.26)	< 0.001
HDL-C (mmol/L)	1.37 (1.16–1.67)	1.23 (1.08–1.47)	1.54 (1.30–1.88)	< 0.001
LDL-C (mmol/L)	2.84 ± 0.86	2.97 ± 0.81	2.69 ± 0.90	0.001
Values are presented as mean $\pm$ standard deviation; or median (interquartile range).				
p-values were obtained from the student' t text, or Wilcoxon rank sum test.				
<i>BMI</i> , body mass index; <i>BSA</i> , body surface area; <i>SBP</i> , systolic blood pressure; <i>DBP</i> , diastolic blood pressure; <i>FBG</i> , fasting blood glucose; <i>TC</i> , total cholesterol; <i>TG</i> , triglyceride; <i>HDL-C</i> , high-density lipoprotein cholesterol; <i>LDL-C</i> , low-density lipoprotein cholesterol.				

Effect of gender on LA, RA volumes and phasic function

The reference values of LA volumes and phasic function for both sexes are shown in Table 2. LA Vmax, LA Vmin, and LA Vpac in men were all greater than those in women (all $p < 0.01$). After indexing by BSA, LA Vmax and LA Vpac were greater for women (both $p < 0.05$), while no significant sex difference was observed in LA Vmin ($p = 0.618$). LAEF total and LAEF booster in women were higher than those in men (both $p < 0.001$), but LAEF passive showed no significant gender difference ($p = 0.404$). LATEV, LAPEV, and LAAEV were comparable between both sexes ($p = 0.157$, $p = 0.055$, and $p = 0.861$, respectively), while women had a significantly higher LAEI ($p < 0.001$).

Table 2

LA and RA volumes and phasic function parameters for all the subjects and stratified according to gender

	Total (n = 408)	Men (n = 220)	Women (n = 188)	p-value
LA parameters				
LA volume				
LA Vmax (mL)	63.3 ± 14.2	65.2 ± 14.6	61.0 ± 13.3	0.002
LA Vmin (mL)	24.8 ± 7.7	26.2 ± 7.3	23.1 ± 7.7	< 0.001
LA Vpac (mL)	40.7 ± 11.1	42.0 ± 10.9	39.1 ± 11.2	0.007
LA volume/BSA				
Indexed LA Vmax (mL/m ²)	36.9 ± 7.7	35.7 ± 7.5	38.4 ± 7.7	< 0.001
Indexed LA Vmin (mL/m ²)	14.4 ± 4.1	14.3 ± 3.8	14.5 ± 4.4	0.618
Indexed LA Vpac (mL/m ²)	23.7 ± 6.2	23.0 ± 5.8	24.6 ± 6.6	0.011
LA reservoir function				
LAEF total (%)	61.1 ± 6.2	60.0 ± 6.2	62.5 ± 5.9	< 0.001
LATEV (mL)	38.5 ± 8.6	39.1 ± 9.3	37.9 ± 7.6	0.157
LAEI (%)	1.6 ± 0.4	1.6 ± 0.4	1.7 ± 0.4	< 0.001
LA conduit function				
LAEF passive (%)	35.9 ± 8.3	35.6 ± 8.4	36.3 ± 8.2	0.404
LAPEV (mL)	22.6 ± 6.8	23.3 ± 7.4	21.9 ± 5.9	0.055
LA booster function				
LAEF booster (%)	39.1 ± 8.0	37.6 ± 7.9	40.9 ± 7.6	< 0.001
LAAEV (mL)	15.9 ± 5.4	15.9 ± 5.5	16.0 ± 5.2	0.861
RA parameters				
RA volume				
RA Vmax (mL)	58.6 ± 17.1	63.9 ± 17.5	52.4 ± 14.5	< 0.001
RA Vmin (mL)	29.7 ± 10.9	33.8 ± 11.2	24.9 ± 8.3	< 0.001

Data are presented as means ± SD. p-values were obtained from the student' *t* text.

LA, left atrial; RA, right atrial; Vmax, maximum volume; Vmin, minimum volume; Vpac, pre-atrial contraction volume; BSA, body surface area; EF, emptying fraction; TEV, total emptying volume; PEV, passive emptying volume; AEV, active emptying volume; EI, expansion index.

	Total (n = 408)	Men (n = 220)	Women (n = 188)	p-value
RA Vpac (mL)	45.1 ± 14.8	50.2 ± 15.0	39.1 ± 12.1	< 0.001
RA volume/BSA				
Indexed RA Vmax (mL/m ²)	34.0 ± 8.8	35.0 ± 9.2	32.9 ± 8.3	0.015
Indexed RA Vmin (mL/m ²)	17.1 ± 5.6	18.5 ± 6.0	15.5 ± 4.7	< 0.001
Indexed RA Vpac (mL/m ²)	26.1 ± 7.7	27.5 ± 8.0	24.5 ± 7.0	< 0.001
RA reservoir function				
RAEF total (%)	49.8 ± 9.3	47.4 ± 8.7	52.6 ± 9.3	< 0.001
RATEV (mL)	29.0 ± 9.3	30.2 ± 9.4	27.6 ± 8.9	0.005
RAEI (%)	1.1 ± 0.5	1.0 ± 0.4	1.2 ± 0.5	< 0.001
RA conduit function				
RAEF passive (%)	23.4 ± 9.7	21.6 ± 8.7	25.5 ± 10.3	< 0.001
RAPEV (mL)	13.6 ± 6.3	13.8 ± 6.3	13.3 ± 6.4	0.462
RA booster function				
RAEF booster (%)	34.3 ± 10.2	32.7 ± 9.7	36.1 ± 10.6	0.001
RAAEV (mL)	15.4 ± 6.9	16.4 ± 7.0	14.2 ± 6.5	0.002
Data are presented as means ± SD. p-values were obtained from the student' <i>t</i> text.				
LA, left atrial; RA, right atrial; Vmax, maximum volume; Vmin, minimum volume; Vpac, pre-atrial contraction volume; BSA, body surface area; EF, emptying fraction; TEV, total emptying volume; PEV, passive emptying volume; AEV, active emptying volume; EI, expansion index.				

The normal parameters of RA volumes and phasic function for men and women are presented in Table 2. The absolute and indexed RA Vmax, RA Vmin, and RA Vpac were all greater in men (all $p < 0.05$), while RAEFs (including RAEF total, RAEF passive, and RAEF booster) were higher in women (all $p \leq 0.001$). Men had significantly greater RATEV and RAAEV compared with women, but a lower RAEI (all $p < 0.01$). There was no significant sex difference in RAPEV ($p = 0.462$).

Age-related differences in atrial volumes and phasic function

LA, RA volumes and phasic function parameters by age decades for both sexes are shown in Tables 3 and 4. Simple linear regression analysis showed that age was positively correlated with the absolute and

indexed LA Vmin, LA Vpac, RA Vmax, RA Vmin, and RA Vpac (all $p < 0.05$), while there was no significant correlation between the absolute and indexed LA Vmax and age ($p = 0.463$ and $p = 0.165$).

Table 3

Normal values of LA volumes and phasic function parameters for men and women by age decile

	Men					Women				
	21– 30 years (n = 32)	31– 40 years (n = 65)	41– 50 years (n = 67)	51– 60 years (n = 35)	61– 70 years (n = 21)	21– 30 years (n = 28)	31– 40 years (n = 47)	41– 50 years (n = 49)	51– 60 years (n = 31)	61– 70 years (n = 33)
LA volume										
LA Vmax (mL)	64.6 ± 15.6	65.7 ± 14.3	65.7 ± 14.2	65.9 ± 16.6	62.3 ± 12.5	55.7 ± 8.6	60.3 ± 10.7	63.5 ± 15.5	59.9 ± 13.5	63.8 ± 15.3
LA Vmin (mL)	25.8 ± 8.2	25.6 ± 6.9	26.0 ± 7.0	28.2 ± 8.2	25.7 ± 6.3	19.1 ± 4.1	22.3 ± 6.5	24.5 ± 10.1	23.3 ± 6.2	25.5 ± 7.9
LA Vpac (mL)	38.9 ± 11.9	40.0 ± 9.8	42.2 ± 10.0	46.6 ± 12.4	44.6 ± 10.4	30.7 ± 7.4	36.8 ± 8.0	40.5 ± 12.7	40.4 ± 9.2	46.0 ± 12.2
LA volume/BSA										
Indexed LA Vmax (mL/m ²)	34.8 ± 7.5	35.8 ± 6.9	35.8 ± 7.6	35.9 ± 9.3	36.1 ± 6.7	35.8 ± 6.1	38.5 ± 6.4	39.6 ± 8.3	37.0 ± 7.6	39.9 ± 9.3
Indexed LA Vmin (mL/m ²)	13.8 ± 4.0	13.9 ± 3.5	14.2 ± 3.9	15.4 ± 4.4	14.8 ± 3.3	12.2 ± 2.7	14.1 ± 3.7	15.3 ± 5.4	14.4 ± 3.6	15.9 ± 4.9
Indexed LA Vpac (mL/m ²)	21.0 ± 6.1	21.8 ± 4.8	23.1 ± 5.5	25.4 ± 6.8	25.8 ± 5.2	19.8 ± 5.5	23.5 ± 4.8	25.3 ± 6.9	24.9 ± 5.2	28.7 ± 7.6
LA reservoir function										
LAEF total (%)	60.4 ± 6.2	61.1 ± 6.2	60.6 ± 5.3	57.1 ± 7.5	58.9 ± 5.4	65.9 ± 3.9	63.4 ± 6.9	61.9 ± 5.8	61.1 ± 5.2	60.3 ± 5.4
LATEV (mL)	38.8 ± 9.1	40.1 ± 9.6	39.7 ± 8.7	37.7 ± 10.9	36.6 ± 7.9	36.6 ± 5.7	38.0 ± 6.9	38.9 ± 7.5	36.6 ± 8.7	38.4 ± 8.8
LAEI (%)	1.6 ± 0.4	1.6 ± 0.4	1.6 ± 0.4	1.4 ± 0.5	1.5 ± 0.3	2.0 ± 0.4	1.8 ± 0.5	1.7 ± 0.4	1.6 ± 0.4	1.6 ± 0.4

LA, left atrial; Vmax, maximum volume; Vmin, minimum volume; Vpac, pre-atrial contraction volume; BSA, body surface area; EF, emptying fraction; TEV, total emptying volume; PEV, passive emptying volume; AEV, active emptying volume; EI, expansion index.

	Men				Women					
LA conduit function										
LAEF passive (%)	39.9 ± 10.4	39.0 ± 6.9	35.6 ± 6.8	29.4 ± 6.0	28.5 ± 6.8	45.3 ± 6.6	39.1 ± 5.3	36.5 ± 5.9	32.2 ± 7.8	28.1 ± 5.7
LAPEV (mL)	25.7 ± 8.2	25.6 ± 7.1	23.5 ± 6.9	19.3 ± 6.2	17.6 ± 5.1	25.1 ± 4.6	23.4 ± 4.7	22.9 ± 5.3	19.5 ± 7.3	17.9 ± 5.1
LA booster function										
LAEF booster (%)	33.3 ± 9.2	36.2 ± 7.8	38.7 ± 6.1	39.3 ± 8.9	42.3 ± 6.5	37.2 ± 8.0	40.0 ± 8.8	40.1 ± 6.3	42.4 ± 7.5	44.9 ± 5.6
LAAEV (mL)	13.1 ± 5.9	14.5 ± 4.7	16.3 ± 4.3	18.3 ± 6.6	19.0 ± 5.8	11.6 ± 4.6	14.6 ± 3.9	16.0 ± 3.9	17.1 ± 4.8	20.5 ± 5.5
LA, left atrial; Vmax, maximum volume; Vmin, minimum volume; Vpac, pre-atrial contraction volume; BSA, body surface area; EF, emptying fraction; TEV, total emptying volume; PEV, passive emptying volume; AEV, active emptying volume; EI, expansion index.										

Table 4

Normal values of RA volumes and phasic function parameters for men and women by age decile

	Men					Women				
	21– 30 years (n = 32)	31– 40 years (n = 65)	41– 50 years (n = 67)	51– 60 years (n = 35)	61– 70 years (n = 21)	21– 30 years (n = 28)	31– 40 years (n = 47)	41– 50 years (n = 49)	51– 60 years (n = 31)	61– 70 years (n = 33)
RA volume										
RA Vmax (mL)	57.5 ± 18.2	64.4 ± 15.1	64.7 ± 17.1	69.0 ± 22.8	61.3 ± 11.6	49.9 ± 12.7	49.2 ± 13.3	52.1 ± 15.7	53.6 ± 15.2	58.7 ± 13.8
RA Vmin (mL)	28.5 ± 10.5	34.2 ± 10.3	34.3 ± 10.1	37.6 ± 15.1	32.7 ± 9.1	21.5 ± 6.8	21.5 ± 7.3	25.9 ± 8.5	27.6 ± 8.1	28.6 ± 8.1
RA Vpac (mL)	42.0 ± 14.5	49.2 ± 12.5	51.6 ± 15.2	55.6 ± 18.6	51.9 ± 11.4	32.0 ± 9.4	34.5 ± 10.4	40.3 ± 12.3	42.2 ± 11.5	47.2 ± 10.7
RA volume/BSA										
Indexed RA Vmax (mL/m ²)	30.9 ± 9.4	35.1 ± 7.5	35.3 ± 8.8	37.6 ± 12.4	35.7 ± 7.4	31.7 ± 7.1	31.2 ± 7.0	32.4 ± 9.1	33.1 ± 8.8	36.6 ± 8.4
Indexed RA Vmin (mL/m ²)	15.2 ± 5.1	18.6 ± 5.3	18.7 ± 5.4	20.5 ± 8.1	19.1 ± 5.7	13.5 ± 3.6	13.6 ± 3.9	16.1 ± 4.8	17.1 ± 4.8	17.8 ± 4.7
Indexed RA Vpac (mL/m ²)	22.4 ± 7.1	26.8 ± 6.3	28.1 ± 7.9	30.3 ± 10.2	30.3 ± 7.0	20.3 ± 5.1	21.9 ± 5.8	25.0 ± 7.1	26.0 ± 6.5	29.5 ± 6.7
RA reservoir function										
RAEF total (%)	49.9 ± 9.1	47.4 ± 8.4	47.2 ± 8.7	45.7 ± 9.2	47.0 ± 7.8	57.0 ± 9.4	56.7 ± 8.1	50.0 ± 9.3	48.0 ± 8.4	51.2 ± 7.9
RATEV (mL)	29.0 ± 10.3	30.3 ± 8.0	30.5 ± 10.0	31.3 ± 11.8	28.5 ± 5.7	28.4 ± 8.4	27.7 ± 7.9	26.2 ± 9.7	26.0 ± 9.6	30.1 ± 8.8

RA, right atrial; Vmax, maximum volume; Vmin, minimum volume; Vpac, pre-atrial contraction volume; BSA, body surface area; EF, emptying fraction; TEV, total emptying volume; PEV, passive emptying volume; AEV, active emptying volume; EI, expansion index.

	Men					Women				
RAEI (%)	1.1 ± 0.4	1.0 ± 0.4	1.0 ± 0.5	0.9 ± 0.3	0.9 ± 0.3	1.5 ± 0.6	1.4 ± 0.5	1.1 ± 0.4	1.0 ± 0.3	1.1 ± 0.3
RA conduit function										
RAEF passive (%)	26.4 ± 10.8	23.7 ± 7.5	20.4 ± 8.2	19.3 ± 7.7	15.5 ± 7.0	35.7 ± 11.8	30.3 ± 8.4	22.7 ± 7.4	20.7 ± 6.2	18.7 ± 8.7
RAPEV (mL)	15.5 ± 7.1	15.2 ± 5.8	13.2 ± 6.2	13.3 ± 6.6	9.4 ± 4.1	17.9 ± 7.9	14.7 ± 5.4	11.8 ± 5.6	11.4 ± 5.0	11.5 ± 6.4
RA booster function										
RAEF booster (%)	31.7 ± 9.8	31.1 ± 9.2	33.4 ± 9.8	32.6 ± 10.3	37.2 ± 8.7	32.8 ± 10.3	37.7 ± 9.9	35.2 ± 11.2	34.4 ± 9.1	39.4 ± 11.3
RAAEV (mL)	13.5 ± 6.4	15.1 ± 5.3	17.3 ± 7.8	18.0 ± 8.2	19.2 ± 5.6	10.5 ± 5.1	13.0 ± 4.9	14.4 ± 6.8	14.6 ± 6.2	18.6 ± 7.1
RA, right atrial; <i>Vmax</i> , maximum volume; <i>Vmin</i> , minimum volume; <i>Vpac</i> , pre-atrial contraction volume; <i>BSA</i> , body surface area; <i>EF</i> , emptying fraction; <i>TEV</i> , total emptying volume; <i>PEV</i> , passive emptying volume; <i>AEV</i> , active emptying volume; <i>EI</i> , expansion index.										

There was a significantly negative correlation between age and LA and RA reservoir function ($r = -0.19$, $r = -0.19$, $r = -0.16$, and $r = -0.17$ for LAEF total, LAEI, RAEF total, and RAEI, respectively; all $p < 0.001$), except for LATEV and RATEV ($p = 0.335$ and $p = 0.747$). Moreover, age was inversely related to LA and RA conduit function ($r = -0.57$, $r = -0.40$, $r = -0.42$, and $r = -0.28$ for LAEF passive, LAPEV, RAEF passive, and RAPEV, respectively; all $p \leq 0.001$), while was positively correlated with biatrial booster function ($r = 0.34$, $r = 0.43$, $r = 0.14$, and $r = 0.28$ for LAEF booster, LAAEV, RAEF booster, and RAAEV, respectively; all $p < 0.01$) (Table 5).

Table 5

Correlation between age and atrial parameters for all the subjects

	Left atrium		Right atrium	
Parameter	Correlation coefficient	p-value	Correlation coefficient	p-value
Atrial volume				
Vmax (mL)	0.036	0.463	0.113	0.022
Vmin (mL)	0.121	0.015	0.164	0.001
Vpac (mL)	0.293	< 0.001	0.25	< 0.001
Atrial volume/BSA				
Indexed Vmax (mL/m ²)	0.069	0.165	0.162	0.001
Indexed Vmin (mL/m ²)	0.159	0.001	0.221	< 0.001
Indexed Vpac (mL/m ²)	0.332	< 0.001	0.321	< 0.001
Reservoir function				
EF total (%)	-0.193	< 0.001	-0.163	0.001
TEV (mL)	-0.048	0.335	0.016	0.747
EI (%)	-0.194	< 0.001	-0.174	< 0.001
Conduit function				
EF passive (%)	-0.573	< 0.001	-0.422	< 0.001
PEV (mL)	-0.402	< 0.001	-0.277	< 0.001
Booster function				
EF booster (%)	0.336	< 0.001	0.142	0.004
AEV (mL)	0.434	< 0.001	0.278	< 0.001
<i>Vmax</i> , maximum volume; <i>Vmin</i> , minimum volume; <i>Vpac</i> , pre-atrial contraction volume; <i>BSA</i> , body surface area; <i>EF</i> , emptying fraction; <i>TEV</i> , total emptying volume; <i>PEV</i> , passive emptying volume; <i>AEV</i> , active emptying volume; <i>EI</i> , expansion index.				

Intra-observer and inter-observer reproducibility

Intra-observer and inter-observer reproducibility are presented in Table **S1**. and as Bland-Altman plots in Fig. 2 and Fig. 3. There were excellent intra- and inter-observer reproducibility with ICC of more than 0.85 in both LA and RA volumes.

Discussion

In this CMR study, we systematically established age- and sex-specific reference values for LA, RA volumes and phasic function based on a large sample of validated healthy Chinese adults free of hypertension, diabetes, and obesity. Moreover, we further confirmed that both sex and age had a considerable impact on atrial volumes and phasic function.

Comparison with previous studies

At present, although there are a few CMR studies on normal biatrial reference values for Chinese adults, this study still presents certain advantages by providing more comprehensive atrial volume and function parameters based on a significantly larger sample size. Specifically, compared with the present study, a study on 200 healthy Chinese volunteers by Zhuang *et al.* [17] reported comparable normal values of LA Vmax, LA Vmin, and RA Vmax, but significantly greater RA Vmin (29.7 ± 10.9 mL versus 53.52 ± 16.12 mL). However, they did not provide atrial phasic function parameters including EF, EV, and EI. In addition, another CMR study by Li *et al.* [16] reported similar normal reference values of biatrial Vmax, Vmin, Vpac, EF total, EF passive, and EF booster based on 135 healthy Chinese adults. However, their provided parameters were not further stratified by age. Finally, as definitive indicators of adverse atrial remodeling in the clinical scenario such as acute coronary syndrome [23, 24], information regarding normal values of atrial EV and EI has scarcely been reported. To the best of our knowledge, this is the first CMR study to establish age- and sex-specific normal values of atrial EV and EI in Chinese adults.

Previous multi-ethnic studies have confirmed that there are significant racial differences in atrial volumes and function, as described by the smaller atrial sizes and higher atrial function parameters for Asians compared with those for whites [14, 15]. Compared with several studies in western populations [11, 13, 21, 25], LA and RA volumetric parameters (including Vmax, Vmin, and Vpac) in the present study were smaller, while the phasic function parameters (including EF, EV, and EI) were slightly higher, which may confirm the racial difference in atrial volumes and function as well.

Gender differences in LA and RA volumes and phasic function

In general, men presented with higher absolute LA Vmax, LA Vmin, and LA Vpac than women, which was consistent with a few previous studies [26, 27]. Interestingly, we found that BSA-indexed LA Vmax and LA Vpac in women were significantly greater than those in men. Besides, we confirmed that LA phasic function was also affected by sex. Specifically, women showed higher LAEF total and LAEF booster than men, which was in accordance with the findings of Vasconcellos *et al.* [14]. In contrast, some other studies, such as those by Maceira *et al.* [13] and Truong *et al.* [26], did not observe these sex differences. Currently, there are still few studies on gender difference in LAEV and LAEI. Maceira *et al.* [13] reported that women presented with significantly smaller LAPEV and higher LAEI than men. Different from their study, we demonstrated that there was no significant sex difference in LATEV, LAPEV, and LAAEV, while women had a significantly higher LAEI.

For the right atrium, in line with several previous studies [15, 28], we demonstrated that the absolute and indexed RA Vmax, RA Vmin, and RA Vpac for men were all significantly greater than those for women. However, there are still considerable controversies about gender differences in RAEFs. For example, several studies showed that RAEF booster was not associated with gender [13, 15, 16]. In comparison, our study demonstrated that female sex was associated with greater RAEFs including RAEF total, RAEF passive, and RAEF booster, which was consistent with the findings from Peluso et al. [28]. We speculated that the differences in sample size, ethnicity, and baseline characteristics of subjects may together contribute to these inconsistencies among studies. Furthermore, we confirmed that men had significantly greater RATEV and RAAEV and a lower RAEI compared with women, while there was no significant sex difference in RAPEV, which was generally agree with the study by Maceira et al. [13].

Correlation between atrial volumes, phasic function, and age

It is controversial regarding the correlation between atrial volumes and age. For example, Petersen et al. [21] showed that aging was associated with decreased LA Vmax based on 804 Caucasian adults aged 45 to 74 years. A CMR study by Li et al. [16] in 135 healthy Chinese volunteers aged 49.9 ± 17.1 years showed that age was positively correlated with LA Vmax, LA Vmin, and LA Vpac. In line with the study by Van Grootel et al. [29], we found that age showed no significant correlation with LA Vmax, while was associated with increased LA Vmin and LA Vpac. Besides, with respect to the right atrium, most previous studies reported aging was associated with no change in or decreased RA Vmax [16, 21, 27]. In contrast, we demonstrated that age was positively correlated with all the RA volumetric parameters including RA Vmax, RA Vmin, and RA Vpac, even after normalized by BSA. These differences may be related to the narrow age range as well as the limited sample size in previous studies.

Our study demonstrated that age was a major determinant of biatrial phasic function, as found that the measurements of LA and RA reservoir and conduit function were decreased, whereas booster function was increased with advancing age. These findings further reinforced the previously described associations between age and atrial function [13, 15]. The observed age-related variations in atrial function were in accordance with physiologic knowledge. Normal aging is associated with loss of cardiomyocytes, myocardial fibrosis, and impaired ventricular relaxation, which may together contribute to the increased atrial booster function, decreased atrial reservoir and conduit function [30–32].

Limitations

There were several limitations in the present study. Firstly, normal reference values of elderly over 70 years old were not covered due to the limited healthy elderly population. In addition, this study is a single-ethnic, cross-sectional study, and the relationship between age, sex, and atrial parameters needs to be further verified by multi-ethnic, longitudinal studies.

Conclusion

The present study systematically provides age- and sex-specific CMR reference values for LA, RA volumes and phasic function based on a large sample of validated healthy Chinese adults. Both age and sex are closely associated with the majority of atrial volumes and function parameters. The establishment of normal values may facilitate the application of CMR to assess atrial structure and function in both clinical practice and research.

Declarations

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Author contributions

Yiyuan Gao and Zhen Zhang contributed to data acquisition, analysis, interpretation, drafting of manuscript, and revisions. Shanshan Zhou and Gengxiao Li contributed to data acquisition, analysis and interpretation. Mingwu Lou contributed to data interpretation, and study supervision. Zhiwei Zhao and Jun Zhao contributed to data acquisition and interpretation. Kuncheng Li contributed to study conception and design, data interpretation, manuscript revisions, and study supervision. Gerald M. Pohost contributed to study conception and design, and study supervision. All authors read and approved the final manuscript.

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Data availability

The datasets are available from the corresponding author on reasonable request.

Code availability

Not applicable.

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Figures

Figure 1

Example of atrial volumetric analysis in the 2- and 4-chamber views. Manual delineation of the atrial endocardial contours in end-systolic, pre-atrial contraction, and end-diastolic phase, respectively.

Figure 2

Bland-Altman plots for intra-observer and inter-observer reproducibility of LA V_{max} , LA V_{min} , and LA V_{pac} .

Figure 3

Bland-Altman plots for intra-observer and inter-observer reproducibility of RA Vmax, RA Vmin, and RA Vpac.

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