Received: 25 July 2019 | Revised: 4 October 2019 | Accepted: 25 October 2019

DOI: 10.1002/jcu.22795

RESEARCH ARTICLE

WILEY

Normal reference values of three-dimensional speckle-tracking echocardiography-derived right atrial volumes and volume-based functional properties in healthy adults (Insights from the MAGYAR-Healthy Study)

Attila Nemes MD, PhD, DSc, FESC[1] | **Árpád Kormányos MD[1]** | **Péter Domsik MD, PhD[1]** | **Anita Kalapos MD, PhD[1]** | **Nóra Ambrus MD, PhD[1]** | **Csaba Lengyel MD, PhD[2]**

[1]2nd Department of Medicine and Cardiology Centre, Medical Faculty, Albert Szent-Györgyi Clinical Center, University of Szeged, Szeged, Hungary

[2]1st Department of Medicine, Medical Faculty, Albert Szent-Györgyi Clinical Center, University of Szeged, Szeged, Hungary

Correspondence
Attila Nemes, MD, PhD, DSc, FESC, 2nd Department of Medicine and Cardiology Center, Medical Faculty, Albert Szent-Györgyi Clinical Center, University of Szeged, H-6725 Szeged, Semmelweis Street 8, P.O. Box 427, Szeged, Hungary.
Email: nemes.attila@med.u-szeged.hu

Abstract

Introduction: The right atrium (RA) roles include being a systolic reservoir, an early diastolic conduit, and a late-diastolic booster pump. The present study aimed to assess normal reference values of three-dimensional speckle-tracking echocardiography (3DSTE)-derived RA volumetric data and volume-based functional properties in healthy adult subjects.

Methods: We included 260 healthy adult subjects in sinus rhythm with complete clinical and demographic dataset, but excluded 110 of them because of inferior image quality. The remaining population sample comprised 150 subjects (31.0 ± 11.6 years, 79 males). Complete two-dimensional Doppler echocardiography and 3DSTE have been performed in all subjects.

Results: Systolic RA volumetric variables did not show changes over time, but after 50 years, a significant reduction could be demonstrated in RA stroke volume and emptying fraction. While early diastolic RA volume increased over time, RA stroke volume and emptying fraction decreased. While late-diastolic RA volume increased over age decades, similar increase could be detected in RA stroke volume but a reduction occurred in older ages. Late-diastolic RA emptying fraction showed an increasing (after the 40s)—decreasing (after the 50s) pattern.

Conclusions: Our study provides normal reference values of 3DSTE-derived RA volumes and volume-based functional properties and their age- and gender dependency in healthy adult subjects.

KEYWORDS

echocardiography, healthy subjects, right atrium, speckle-tracking, three-dimensional

1 | INTRODUCTION

The right atrium (RA) is an important part of the right heart, loaded by the caval veins and the coronary sinus and communicating with the right ventricle (RV) via the tricuspid annulus.[1,2] It serves as a reservoir in systole, is a conduit in early diastole, and is a booster pump in late diastole.[1,2] Due to novel opportunities of treatment of right heart diseases, there is an increased focus on accurate assessment of right heart chambers, including the RA. Three-dimensional speckle-tracking echocardiography (3DSTE) is a novel, validated clinical tool with capability of 3D assessment of atria.[3-6] By using 3D virtual atrial models, volumetric and functional variables can be assessed simultaneously.[7,8] However, limited information is available regarding the 3DSTE-derived volumetric variables in the literature, including their normal values. The present study aimed to determine normal reference values of 3DSTE-derived RA volumetric data and volume-based functional properties in healthy adult subjects.

2 | PATIENTS AND METHODS

2.1 | Study population

We included 260 healthy adult subjects in sinus rhythm with complete clinical and demographic dataset, but we excluded 110 of them because of inadequate image quality. The remaining 150 subjects undergone complete two-dimensional (2D) Doppler echocardiography and 3DSTE. Subjects had no history of cardiovascular symptoms or known disorders. None of them received any medication, while physical examination, electrocardiography and echocardiography proved to be normal in all cases. The present study is a part of MAGYAR-Healthy Study (Motion Analysis of the heart and Great vessels by three-dimension AI speckle-tracking echocardiography in Healthy subjects). This study was created to determine normal values of 3DSTE-derived parameters in healthy adults among others ('magyar' means 'Hungarian' in Hungarian language). All subjects gave informed consent. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the institution's human research committee.

2.2 | 2D echocardiography

An Artida echocardiography equipment (Toshiba Medical Systems, Tokyo, Japan) with a PST-30SBP (1-5 MHz) phased-array transducer was used for standard examination of heart chambers.[3-6] Left ventricle (LV) dimensions, volumes, and ejection fraction, and atrial dimensions were measured according to the guidelines.[9] Doppler echocardiography was used for visual quantification of valvular regurgitations and to exclude valvular stenoses.

2.3 | Three-dimensional speckle-tracking echocardiography

3DSTE analysis was performed using the same echocardiography machine. During data acquisitions using a 1 to 4 MHz matrix phased-array transducer (PST-25SX), six sub-volumes were collected digitally from an apical window within a single breath-hold, from which the software created a pyramid-shaped volume dataset.[3-6] RA measurements were performed on RA-focused volumes. We used 3D Wall Motion Tracking software version 2.7 (Toshiba Medical Systems) for RA volumetric quantification.[8] Acquired 3D echocardiographic datasets were then displayed in apical two- (AP2CH) and four-chamber (AP4CH) views and three short-axis views at different RA levels (basal, mid-atrial, superior). After definition of several reference points on the RA endocardium in AP2CH and AP4CH views (edges of tricuspid annular ring and RA apex) at end-diastole, automatic reconstruction was started to define complete endocardial RA surface. From these reconstructed volumes, a 3D RA cast was created for volumetric analysis (Figure 1).[8] Several RA volumes were obtained along the cardiac cycle:

- Maximum RA volume, measured at end-systole, just before tricuspid valve opening (V_{max}).
- RA volume before atrial contraction, measured at early-diastole at the time of P wave on ECG (V_{preA}).
- Minimum RA volume measured at end-diastole, just before mitral valve closure (V_{min}).

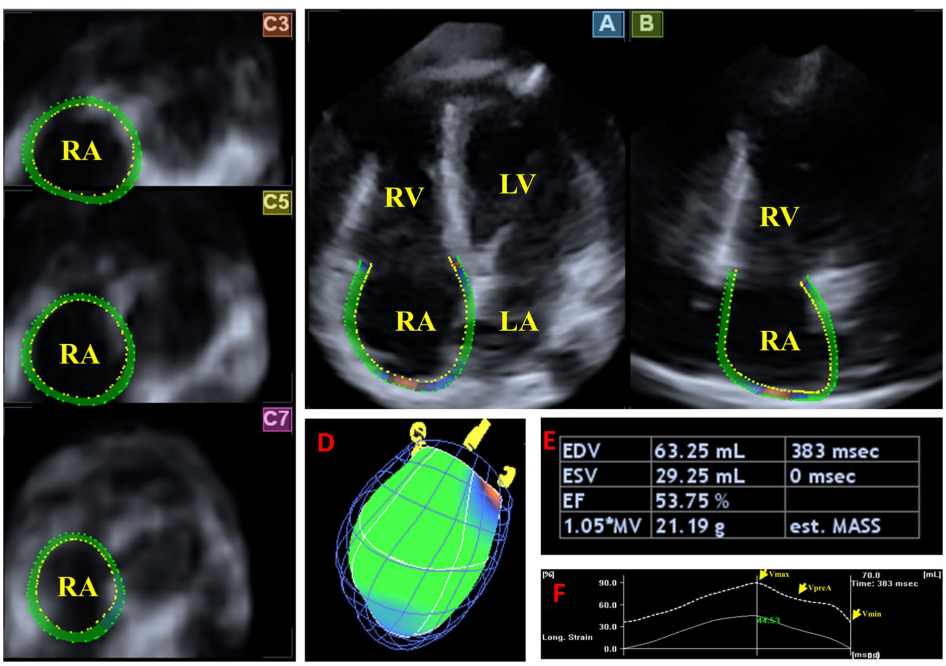

FIGURE 1 Images from three-dimensional (3D) echocardiographic full-volume dataset demonstrating the right atrium (RA) in a healthy subject: A, apical four-chamber view; B, apical two-chamber view; C3, short-axis views at basal; C5, mid-atrial; and C7, superior RA level. D, Virtual 3D model of the RA; E, calculated RA volumetric variables and F, RA volume changes over time (dashed line) based on 3D speckle-tracking echocardiographic analysis are also presented. EDV, maximum volume end-diastolic minimum RA volume; EF, ejection fraction; MV, estimated mass; ESV, minimum volume end-systolic maximum RA volume; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle

From these RA volumes, the following RA stroke volumes (SV) and RA emptying fractions (EF) were calculated to characterize reservoir, conduit, and active contraction phases of the RA function[8]:

Reservoir function:

- Total Atrial Stroke Volume (TASV): $V_{max} - V_{min}$.
- Total Atrial Emptying Fraction (TAEF): TASV/V_{max} × 100.

Conduit function:

- Passive Atrial Stroke Volume (PASV): $V_{max} - V_{preA}$.
- Passive Atrial Emptying Fraction (PAEF): PASV/V_{max} × 100.

Active contraction:

- Active Atrial Stroke Volume (AASV): $V_{preA} - V_{min}$.
- Active Atrial Emptying Fraction (AAEF): AASV/V_{preA} × 100.

2.4 | Statistical analysis

All data are reported as mean ± *SD* or number and percentages. All values were considered significantly different at $P < .05$. Student *t* test was used to compare continuous variables. Statistical calculations were performed using MedCalc software (MedCalc, Mariakerke, Belgium).

TABLE 1 Clinical, two-dimensional, and volumetric three-dimensional speckle-tracking echocardiographic data of healthy subjects

	Data
n	150
Age (years)	31.0 ± 11.6
Male gender (%)	79 (53)
Weight (kg)	69.5 ± 14.1
Height (m)	172.2 ± 9.9
Body surface area (kg/m^2)	1.84 ± 0.24
Two-dimensional echocardiography	
Left atrium (mm)	36.1 ± 4.0
Left ventricular end-diastolic diameter (mm)	48.0 ± 3.7
Left ventricular end-diastolic volume (mL)	105.6 ± 22.8
Left ventricular end-systolic diameter (mm)	34.5 ± 12.4
Left ventricular end-systolic volume (mL)	36.0 ± 9.0
Interventricular septum (mm)	8.92 ± 1.63
Left ventricular posterior wall (mm)	9.06 ± 1.68
Left ventricular ejection fraction (%)	66.0 ± 4.9
E (cm/s)	82.7 ± 16.3
A (cm/s)	64.4 ± 19.6

3 | RESULTS

3.1 | Demographic data

Baseline demographic data of healthy adult subjects are presented in Table 1. The 150 healthy volunteers were assigned to the following groups depending on their age: 18 to 29 years (n = 90; mean age: 23.5 ± 2.9 years, 47 males), 30 to 39 years (n = 32; mean age: 34.0 ± 2.9 years, 23 males), 40 to 49 years (n = 11; mean age: 42.9 ± 2.7 years, 4 males), and >50 years (n = 17, mean age: 57.2 ± 5.4 years, 5 males). The mean heart rate of subjects was in the normal range (73 ± 8 bpm).

3.2 | 2D echocardiographic data

Routine 2D Doppler echocardiographic variables are presented in Table 1. None of the healthy adult cases showed ≥ grade 1 valvular regurgitations or had significant valvular stenosis.

3.3 | Changes in 3DSTE-derived RA volumes over age decades

While end-systolic V_{max} did not change over age decades, early and end-diastolic V_{preA} and V_{min} increased over time. Significantly larger values could be detected in healthy subjects >50 year old than in younger subjects (Table 2, Figure 2). The rate of volume acquisition for 3DSTE-derived measurements was 25 ± 2 volumes per second.

3.4 | 3DSTE-derived changes in RA stroke volumes over age decades

TASV remained almost unchanged over age decades until 50 years, after which it showed a significant reduction. PASV showed a continuous reduction over age decades and exhibited significant difference between subjects aged 18 to 29 years and >50 years. AASV increased over age decades until 50 years, after which it showed a reduction (Table 2, Figure 3).

3.5 | 3DSTE-derived changes in RA emptying fractions over age decades

TAEF did not show any changes over age decades, but a significant reduction could be demonstrated in subjects aged >50 years. PAEF showed significant continuous reduction over age decades. AAEF did not change in younger ages, reached its highest values at ages 40 to 49 years, then decreased significantly after 50 years (Table 2, Figure 4).

3.6 | Gender differences in 3DSTE-derived RA parameters

Males had nonsignificantly higher RA volumes than females along the cardiac cycle regardless of their age. No significant differences could

TABLE 2 Age-dependency of three-dimensional speckle-tracking echocardiography-derived right atrial volumes and volume-based functional properties

	All (n = 150)	Aged 18-29 years (n = 90)	Aged 30-39 years (n = 32)	Aged 40-49 years (n = 11)	Aged >50 years (n = 17)
RA volumetric data					
V_{max} (mL)	46.8 ± 14.7	46.6 ± 15.8	47.0 ± 15.4	48.0 ± 6.4	46.1 ± 11.9
V_{max}-indexed (mL)	25.5 ± 8.1	26.0 ± 9.0	23.7 ± 6.8	27.0 ± 4.0	25.3 ± 7.2
V_{preA} (mL)	33.3 ± 11.3	31.6 ± 12.0	34.4 ± 10.4	36.7 ± 7.1	38.2 ± 10.6[a]
V_{preA}-indexed (mL)	18.1 ± 5.8	17.5 ± 6.3	17.3 ± 4.5	20.5 ± 3.4[b]	20.7 ± 5.2[a,b]
V_{min} (mL)	26.0 ± 10.0	24.8 ± 10.3	27.2 ± 10.0	26.1 ± 7.4	30.5 ± 9.8[a]
V_{min}-indexed (mL)	14.1 ± 5.0	13.7 ± 5.4	13.6 ± 4.5	14.4 ± 3.0	16.5 ± 5.0[a,b]
RA volume-based functional properties					
TASV (mL)	20.7 ± 9.3	21.9 ± 9.7	19.8 ± 8.8	21.9 ± 6.6	15.6 ± 8.8[a,c]
TASV-indexed (mL)	11.4 ± 5.5	12.3 ± 5.8	10.1 ± 4.4	12.6 ± 4.6	8.7 ± 5.4[a]
PASV (mL)	13.4 ± 7.8	15.0 ± 7.5	12.6 ± 8.4	11.3 ± 3.7	7.9 ± 8.3[a]
PASV-indexed (mL)	7.4 ± 4.5	8.5 ± 4.5	6.5 ± 4.1	6.5 ± 2.4	4.6 ± 5.1[a]
AASV (mL)	7.3 ± 4.4	6.9 ± 4.7	7.2 ± 3.5	10.6 ± 4.6[a,b]	7.7 ± 4.3
AASV-indexed (mL)	4.0 ± 2.5	3.8 ± 2.6	3.7 ± 1.7	6.1 ± 3.0[a,b]	4.2 ± 2.3
TAEF (%)	44.2 ± 13.3	46.8 ± 12.7	42.3 ± 12.4	45.8 ± 12.2	33.2 ± 14.1[a,b,c]
TAEF-indexed (%)	24.8 ± 9.9	26.8 ± 10.2	22.0 ± 12.4	26.2 ± 8.6	18.6 ± 8.8[a,c]
PAEF (%)	28.3 ± 12.5	32.1 ± 11.4	25.8 ± 11.9[a]	23.9 ± 7.4[a]	16.1 ± 13.4[a,b]
PAEF-indexed (%)	16.0 ± 8.5	18.4 ± 8.5	13.5 ± 7.2[a]	13.7 ± 4.8	9.2 ± 8.2[a]
AAEF (%)	22.4 ± 11.4	22.0 ± 11.6	22.2 ± 11.3	29.1 ± 12.1	20.4 ± 10.0[c]
AAEF-indexed (%)	12.5 ± 7.1	12.6 ± 7.4	11.6 ± 6.4[c]	16.7 ± 7.9	11.3 ± 5.8[c]

Abbreviations: AAEF, active RA emptying fraction; AASV, active RA stroke volume; PASV, passive RA stroke volume; PASV, early diastolic passive RA stroke volume; RA, right atrium; TAEF, total RA emptying fraction; TASV, total RA stroke volume; V_{max}, end-systolic maximum RA volume; V_{min}, end-diastolic minimum RA volume; V_{preA}, early diastolic pre-atrial contraction RA volume.

[a]$P < .05$ vs Aged 18-29 years.

[b]$P < .05$ vs Aged 30-39 years.

[c]$P < .05$ vs Aged 40-49 years.

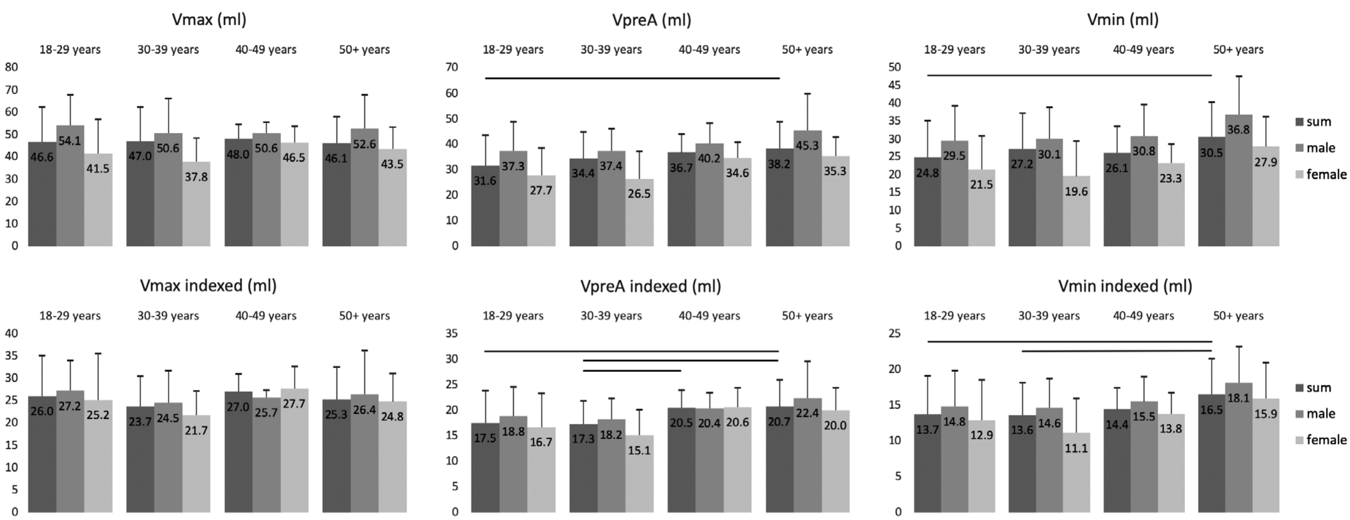

FIGURE 2 Gender-dependency of nonindexed and indexed right atrial volumes over age decades as assessed by three-dimensional speckle-tracking echocardiography. Lines represent significant differences between the groups. V_{max}, end-systolic maximum RA volume; V_{min}, end-diastolic minimum RA volume; V_{preA}, early diastolic pre-atrial contraction RA volume

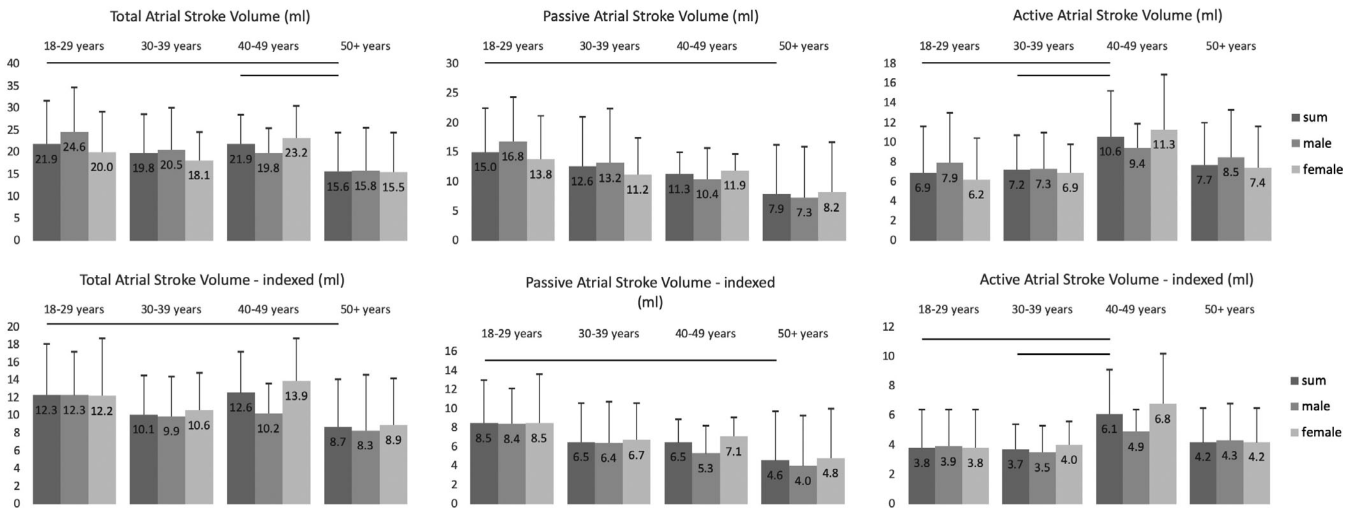

FIGURE 3 Gender-dependency of right atrial stroke volumes over age decades as assessed by three-dimensional speckle-tracking echocardiography. Lines represent significant differences between the groups

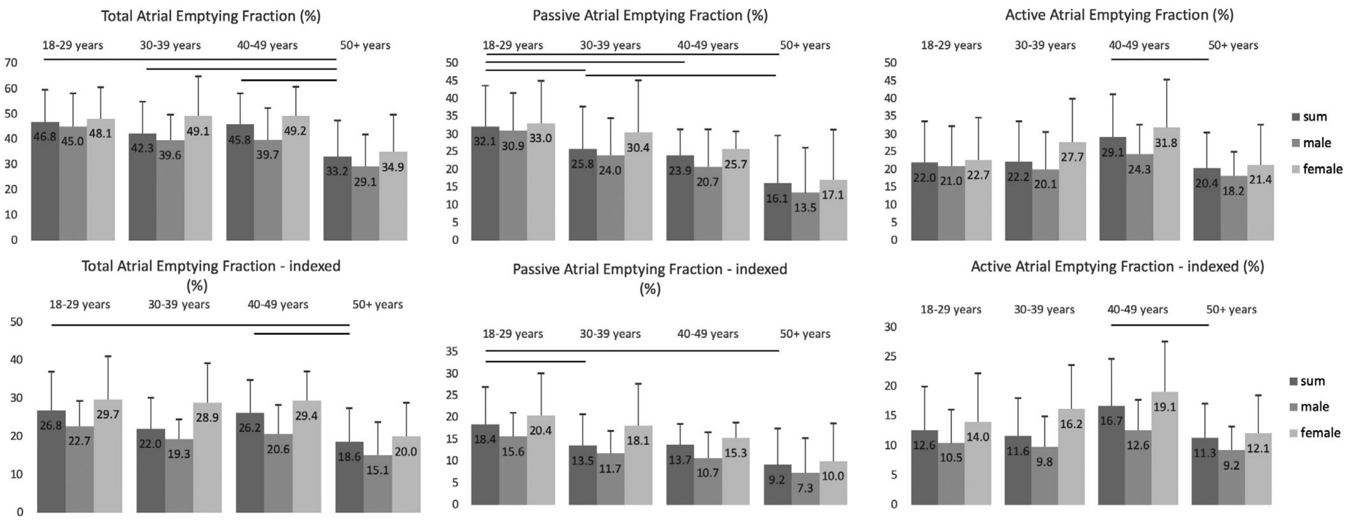

FIGURE 4 Gender-dependency of nonindexed and indexed right atrial emptying fractions over age decades as assessed by three-dimensional speckle-tracking echocardiography. Lines represent significant differences between the groups

be demonstrated between RA stroke volumes between genders except in the 40 to 49 years age range when females had nonsignificantly higher values. RA emptying fractions were nonsignificantly higher in females than in males regardless of age (Figures 2–4).

4 | DISCUSSION

To the best of our knowledge, this is the first study to define normal reference values of 3DSTE-derived RA volumes and volume-based functional properties and their age- and gender-dependency in healthy adult subjects. Systolic RA volumetric parameters did not show changes over time until 50 years, but a significant reduction could be demonstrated in RA stroke volume and emptying fraction afterward. While early diastolic RA volume and emptying fraction increased over time, RA stroke volume decreased. While late-diastolic RA volume increased over age decades, similar increase could be detected in RA stroke volume followed by a significant reduction in older ages. Late-diastolic RA emptying fraction showed an increasing (after the 40s)—decreasing (after the 50s) pattern. These results suggest special changes of RA volumes and volume-based functional properties over age decades.

There are limited opportunities featuring RA morphology in the routine clinical practice.[1,2,9,10] According to recent guidelines, RA diameters and areas are suggested to be measured in AP4CH view when they are the largest at end-systole.[1,10] Theoretically, 2D echocardiography-based volumetric measurements are possible using RA area and length data, but literature data based on clinical results are limited.[9,10] Moreover, 2DSTE can also be performed for RA quantifications.[2] The newly developed and just clinically spreading 3DSTE seems to be an optimal and reliable tool for this sort of detailed assessment due to its noninvasiveness and ability for 3D volumetric and functional evaluation at the same time from the same virtual 3D atrial cast.[3-6] Functional assessment may involve calculation of RA volume-based functional properties and strain variables. In recent studies, detailed disease-related 3DSTE-derived RA volumetric and functional abnormalities were suggested.[8] However, further validation studies are warranted to compare 3DSTE-derived vs other imaging method-derived RA volumes.[11,12]

4.1 | Limitations

The present study suffers from several important limitations that should be taken into consideration.

- First, the image quality for 3DSTE is worse than that of 2D echocardiography due to its low temporal and spatial image resolutions (we had to exclude almost half of the examined subjects).
- The low frame rate and the large-sized 3DSTE-capable transducer could affect data acquisition and findings.
- Further validation studies are warranted for 3DSTE-derived RA volumetric measurements against other imaging methods like other echocardiographic techniques, computed tomography, or magnetic resonance imaging.
- During creation of 3D virtual model of RA, its appendage, the caval veins, and the coronary sinus were excluded from the assessments.
- Although RA strains and strain rates could be measured from the same 3DSTE-acquired datasets, the present study did not define their normal reference values.
- The present study did not aim to compare 2D echocardiography- vs 3DSTE-derived RA variables.
- Only RA volume and calculated volume-based functional properties were calculated. Featuring RA morphological abnormalities or measuring RA diameters or areas in selected planes were not part of this study.
- Moreover, 3DSTE-derived volumetric and functional measurement of other heart chambers was also not performed in this study.
- Atrial septum was considered as a part of the RA.
- Due to absence of special 3DSTE-derived RA segmentation model, LV cast was used during measurements.
- (Patho)physiology of the right ventricle and pulmonary artery could theoretically have effects on RA volumetric and functional status, which was not examined in this study. All subjects were healthy without known factors (such as pulmonary disease) affecting results.

5 | CONCLUSIONS

Our study provides normal reference values of 3DSTE-derived RA volumes and volume-based functional properties and their age- and gender dependency in healthy adult subjects.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

ETHICS STATEMENT

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent was obtained from all individual participants included in the study. This work was supported by a grant from the National Research, Development and Innovation Office (GINOP-2.3.2-15-2016-00047).

ORCID

Attila Nemes https://orcid.org/0000-0002-7570-6214

REFERENCES

1. Tadic M. The right atrium, a forgotten cardiac chamber: an updated review of multimodality imaging. *J Clin Ultrasound*. 2015;43:335-345.
2. Rai AB, Lima E, Munir F, et al. Speckle tracking echocardiography of the right atrium: the neglected chamber. *Clin Cardiol*. 2015;38:692-697.
3. Ammar KA, Paterick TE, Khanderia BK, et al. Myocardial mechanics: understanding and applying three-dimensional speckle tracking echocardiography in clinical practice. *Echocardiography*. 2012;29:861-872.
4. Urbano-Moral JA, Patel AR, Maron MS, Arias-Godinez JA, Pandian NG. Three-dimensional speckle-tracking echocardiography: methodological aspects and clinical potential. *Echocardiography*. 2012;29:997-1010.
5. Seo Y, Ishizu T, Aonuma K. Current status of 3-dimensional speckle tracking echocardiography: a review from our experiences. *J Cardiovasc Ultrasound*. 2014;22:49-57.
6. Seo Y, Ishizu T, Atsumi A, Kawamura R, Aonuma K. Three-dimensional speckle tracking echocardiography. *Circ J*. 2014;78:1290-1301.
7. Mohty D, Petitalot V, Magne J, et al. Left atrial function in patients with light chain amyloidosis: a transthoracic 3D speckle tracking imaging study. *J Cardiol*. 2018;71:419-427.
8. Nemes A, Domsik P, Kalapos A, Kormányos Á, Ambrus N, Forster T. Three-dimensional speckle-tracking echocardiography detects different patterns of right atrial dysfunction in selected disorders: a short summary from the MAGYAR-Path study. *Quant Imaging Med Surg*. 2018;8:182-186.
9. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging*. 2015;16:233-270.
10. Rudski LG, Lai WW, Afilalo J, et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. *J Am Soc Echocardiogr*. 2010;23:685-713.
11. Kleijn SA, Aly MF, Terwee CB, van Rossum AC, Kamp O. Comparison between direct volumetric and speckle tracking methodologies for left ventricular and left atrial chamber quantification by three-dimensional echocardiography. *Am J Cardiol*. 2011;108:1038-1044.
12. Nagaya M, Kawasaki M, Tanaka R, et al. Quantitative validation of left atrial structure and function by two-dimensional and three-dimensional speckle tracking echocardiography: a comparative study with three-dimensional computed tomography. *J Cardiol*. 2013;62:188-194.

How to cite this article: Nemes A, Kormányos Á, Domsik P, Kalapos A, Ambrus N, Lengyel C. Normal reference values of three-dimensional speckle-tracking echocardiography-derived right atrial volumes and volume-based functional properties in healthy adults (Insights from the MAGYAR-Healthy Study). *J Clin Ultrasound*. 2019;1–6. https://doi.org/10.1002/jcu.22795