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RESEARCH ARTICLE

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Autonomic function and specific right atrial functions – Is there a relationship? Correlations from the three-dimensional speckle-tracking echocardiographic MAGYAR-Healthy Study

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Abstract

Introduction: Similarly to the ventricles, the atria are under sympathetic/parasympathetic neural regulation. Accordingly, correlations were investigated between Ewing's standard cardiovascular reflex tests (SCRTs) and three-dimensional speckle-tracking echocardiography (3DSTE)-derived right atrial (RA) volumes and strains in healthy subjects.

Materials and Methods: The study comprised 45 healthy adults, but 5 subjects were excluded due to inferior image quality for 3DSTE-derived RA assessments. The remaining 40 individuals being in sinus rhythm had a mean age of 35.1 ± 3.5 years (20 men). Two-dimensional, Doppler, 3DSTE and SCRTs were performed in all cases.

Results: RA maximum volume and total and passive RA stroke volumes correlated with the Valsalva ratio. Active RA stroke volume and emptying fraction showed correlations with 30/15 ratio. Peak global and mean segmental RA circumferential (CS) and longitudinal strains (LS) showed correlation with the Valsalva ratio. At atrial contraction, global RA-LS and mean segmental RA-CS showed correlations with the Valsalva ratio. Moreover, mean segmental RA-CS correlated with 30/15 ratio and mean segmental RA radial strain showed correlations with systolic blood pressure in response to standing. Autonomic neuropathy score correlated with peak global RA-LS.

Conclusions: Autonomic function parameters have significant associations with specific RA functions in healthy adults, making the latter possible indicators of autonomic dysregulation.

KEYWORDS
autonomic, correlation, echocardiography, right atrial, speckle-tracking, three-dimensional

1 | INTRODUCTION

Atria and ventricles are under sympathetic/parasympathetic autonomic functional regulation. The right atrium (RA), similarly to the left atrium (LA), has a special functional pattern and serves as a systolic reservoir, an early diastolic conduit and a late diastolic booster pump chamber helping filling the right ventricle from the caval veins and the coronary sinus.[1] Previously, it was a professional challenge to perform detailed volumetric and functional examination of the RA during cardiac imaging. Due to significant improvements in cardiovascular imaging, atrial and ventricular mechanics could be analyzed in details. Three-dimensional (3D) speckle-tracking echocardiography (3DSTE) is one these methods with its easy-to-learn and non-invasive nature, where volumes, functional properties based on volumes and strains, quantitative features of deformation of a certain cardiac chamber can be determined using the same digitally acquired 3D echocardiographic datasets at the same time.[2–5] 3DSTE takes into account chamber volume and wall contractility changes respecting the cardiac cycle.[2–5] The relationship between autonomic function represented by Ewing's standard cardiovascular reflex tests (SCRTs) and 3DSTE-derived RA quantitative parameters has never been investigated. Accordingly, correlations were investigated between SCRTs and RA volumes and strains.

2 | METHODS

2.1 | Study population

The study comprised 45 healthy individuals, but 5 subjects were excluded due to poor quality of images for 3DSTE-derived RA assessments. The final 40 individuals being in sinus rhythm had an average age of 35.1 ± 3.5 years (20 men). All cases were volunteers, electrocardiography (ECG), 5 Ewing's SCRTs, blood pressure (BP) measurement, two-dimensional Doppler echocardiography and 3DSTE were established in all participants. Calculated variables of the above mentioned techniques were within normal ranges. Obese (BMI > 25 kg/m^2) or smoker subjects, or individuals having hypertension, hypercholesterolaemia, diabetes mellitus, or other known disease were not enrolled into this study. The present study is the part of the Motion Analysis of the heart and Great vessels bY three-dimension Al speckle-tRacking echocardiography in Healthy subjects (MAGYAR-Healthy) Study, which was organized at the Department of Medicine, University of Szeged partly for physiologic analyses between 3DSTE-derived parameters among healthy individuals ('magyar' means 'Hungarian' in Hungarian language). Declaration of Helsinki was complied. All subjects gave informed consent, Institutional and Regional Human Biomedical Research Committee of University of Szeged, Hungary approved the study with the following registration number No. 71/2011 (prolonged February 20/2023).

2.2 | Two-dimensional Doppler echocardiography

A Toshiba Artida™ cardiac ultrasound equipment (Toshiba Medical Systems, Tokyo, Japan) was used for routine two-dimensional Doppler echocardiographic measurements using a 1–5 MHz PST-30BT phased-array transducer. Diameter of the left atrium in parasternal long-axis view, LV dimensions and Simpson's LV ejection fraction in apical long-axis view were obtained. With color Doppler echocardiography, significant valvular regurgitations and stenoses were excluded in case of all valves. Early and late diastolic mitral inflow velocities were also established in all cases by pulsed Doppler.[6]

2.3 | Three-dimensional speckle-tracking echocardiography

Using recent guidelines and practices, the same echocardiographic tool was utilized for 3DSTE, but the transducer was replaced with one suitable for 3D scanning (PST-25SX matrix phased-array transducer, 1–4 MHz).[2–5] In the first part, 3DSTE datasets were acquired immediately after gain and magnitude optimizations during breathhold and lying in the left decubitus position, 6 wedge-shaped so-called subvolumes were digitally acquired from the apical window. Subsequent analyses has been performed offline, when the software created a 'full-volume' dataset. A special software (3D Wall Motion Tracking software version 2.7, Toshiba Medical Systems, Tokyo, Japan) was used demonstrating datasets in apical two- (AP2CH) and four-chamber (AP4CH) longitudinal views and short-axis views at basal, midatrial and superior regions following automatic slicing. Reference points were set by the observer on the edge of septum – tricuspid annulus, then, using the software, we placed signals counterclockwise around RA towards the edge of the lateral wall – TA in AP4CH and AP2CH views. The RA appendage and the pulmonary veins were not the subject of the evaluations. Finally, 3DSTE-derived sequential analysis was performed through the heart cycle creating a virtual RA model, on which measurements could be done (Figure 1).[7] The following RA volumetric and strain characteristics were calculated in all subjects:

RA volumes:

- End-systolic maximum RA volume, which is the largest volume just before tricuspid valve opening (V_{max}),
- Early diastolic RA volume measured before atrial contraction, which was measured at the last frame before tricuspid valve reopening or at the time of the P wave on the ECG (V_{preA}),
- End-diastolic minimum RA volume, which is the lowest volume just before tricuspid valve closure (V_{min}).

RA volume-based functional properties for systolic reservoir function:

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

RA volume-based functional properties for early diastolic conduit function:

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

RA volume-based functional properties for late diastolic active contraction:

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

Global and mean segmental peak RA strains and RA strains at atrial contraction:

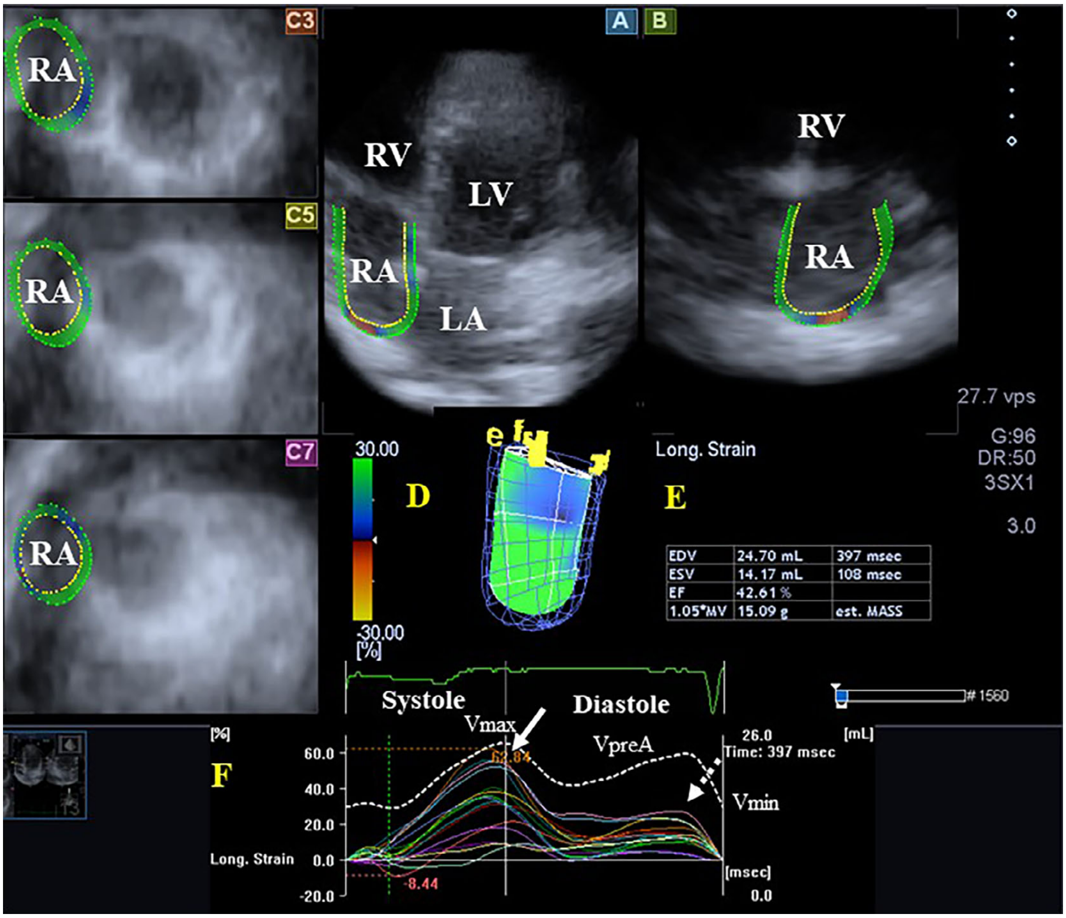

FIGURE 1 Three-dimensional speckle-tracking echocardiography-derived right atrial (RA) analysis in a healthy subject: apical four-chamber (A) and two-chamber (B) longitudinal views and basal (C3), midatrial (C5) and apical (C7) RA short-axis views are presented. Virtual three-dimensional model of the RA (yellowD), calculated volumetric data (yellowE) and time – global and segmental RA strains (white and colored lines) and time – global RA volume changes (dashed white line) (yellowF) are demonstrated. White arrow represents peak RA strains, while white dashed arrow represents RA strains at atrial contraction. EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle; Vmax, end-systolic maximum RA volume; VpreA, early diastolic pre-atrial contraction RA volume; Vmin, end-diastolic minimum RA volume.

- Longitudinal strain, which represents lengthening and shortening (LS),
- Circumferential strain, which represents widening and narrowing (CS),
- Radial strain, which represents thickening and thinning (RS),
- Area strain was defined as combined LS and CS (AS),
- 3D strain was defined as combined RS, LS and CS (3DS).

Using the twin-peak RA strain curves, systolic RA reservoir function was represented by the first one (peak RA strain), while end-diastolic booster bump function was represented by the second one (RA strain at atrial contraction).[7]

2.4 | Autonomic function

The following widely used 5 standard SCRTs were used in all cases.[8,9] For predominantly characterizing parasympathetic function:

- Heart rate response to deep breathing was evaluated by asking the subject to take a deep breath at the rate of six breaths per minute (5 s-in and 5 s-out). The results were expressed as the difference between the maximum and minimum heart rate values (beats/min) measured during the six breathing cycles (normal value: ≥15 bpm, abnormal value: ≤10 bpm).
- Valsalva ratio was calculated by asking the subject to blow into a mouthpiece connected to a modified manometer and to hold it at a pressure of 40 mmHg for 15 s while an ECG was registered continuously. The Valsalva ratio expressed as the ratio of the longest R-R interval after the procedure and the shortest R-R interval during the maneuver (normal value: ≥1.21, abnormal value: ≤1.10).
- 30/15 ratio was determined by asking the subjects to remain in supine position while continuous ECG was recorded, and then by asking the subjects to stand up without interrupting the recording. The 30/15 ratio was calculated as the ratio of the longest R-R interval (at around the 30th beat) to the shortest R-R interval

(at around the 15th beat) following standing up (normal value: ≥1.03, abnormal value: ≤1.00).

For predominantly characterizing sympathetic function:

- In case of sustained handgrip test, first the subject was asked to squeeze a ball with maximal pressure, then this maximal contraction was maintained at 30% of that maximum for as long as possible up to 5 min. BP was measured 3 times before the test and then at 1-min intervals. The difference between the highest diastolic BP during the handgrip exercise and the mean of the three diastolic BP readings before the handgrip was started was calculated (normal value: ≥16 mmHg, abnormal value: ≤10 mmHg).
- Systolic BP response to standing was measured by evaluating the BP in lying position and following standing up. The postural fall in the BP was defined as the difference between the systolic BP after 10 min of standing and systolic BPs 1, 5 and 10 min after standing up. The largest difference from the systolic BP in lying position was evaluated as the BP response to standing (normal value: ≤10 mmHg, abnormal value: ≥30 mmHg).

The severity of autonomic dysfunction was demonstrated by the autonomic neuropathy score (ANS). In all tests, normal, borderline and abnormal values were scored 0,1 and 2, respectively. The sum of the scores gave the total ANS ranging 0-10. A score was considered to be normal, borderline and abnormal if 0-1, 2-3 and larger than 3, respectively.

2.5 | Statistical analysis

Continuous parameters were demonstrated in a format 'average ± standard deviation,' while categorical parameters were presented in format 'n (%).' A significance was considered in case of *p* value less than 0.05. To establish correlations, Spearman's correlation coefficients were calculated between the 5 SCRTs and RA volumes, functional properties based on volumes and strains. The Bland–Altman method was used to determine intraobserver and interobserver agreements. For intraobserver and interobserver correlations, intraclass correlation coefficients (ICCs) were calculated. SPSS software package (SPSS Inc, Michigan, IL, USA) was utilized during statistical analyses.

3 | RESULTS

3.1 | Standard cardiovascular reflex tests

Both Ewings' SCRTs mainly characterizing parasympathetic function including heart rate response to deep breathing (24.3 ± 8.2 bpm), Valsalva (1.84 ± 0.26) and 30:15 (1.43 ± 0.26) ratios and SCRTs mainly characterizing sympathetic function including sustained handgrip test (21.3 ± 7.2 mmHg) and systolic BP response to standing (3.20 ± 4.05 mmHg) and ANS (0.44 ± 1.22) were in the normal ranges.

3.2 | Two-dimensional Doppler echocardiography

Parasternal long-axis view was used for LA diameter measurement (39.1 ± 2.2 mm). LV end-diastolic diameter and volume (48.1 ± 2.2 mm and 107.9 ± 16.0 mL, respectively), LV end-systolic diameter and volume (32.7 ± 3.3 mm and 38.4 ± 8.0 mL, respectively), LV posterior wall (8.5 ± 1.5 mm), interventricular septum (8.9 ± 1.3 mm) and LV ejection fraction (63.5 ± 2.4%) were within the normal references. Average transmitral E and A inflow velocities were 76.2 ± 16.3 cm/s and 57.5 ± 14.3 cm/s, respectively. None of the subjects had significant (≥grade 1) regurgitations or stenoses on any valves.

3.3 | Three-dimensional speckle-tracking echocardiography

The frame rate for 3DSTE-derived strain assessments proved to be 30 ± 2 fps. RA-V_{max} (52.1 ± 15.6%), RA-V_{preA} (35.2 ± 8.7%), RA-V_{min} (25.5 ± 8.3%), RA-TASV (27.2 ± 13.7%), RA-PASV (17.2 ± 9.8%), RA-AASV (7.3 ± 3.5%), RA-TAEF (49.3 ± 17.6%), RA-PAEF (31.3 ± 12.3%) and RA-AAEF (26.7 ± 18.5%) assessed by 3DSTE were in the normal ranges. Similarly, peak global and mean segmental RA-RS (−13.3 ± 9.9 and −19.5 ± 8.5, respectively), RA-CS (31.4 ± 23.3% and 37.5 ± 22.4%, respectively), RA-LS (39.2 ± 9.3% and 43.9 ± 9.0%, respectively), RA-3DS (−5.5 ± 4.6% and −10.4 ± 6.2%, respectively) and RA-AS (91.2 ± 66.3% and 100.1 ± 66.3%, respectively), as well as global and mean segmental RA-RS (−4.5 ± 4.2 and −8.1 ± 4.6, respectively), RA-CS (10.5 ± 7.1% and 15.2 ± 6.5%, respectively), RA-LS (7.7 ± 6.3% and 12.3 ± 3.7%, respectively), RA-3DS (−0.6 ± 3.9% −3.7 ± 4.1%, respectively) and RA-AS (25.3 ± 21.7% and 30.7 ± 13.7%, respectively) at atrial contraction proved to be normal.

3.4 | Correlations

From RA volumetric parameters, RA-V_{max}, TASV, PASV representing systolic and early diastolic RA volumes and functions showed correlations with Valsalva ratio, which mainly represent parasympathetic function. AASV and AAEF representing late diastolic RA booster pump function showed correlations with 30/15 ratio similarly mainly representing parasympathetic autonomic function. None of the parameters representing sympathetic autonomic function correlated with any RA volumes or functional properties based on RA volume.

From peak RA strains, mean segmental and global RA-CS and RA-LS, which represents systolic phase of RA function showed correlations with the Valsalva ratio, which represents parasympathetic function. At atrial contraction, global RA-LS and mean segmental RA-CS, which represents late-diastolic RA booster pumping function showed correlations with Valsalva ratio. At atrial contraction, mean segmental RA-CS correlated with 30/15 ratio, as well. At atrial

TABLE 1 Spearman correlation coefficients between right atrial volumes and volumes-based functional properties and standard cardiovascular reflex tests in healthy adults.

	Parasympathetic function			Sympathetic function		
	Heart rate response to deep breathing	Valsalva ratio	30/15 ratio	Sustained handgrip test	Systolic blood pressure response to standing	Autonomic neuropathy score
Right atrial volumes						
V_{max}	−0.081 (*p* = 0.827)	**0.742 (*p* = 0.008)**	−0.417 (*p* = 0.213)	−0.382 (*p* = 0.261)	0.279 (*p* = 0.401)	0.250 (*p* = 0.451)
V_{preA}	0.023 (*p* = 0.951)	0.521 (*p* = 0.113)	−0.462 (*p* = 0.167)	−0.166 (*p* = 0.630)	0.189 (*p* = 0.568)	0.244 (*p* = 0.459)
V_{min}	0.213 (*p* = 541)	0.232 (*p* = 0.521)	0.061 (*p* = 0.840)	−0.092 (*p* = 0.783)	0.024 (*p* = 0.954)	0.236 (*p* = 0.471)
Right atrial stroke volumes						
TASV	−0.221 (*p* = 0.532)	**0.721 (*p* = 0.014)**	−0.511 (*p* = 0.113)	−0.368 (*p* = 0.236)	0.320 (*p* = 0.347)	0.149 (*p* = 0.651)
PASV	−0.162 (*p* = 0.653)	**0.734 (*p* = 0.012)**	−0.249 (*p* = 0.460)	−0.450 (*p* = 0.158)	0.291 (*p* = 0.392)	0.182 (*p* = 0.580)
AASV	−0.213 (*p* = 0.514)	0.420 (*p* = 0.221)	**−0.666 (*p* = 0.026)**	−0.112 (*p* = 0.762)	0.223 (*p* = 0.509)	0.043 (*p* = 0.901)
Right atrial emptying fractions						
TAEF	−0.392 (*p* = 0.223)	0.411 (*p* = 0.213)	−0.471 (*p* = 0.139)	−0.256 (*p* = 0.471)	0.183 (*p* = 0.576)	0.069 (*p* = 0.834)
PAEF	−0.291 (*p* = 0.401)	0.471 (*p* = 0.151)	−0.065 (*p* = 0.841)	−0.432 (*p* = 0.191)	0.169 (*p* = 0.607)	0.131 (*p* = 0.705)
AAEF	−0.321 (*p* = 0.352)	0.233 (*p* = 0.491)	**−0.584 (*p* = 0.053)**	−0.070 (*p* = 0.830)	0.172 (*p* = 0.610)	0.004 (*p* = 0.991)

Note: The bold value indicate the $p < 0.05$.

contraction, mean segmental RA-RS showed correlations with systolic BP response to standing mainly representing sympathetic function. ANS correlated with peak global RA-LS. Correlation analysis between Ewing's SCRTs and RA volumetric and strain parameters are demonstrated in Tables 1 and 2.

3.5 | Inter- and intraobserver variabilities

The mean difference of RA-V_{max}, RA-V_{preA}, RA-V_{min} and peak RA-RS, RA-LS, RA-CS, RA-AS and RA-3DS by two examiners were 1.1 ± 4.9 mL, −1.3 ± 8.1 mL, 1.1 ± 4.1 mL, −3.0 ± 11.2%, 6.0 ± 12.3%, 0.9 ± 7.8%, 9.6 ± 32.9% and −1.5 ± 9.6%, respectively, with an ICC between these independent measurements of 0.95 ($P < 0.01$), 0.90 ($P < 0.01$), 0.93 ($P < 0.01$), 0.65 ($P < 0.01$), 0.79 ($P < 0.01$), 0.65 ($P < 0.01$), 0.65 ($P < 0.01$) and 0.68 ($P < 0.01$), respectively (interobserver variability). The mean difference of the same parameters measured 2 times by the same examiner was 1.3 ± 6.1 mL, −1.4 ± 10.2 mL, 0.8 ± 5.3 mL, −1.3 ± 8.9%, 5.9 ± 15.8%, 1.4 ± 16.0%, 5.3 ± 35.1% and 1.2 ± 9.1%, respectively, with a correlation coefficient between these independent measurements of 0.96 ($P < 0.01$), 0.88 ($P < 0.01$), 0.94 ($P < 0.01$), 0.76 ($P < 0.01$), 0.77 ($P < 0.01$), 0.63 ($P = 0.03$), 0.75 ($P < 0.01$) and 0.73 ($P < 0.01$), respectively (intraobserver variability).

4 | DISCUSSION

The relationships between RA volumes and quantitative features of RA wall contractility (strains) and autonomic function were investigated for the first time in healthy adults. Moreover, RA parameters were examined on 3DSTE-derived virtual models of the RA, the use of which appropriate physiologic investigations is carried out. Based on literature data, 3DSTE is validated for atrial chamber quantifications and strain measurements,[10–13] and normal reference values have also been published.[14,15]

The cardiac plexus provides the autonomic innervation of the heart, this network consists of autonomic nerves and ganglia. While the vagal nerve is responsible for the parasympathetic innervation of the heart, the sympathetic cardiac nerves arise from the T1 to T4 segments and partly from the T5 segment of the spinal cord. The cardiac plexus is divided into two closely connected parts, a superficial and a deep part contributing to the left and right coronary plexuses. The right coronary plexus innervates the right atrium and right ventricle.[16,17]

In recent studies, correlations between Ewing's SCRTs, which represent autonomic function and aortic stiffness,[18] LV rotational parameters[19] and LA volumes and strains[20] were detected. With correlations between SCRTs and PWV, augmentation index, aortic strain, distensibility and stiffness index, higher parasympathetic

TABLE 2 Spearman correlation coefficients between right atrial strains and standard cardiovascular reflex tests in healthy adults.

	Parasympathetic function			Sympathetic function		
	Heart rate response to deep breathing	Valsalva ratio	30/15 ratio	Sustained handgrip test	Systolic blood pressure response to standing	Autonomic neuropathy score
Peak right atrial strains						
Global RA-RS	0.002 ($p = 0.997$)	0.162 ($p = 0.642$)	0.121 ($p = 0.720$)	−0.018 ($p = 0.973$)	0.212 ($p = 0.540$)	−0.312 ($p = 0.352$)
Mean segmental RA-RS	0.031 ($p = 0.931$)	0.162 ($p = 0.640$)	0.111 ($p = 0.761$)	0.069 ($p = 0.842$)	0.291 ($p = 0.392$)	−0.361 ($p = 0.282$)
Global RA-CS	−0.111 ($p = 0.730$)	**0.685 ($p = 0.021$)**	−0.452 ($p = 0.168$)	−0.210 ($p = 0.533$)	0.002 ($p = 0.998$)	−0.063 ($p = 0.861$)
Mean segmental RA-CS	−0.062 ($p = 0.862$)	**0.701 ($p = 0.021$)**	−0.401 ($p = 0.222$)	−0.175 ($p = 0.612$)	0.012 ($p = 0.981$)	−0.114 ($p = 0.732$)
Global RA-LS	0.440 ($p = 0.183$)	**0.686 ($p = 0.019$)**	0.122 ($p = 0.712$)	0.335 ($p = 0.312$)	0.523 ($p = 0.081$)	**−0.593 ($p = 0.051$)**
Mean segmental RA-LS	0.412 ($p = 0.211$)	**0.742 ($p = 0.010$)**	0.150 ($p = 0.650$)	0.320 ($p = 0.340$)	0.572 ($p = 0.071$)	−0.511 ($p = 0.110$)
Right atrial strains at atrial contraction						
Global RA-RS	−0.291 ($p = 0.390$)	−0.093 ($p = 0.783$)	−0.131 ($p = 0.702$)	−0.161 ($p = 0.641$)	0.353 ($p = 0.285$)	0.233 ($p = 0.482$)
Mean segmental RA-RS	−0.235 ($p = 0.487$)	0.179 ($p = 0.600$)	0.211 ($p = 0.542$)	−0.278 ($p = 0.414$)	**0.614 ($p = 0.041$)**	0.266 ($p = 0.419$)
Global RA-CS	−0.282 ($p = 0.390$)	0.323 ($p = 0.321$)	−0.295 ($p = 0.367$)	0.202 ($p = 0.557$)	−0.418 ($p = 0.201$)	0.020 ($p = 0.961$)
Mean segmental RA-CS	−0.210 ($p = 0.559$)	**0.593 ($p = 0.051$)**	**−0.691 ($p = 0.020$)**	−0.124 ($p = 0.730$)	−0.024 ($p = 0.948$)	0.005 ($p = 0.982$)
Global RA-LS	0.562 ($p = 0.072$)	**0.595 ($p = 0.052$)**	0.142 ($p = 0.680$)	0.154 ($p = 0.655$)	0.006 ($p = 0.989$)	−0.321 ($p = 0.342$)
Mean segmental RA-LS	0.183 ($p = 0.601$)	0.511 ($p = 0.113$)	−0.320 ($p = 0.333$)	0.010 ($p = 0.981$)	−0.125 ($p = 0.711$)	0.061 ($p = 0.859$)

Note: The bold value indicate the $p < 0.05$.

function was found to be associated with better aortic elasticity.[18] During a 3DSTE study, correlations could be demonstrated between the Valsalva ratio (and heart rate response to deep breathing) and LV twist suggesting that better parasympathetic autonomic function is associated with lower LV rotational mechanics as well.[19]

Although complex correlation analysis was performed in case of the LA, direct relationship between RA volumetric and functional features and autonomic function has never been investigated. Therefore, the present study is the first trying to find correlation between Ewing's SCRTs and RA volumes and strains. Findings suggest substantial differences between parameters mainly featuring parasympathetic and sympathetic functions and volumes of RA and LA according to recent findings from the MAGYAR-Healthy Study.[20] While only LA-TAEF and LA-PAEF showed correlations with systolic BP response to standing, which mainly represents sympathetic function, significant correlations between RA volumes and volume-based functional properties and Ewing's SCRTs mainly representing parasympathetic autonomic function (Valsalva and 30/15 ratios) could be detected.[20]

When atrial strains were examined, from SCRTs, only Valsalva ratio, which mainly represents parasympathetic function correlated with -LA RSs and CSs representing systolic and late-diastolic phases of LA function. According to the presented findings, in addition to RA-CS, Valsalva ratio also correlated with RA-LS, but not with RA-RS both in systole and late diastole. Moreover, another parameter (30/15 ratio) showed correlations as well with RA-CS in booster pump phase of RA function. While LA-CS both measured in systole and late-diastole correlated with the systolic BP response to standing mainly representing sympathetic autonomic function, similar findings could not be detected for the RA. Only RA-RS at atrial contraction correlated with this SCRT.[20] For RA, ANS correlated with peak global RA-LS, similar findings for LA were not present.

These findings could suggest different contributions of the autonomic function to atrial volumes and functional properties in the left and right hearts. However, importance of the parasympathetic nervous system in determining certain atrial function seem to be confirmed, which could promote the development of atrial fibrillation in future, as suggested by recent findings.[21] However, further analysis would be necessary in healthy subjects and in several pathological states.

4.1 | Limitation section

- Small number of healthy individuals were enrolled, in case of whom Ewing's SCRTs and 2D echocardiography extended with Doppler examination and 3DSTE were performed. The study results would have been statistically stronger, if a larger number of healthy individuals had been included.[22,23]
- It is also known that physical training and yoga may affect the results of autonomic function tests. However, to the best of authors' knowledge, none of participants were active athlete or yoga practitioner at the time of examinations.[24,25]
- 3DSTE-derived image quality is still worse as that of routine echocardiography, which may influence our results.
- The study purposed to investigate healthy subjects demonstrating physiological correlations between natural healthy parameters, patients with certain pathologies were not examined in this study, therefore no pathophysiological associations were examined. These facts are important to mention when interpreting the findings.
- Questions may arise as to which atrium part the atrial septum is. In the present study, complete virtual 3D models of the RA were examined, this model included the atrial septum as well. However, if we had made a 3D model of the LA, the affiliation of the atrial septum would have been questionable.
- SCRTs may be influenced by a number of factors, the complete exclusion of which in such a study is limited such as hemodynamics, venous return, afterload, and so forth.

4.2 | Conclusions

Autonomic function parameters have significant associations with specific RA functions in healthy adults, making the latter possible indicators of autonomic dysregulation.

AUTHOR CONTRIBUTIONS

Attila Nemes: Conceptualization, Writing – original draft, Writing – review & editing. **Árpád Kormányos**: Methodology, Software, Investigation, Data curation, Writing – review & editing. **Andrea Orosz**: Investigation, Resources. **Nóra Ambrus**: Writing – original draft. **Tamás T. Várkonyi**: Writing – review & editing. **Csaba Lengyel**: Writing – review & editing.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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