Evaluation of right heart function in heart failure patients using strain imaging and three-dimensional echocardiography

Amal M. Hamdy, Layla A. Mohamed, Nadia A. Agiba, Gehan E. Youssof

Introduction Right heart function is an important predictor of morbidity and mortality in patients with cardiovascular diseases having left ventricular (LV) systolic dysfunction.

Aim Assessment of right ventricular (RV) and right atrial (RA) functions in heart failure patients using strain imaging and three-dimensional echocardiography.

Patients and methods This study included 60 patients (group I) having LV systolic dysfunction with LV ejection fraction less than or equal to 40% in addition to 20 healthy participants (group II) as a control group. LV measures included 2D and 3D-LV ejection fraction, LV-Tei index, and 2D and 3D-LV global longitudinal strain. RV measures included RV dimensions, RV fractional area change, RV-Tei index, 2D-RV global longitudinal strain, 3D-RV ejection fraction, 3D-average longitudinal strain for both interventricular septum, and RV free wall (3D-RVLS-sept and 3D-RVLS-FW, respectively). RA measures included RA dimensions, RA passive, active and total emptying volumes and fractions, peak RA longitudinal, and contractile strain. Parameters of LV, RV, and RA functions were compared between groups I and II.

Results RV and RA dimensions and volumes, and LV-Tei and RV-Tei indexes were significantly higher in group I compared with group II. All other parameters of LV, RV, and RA function except RA-active emptying volumes were significantly lower in group I compared with group II. Cutoff values for parameters of RV and RA function showed good sensitivity and specificity to discriminate group I from group II. Cutoff points were 19.9% for 2D-RV global longitudinal strain, 46.4% for 3D-RV ejection fraction, 11.7% for 3D-RVLS-sept, 18.6% for 3D-RVLS-FW, 29.2% for peak RA longitudinal, and 17.1% for peak RA contractile strain. Sensitivity ranged from 78.3 to 96.7% and specificity ranged from 85 to 100% with a *P* value of less than 0.001.

Conclusion RV and RA functions are impaired in heart failure patients with LV systolic dysfunction. Both 3D and strain imaging are good echo modalities in the evaluation of right heart function.
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Department of Cardiology, Faculty of Medicine for Girls, Al-Azhar University, Cairo, Egypt

Correspondence to Dr. Gehan Youss, Gharbeya Gharbeya, Egypt.
e-mail: gegr108484@gmail.com

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Introduction

The right heart function (RHF) has long been overlooked because it was not considered essential for overall cardiac performance. In the last two decades, it has become more attractive to research because some studies have shown the great importance of right ventricular (RV) structure and function in the cardiovascular morbidity and mortality of patients with congenital heart disease, pulmonary hypertension, heart failure (HF), and ischemic heart disease, even in the general population [1,2].

The role of RV in the clinical presentation of HF patients has been emphasized in a relatively recent study [3]. Although two-dimensional echocardiography (2DE) has been recommended as a useful tool for quantifying RV and right atrial (RA) volume and functions [4], it is limited by the absence of an orthogonal plane and the need for geometric assumptions [5]. Strain rate imaging was recently proposed as a new modality for assessing RV and RA myocardial function; however, this method had a potential limitation because of the angle dependency of the Doppler feature [6].

Real-time three-dimensional echocardiography (RT3DE) is a semiautomatic system that can be used directly with an ultrasound machine. This technique can accurately and rapidly determine cardiac chamber anatomy and function independent of the angle, without making geometric assumptions, and it provides information concerning phasic volume changes during the cardiac cycle [7].

The aim of this study was to evaluate both RV and RA functions in HF patients using strain imaging and 3DE.

Patients and methods

This study comprised two groups: group I included 60 patients having systolic HF with left ventricular ejection fraction (LVEF) of less than or equal to 40% and group II included 20 healthy participants as a control group. The patients were selected from those attending the cardiology outpatient clinic or admitted to the Cardiology Department at Al-Zahraa University Hospital during the period from April 2016 to April 2018. The study protocol was approved by the Medical Ethics Committee of the Faculty of Medicine for Girls, Al-Azhar University and a verbal informed consent was obtained from all participants before enrollment into the study. Patients with recent (≤30 days) acute coronary syndrome, acute pulmonary edema, valvular heart disease, congenital heart diseases, end-stage renal failure requiring hemofiltration, history of malignancy and/or under chemotherapy or radiotherapy, permanent atrial fibrillation, and patients on permanent pacemakers or cardiac resynchronization devices were excluded from the study.

All participants were subjected to the following:

(1) Thorough medical history analysis and clinical evaluation with special emphasis on risk factors for coronary artery disease (CAD) (such as hypertension and diabetes) and New York Heart Association (NYHA) classification [8].
(2) 12-Lead surface ECG: for documenting resting heart rate, detecting any chamber enlargement, ST changes, or arrhythmias, if present.
(3) Transthoracic echo-Doppler assessment:

Transthoracic echo-Doppler studies were performed using Vivid-E9 GE (©2019 General Electric Company, United States), ultrasound system, Horten Norway with tissue Doppler, speckle-tracking imaging, and three-dimensional imaging (3D) capabilities. Standard views were obtained from all available windows, using multifrequency (1.5–4.6 MHz) matrix probe M5S and 4 V probe for 3D acquisition. The images and cine loops were digitally stored for later offline analysis through an echo-pack work station, version 201.

LV parameters included:

(1) M-mode measures: LV end-diastolic and end systolic dimensions, LV percent fractional shortening, and LVEF.
(2) 2DE measures: 2D-LVEF and 2D-STE (ST segment Elevation) to assess 2D-LV global longitudinal strain.
(3) LV-Tei index calculated as LV-IVCT+LV-IVRT/LV-ET [9], where IVCT is the isovolumic contraction time, IVRT is the isovolumic relaxation time, and ET is the ejection time.
(4) 3DE measures: LV volumes, EF, and 3D-STE using 4D autoquantification software to assess 3D-LV global longitudinal strain.

RV parameters included:

(1) M-mode measured tricuspid annular plane systolic excursion (TAPSE).
(2) 2D echo RV measures: from apical four-chamber view:
    (a) Basal RV linear diameter (basal RVD), mid-cavity RV linear diameter (mid-RVD), and longitudinal RV diameter (long RVD).
    (b) RV fractional area change (RV-FAC).
    (c) RV-2D-STE: due to the absence of software dedicated for the RV in our echo machine, we used the software for LV-2D-STE to assess RV global longitudinal strain (2D-RVGLS).
(3) RV-Tei index: RV-IVCT+RV-IVRT/RV-ET [9].
(4) RV-3DE: RV volumes, EF, and 3D-RV-STE using TomTec software (TomTec Imaging Systems, Royal Philips, Amstelplein 2, Amsterdam, The Netherlands) to assess 3D-RV longitudinal strain both at septal and free wall (3D-RVLs-sept and 3D-RVLS-FW, respectively).

RA parameters included:

(1) 2D-RA volumes: maximum, minimum, and pre-P RA volumes were automatically calculated by the software using the area–length method. These volumes were used for the calculation of:
    (a) RA-total emptying volume (RA-TEV) that represents the reservoir function, calculated as: RA maximum volume–RA minimum volume.
    (b) RA passive emptying volume (RA-PEV) that represents the conduit function, calculated as: RA maximum volume–RA pre-P volume.
    (c) RA-active emptying volume (RA-AEV) that represents the booster pump function, calculated as: RA pre-P volume–RA minimum volume.
    (d) RA-total emptying fraction (RA-TEF) calculated as: RA-TEV/RA maximum volume.
    (e) RA passive emptying fraction (RA-PEF) calculated as: RA-PEV/RA maximum volume.
    (f) RA-active emptying fraction (RA-AEF) calculated as: RA-AEV/RA pre-P volume.
(2) 2D-STE: due to the absence of software dedicated for the RA in our echo machine, we used the software for LV-2D-STE, to assess peak RA longitudinal strain (PRALS) that represents the reservoir function and peak RA contractile strain (PRACS) that represents the contractile function.

Statistical analysis

Performed via SPSS statistics (version 23) (IBM Corp. Released 2015; IBM SPSS Statistics for Windows, Version 23.0, Armonk, NY: IBM Corp.). Data were expressed as mean±SD for normally distributed data, or median for not normally distributed data. Comparison between study groups was done using unpaired *t* test in the case of normal distribution, or Mann–Whitney test in the case of non-normal distribution. Receiver operating characteristic analysis was performed to detect the cutoff points of right heart parameters that show good sensitivity and specificity to discriminate between study groups. A *P* value less than 0.05 was considered statistically significant.

Results

Group I included nine women and 51 men while group II included 11 women and nine men. The mean age of group I was 55.5±9.7 years and group II was 46.7±8.9 ($P<0.01$). Among group I, there were 36 (60%) hypertensive patients, 33 (55%) diabetic patients, 49 (81.6%) smokers, and 10 (16.7%) had positive family history of ischemic heart disease (IHD).

Table 1 Comparison between groups I and II with respect to left ventricular echo parameters

	Group I (*N*=60)	Group II (*N*=20)	*P* value
LVEDD (cm)	6.4±0.7	4.7±0.6	0.000
LVESD (cm)	5.4±0.7	2.9±0.4	0.000
LVEF (%)	33.9±8.3	67.5±3.6	0.000
FS (%)	16.8±4.7	37.6±2.7	0.000
LVEF (biplane %)	28.3±7.5	63.4±3.1	0.000
LV-Tei	0.68±0.28	0.42±0.09	0.000
2D-LVGLS (%)	7.1±2.5	22.4±1.5	0.000
3D-LVEDV (ml)	141.7±44	83.9±20.1	0.000
3D-LVESV (ml)	104±37.5	32.2±9.1	0.000
3D-LVEF (%)	27.1±8.2	61.9±3.3	0.000
3D-LVGLS (%)	5.2±2.2	14.4±3.2	0.000

2D-LVGLS, 2D left ventricular global longitudinal strain; 3D-LVEDV, 3D left ventricular end-diastolic volume; 3D-LVEF, 3D-LV ejection fraction; 3D-LVESV, 3D left ventricular end systolic volume; 3D-LVGLS, 3D left ventricular global longitudinal strain; FS (%), percent fractional shortening; LVEDD, LV end-diastolic dimension; LVEF, LV ejection fraction; LVESD, LV end systolic dimensions.

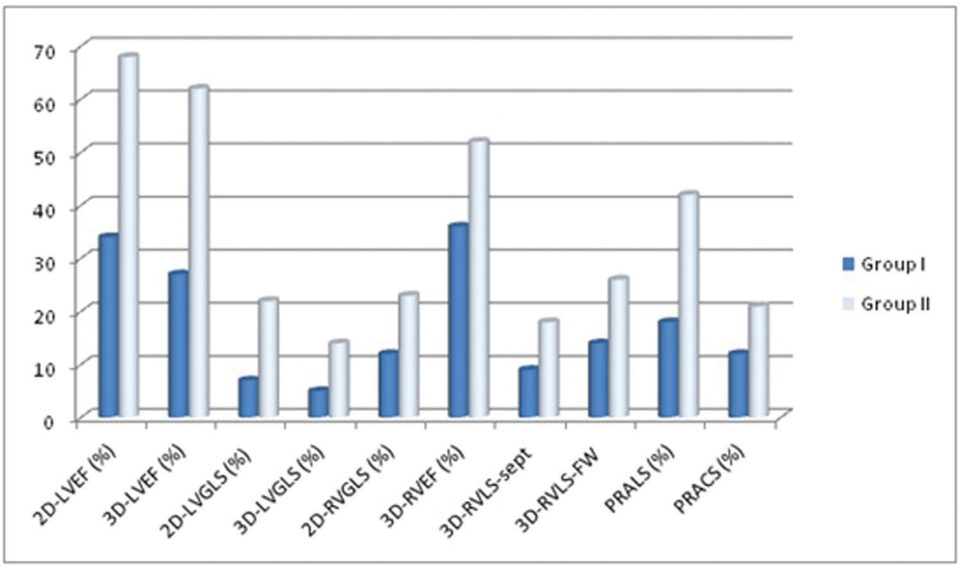
As regards the NYHA functional class, 17 (28.3%) patients had NYHA class II, 31 (51.7%) patients had NYHA class III, and 12 (20%) patients had NYHA class IV. Thirty-three (55%) patients had a history of orthopnea and 32 (53.3%) patients had a history of paroxysmal nocturnal dyspnea and 27 (45%) patients had a history of lower limb edema.

LV dimensions, volumes, and Tei index were significantly higher in group I compared with group II while all other parameters of LV function being lower in group I compared with group II (Table 1, Fig. 1).

RV dimensions, volumes, and RV-Tei index were significantly higher in group I compared with group II. All other parameters of RV function were significantly lower in group I compared with group II (Table 2, Fig. 1).

Group I had significantly higher values of RA volumes, RA-TEV, and RA-AEV. Values of RA-TEF, RA-PEF, and PRALS that represent the RA reservoir function and PRACS that represents the RA contractile function were lower in group I compared with group II. There were no significant differences between the two groups as regards the RA-PEV and RA-AEF (Table 3, Fig. 1).

Figure 1



Comparison between groups I and II with respect to LV and RV echo parameters. LV, left ventricular; RV, right ventricular.

Table 2 Comparison between groups I and II with respect to right ventricular echo parameters

	Group I (*N*=60)	Group II (*N*=20)	*P* value
Basal RVD (cm)	4.3±0.9	3.5±0.4	0.000
Mid-RVD (cm)	2.8±0.8	2.5±0.3	0.007
Long RVD (cm)	7.1±1.2	5.8±0.5	0.000
TAPSE (cm)	1.67±0.33	2.28±0.18	0.000
RV-FAC (%)	34.5±11.1	49.9±4.6	0.000
RV-Tei	0.62±0.26	0.29±0.09	0.000
2D-RVGLS (%)	12.3±4.6	22.8 ±2.2	0.000
3D-RVEDV (ml)	62.6±35.1	28.3±10.1	0.000
3D-RVESV (ml)	42.6±28.8	13.7±5.5	0.000
3D-RVEF (%)	35.7±11	52.1±3.2	0.000
3D-RVLS-sept (%)	8.7±4.8	17.7±4.2	0.000
3D-RVLS-FW (%)	13.8±6.9	25.5±5.2	0.000

2D-RVGLS, 2D right ventricular global longitudinal strain; 3D-RVEF, 3D right ventricular ejection fraction; 3D-RVLS-FW, 3D right ventricular longitudinal strain for free wall; 3D-RVEDV, 3D right ventricular end-diastolic volume; 3D-RVESV, 3D right ventricular end systolic volume; 3D-RVLS-sept, 3D right ventricular longitudinal strain for septum; FAC, fractional area change; RVD, right ventricular diameter; TAPSE, tricuspid annular plane systolic excursion.

Table 3 Comparison between groups I and II as regards right atrial two-dimensional echocardiography parameters

	Group I (*N*=60)	Median	IQR	Group II (*N*=20)	*P* value
2D-RAVmax (ml)	52±27.7			28.8±7.3	0.000
2D-RAVmin (ml)	30.6±22.9			12.1±4.3	0.000
2D-RAVprep (ml)	42±25.4			19.1±5.7	0.000
RA-TEV (ml)	21.4±7.6			16.7±4.8	0.002
RA-PEV (ml)	10.0±6.0	9	6.8	9.8±3.9	0.644
RA-AEV (ml)	11.4±4.9			7±2.6	0.000
RA-TEF (%)	0.46±0.14			0.58±0.09	0.000
RA-PEF (%)	0.22±0.11			0.34±0.10	0.000
RA-AEF (%)	0.32±0.12	0.333	0.195	0.37±10	0.111
PRALS (%)	18.0±9.8			41.8±9.1	0.000
PRACS (%)	12.1±6.5			21.4±5.4	0.000

AEF, active emptying fraction; AEV, active emptying volume; IQR, interquartile range; PEF, passive emptying fraction; PEV, passive emptying volume; PRACS, peak right atrial contractile strain; PRALS, peak right atrial longitudinal strain; RA-TEV, right atrial total emptying volume; RAV max, right atrial volume maximum; RAV min, right atrial volume minimum; TEF, total emptying fraction.

Cutoff values for parameters of RV and RA function that showed good sensitivity and specificity to discriminate group I from group II are shown in Table 4, Fig. 2.

Discussion

The RV has historically received less attention than its counterpart of the left side of the heart, yet there is a substantial body of evidence showing that RV size and function are perhaps equally important in predicting adverse outcomes in cardiovascular disease. RV dysfunction is associated with excess morbidity and mortality in patients with chronic left-sided HF, acute myocardial infarction (with or without RV involvement), pulmonary embolism, pulmonary arterial hypertension, and congenital heart disease [10–12]. The most common cause of RV dysfunction is chronic left-sided HF. LV dilation and dysfunction adversely affect RV function via a complex, systolic, and diastolic ventricular interdependence [13]. In patients with LV systolic dysfunction and HF, RVF has been shown to be predictive of short-term and long-term morbidity and mortality [14]. Recent studies have shown that RA volume and/or function are important predictors of morbidity and mortality in patients with HF, coronary artery disease (CAD), PE, or Eisenmenger's syndrome [4]. Therefore, assessment of RV function is clinically important in almost all patients with heart disease. Although a recently published study showed that 2DE-derived linear RA and RV sizes correlated with CT measurements [15], the complex geometry of the RV poses a significant limitation to the reliable quantitation of RV volumes and RV ejection fraction (RVEF) using 2D transthoracic echocardiography (2D-TTE) [16]. Cardiac magnetic resonance (CMR) imaging is reported to be the gold standard for the evaluation of RV volumes and RVEF [17]; however, factors such as cost, portability, time consumption, and contraindications hinder its routine use in every patient. 3D-TTE has the advantage of full-volume acquisition of the entire RV, which may overcome the technical and clinical limitations of 2D-TTE [18].

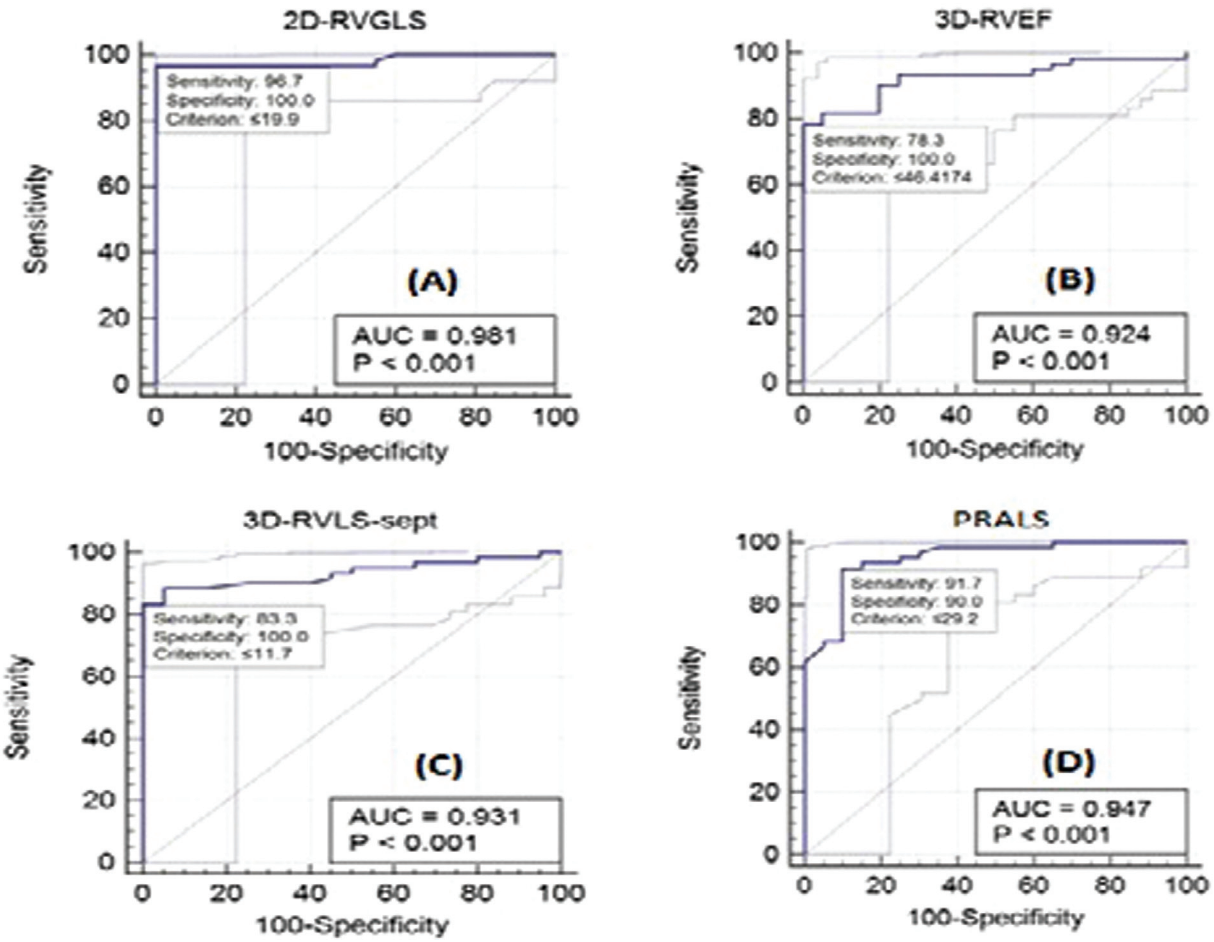
Table 4 Cutoff points, sensitivity, and specificity of right ventricular and right atrial parameters discriminating group I from group II

Parameters	Cutoff point (%)	AUC (cm^2)	Sensitivity (%)	Specificity (%)	*P* value
2D-RVGLS	19.9	0.98	96.7	100	<0.001
3D-RVEF	46.4	0.92	78.3	100	<0.001
3D-RVLS-sept	11.7	0.93	83.3	100	<0.001
3D-RVLS-FW	18.6	0.91	80	95	<0.001
PRALS	29.2	0.95	91.7	90	<0.001
PRACS	17.1	0.86	78.3	85	<0.001

AUC, area under curve; 2D-RVGLS, 2D right ventricular global longitudinal strain; 3D-RVEF, 3D right ventricular ejection fraction; 3D-RVLS-FW, 3D right ventricular longitudinal strain for free wall; 3D-RVLS-sept, 3D right ventricular longitudinal strain for septum; PRACS, peak right atrial contractile strain; PRALS, peak right atrial longitudinal strain.

It is reported that low TAPSE is associated with increased cardiovascular risk and mortality [19].

Figure 2



ROC curves for RV and RA parameters discriminating group I from group II. (a) 2D-RVGLS, (b) 3D-RVEF, (c) 3D-RVLS-sept, (d): PRALS. 2D, two-dimensional; 3D, three-dimensional; PRALS, peak RA longitudinal strain; RA, right atrial; ROC, receiver operating characteristic; RV, right ventricular; RVEF, RV ejection fraction; RVGLS, RV global longitudinal strain; RVLS-sept, RV longitudinal strain both at septal.

Therefore, this parameter can be considered as a conventionally useful measure to assess cardiovascular risk in HF patients. A study conducted by Deveci *et al.* [20] reported a significantly lower TAPSE in HF patients compared with normal participants (15.7±6.0 vs. 27.5 ±3.3, respectively).

Previous studies for the assessment of RV function using TAPSE in HF patients with reduced ejection fraction (HFrEF) compared with HF patients with preserved ejection fraction (HFpEF) reported that TAPSE is lower in HFrEF compared with HFpEF [19,21].

Our findings are in accordance with the previously mentioned reports [19–21], where our HF patients had significantly lower TAPSE than the control group.

In our study, the HF patients showed other echo-Doppler parameters of impaired RV function including lower FAC and higher RV-Tei index in comparison to the control group. These results are concordant with the results of Puwanant *et al.* [21] who reported a lower value of FAC and higher RV-Tei in HFrEF compared with HFpEF.

There are a limited numbers of studies that have investigated the morphology and function of the RV by 3DE. Recently, RT3DE has been shown to have better correlation with CMR, as compared with 2DE in evaluating the RV in healthy patients and in a selected cohort of patients, particularly those with congenital heart disease and pulmonary hypertension [14]. A study done by Kim *et al.* [22] demonstrated that the assessment of RV function using RT3DE in patients with LV dysfunction is both feasible and accurate as compared with CMR. These investigators showed a good correlation in RV volumes and RVEF between RT3DE and CMR and reported that RT3DE measurements were found to be highly reproducible with excellent limits of agreement for intraobserver as well as interobserver variability. They concluded that RT3DE could be used as a reliable and reproducible alterative to CMR for the quantitative assessment of RV function and better prognostication in an important patient population.

Studies that investigated that the morphology and function of the RA are limited. The range references for different variables of RA phasic function (volumes, emptying fraction, strain, and strain rates) are not provided in the current guidelines for echocardiographic assessment of the right heart [23].

Jain *et al.* [24] studied the RA phasic function in HF patients either with reduced or preserved EF using CMR imaging with assessment of its prognostic implications. They concluded that phasic RA function is predictive of the risk of all-cause death in a diverse group of participants with and without HF, and also concluded that RA conduit and reservoir functions are independent predictors of mortality.

The current study demonstrated impaired parameters of RA function including PRALS and PRACS in HF patients compared with normal participants. These findings are consistent with a previous study [6] for quantitative assessment of RA function using strain and strain rate imaging in HF patients with reduced EF which have shown significantly compromised RA deformation indices in HF patients versus normal participants, and concluded that a diminished RA function, assessed by strain imaging, plays a critical role in the pathophysiological process of HF patients. This study [6] also demonstrated a significant correlation between the RA peak systolic strain, RA peak systolic strain rate, and cardiac output. Likewise, Peluso *et al.* [25] found a correlation between RA longitudinal strain and different RA volumes and emptying fractions, illustrating various types of atrial function. These findings are particularly important when considering the simplicity of performing 2D strain analysis in comparison with the time-consuming and complicated evaluation of all kinds of RA volumes, emptying volumes, and fractions.Sakata *et al.* [26] studied the RA function by 2D-STE in patients with pulmonary artery hypertension. They reported that the PRALS was significantly lower in pulmonary artery hypertension patients compared with the control participants (34.6 ±14.1 vs. 58.3±9.9%, $P<0.0001$). It was reported that the PRALS measured by 2D-STE correlates with the invasively measured systolic pulmonary artery pressure and thus assessment of PRALS by 2D-STE could predict pulmonary hypertension in patients with HF due to LV systolic dysfunction [27]. PRALS was found to be the strongest predictor of pulmonary hypertension in patients with HF and LV dysfunction and it showed inverse correlation with pulmonary artery pressure and pulmonary vascular resistance, suggesting that RA function declines with an increase in pulmonary pressure and vascular resistance [27].

Our findings regarding RHF are in agreement with the previous studies [6,20,21,26,27] and highlight the value of strain imaging and 3DE in the detection of RV dysfunction in HF patients with LV systolic dysfunction.

Study limitation

This study is limited by:

First, the use of software dedicated for the LV for the assessment of RV and RA strain. Second, the small number of control group and their younger age compared with the control group.

Conclusion

RV and RA functions are impaired in HF patients with LV systolic dysfunction. Both 3DE and strain imaging are good echo modalities in the evaluation of RHF.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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