## Original Article

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# The Usefulness of 4D Echocardiographic Modality for Assessing RV Affection in Uncontrolled Hypertensive Patients

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#### **Conflict of Interest**

The authors have no financial conflicts of interest.

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## ABSTRACT

BACKGROUND: In many cardiovascular disorders, the contractile performance of the right ventricle (RV) is the primary determinant of prognosis. For evaluating RV volumes and function, 4 dimensional (4D)-echocardiography has become common. This research used 2D and 4D modalities to assess RV contractile performance in hypertensive patients.
METHODS: A total of 150 patients with essential hypertension were enrolled in this study, along with 75 age and sex-matched volunteers. Clinical evaluation and echocardiographic examination (including M-mode, tissue Doppler imaging, and 2D speckle tracking) were conducted on all participants. RV volumes, 4D-ejection fraction (EF), 4D-fractional area change (FAC), 4D-tricuspid annular plane systolic excursion (TAPSE), 4D-septal and free wall (FW) strain were all measured using 4D-echocardiography.

**RESULTS:** Hypertensive patients showed 2D-RV systolic and diastolic dysfunction (including TAPSE, 2D-right ventricular global longitudinal strain, RV-myocardial performance index and average E/EaRV) and 4D-RV impairment (including right ventricular EF, FAC, RV strain and TAPSE, right ventricular end-diastolic volume and right ventricular end-systolic volume) compared to the control group. We verified the prevalence of RV systolic dysfunction in hypertension patients using the following parameters: 1) 15% of them had 2D-TAPSE < 17 mm vs. 40% by 4D-TAPSE; 2) 25% of them had 2D-GLS < 19% vs. 42% by 4D-septal strain and 35% by 4D FW strain; 3) 35% of hypertensive patients had 4D-EF < 45%; and finally; 4) 25% of hypertensive patients had 2D-FAC < 35% compared to 45% by 4D-FAC. **CONCLUSIONS:** The incidence of RV involvement was greater in 4D than in 2D-modality trans-thoracic echocardiography. We speculated that 4D-echocardiography with 4D-strain imaging would be more beneficial for examining RV morphology and function in hypertensive patients than 2D-echocardiography, since 4D-echocardiography could estimate RV volumes and function without making geometric assumptions.

**Keywords:** Hypertension; 4 dimensional echocardiography; Right ventricle; 4 dimensional-fractional area change

#### **Author Contributions**

Conceptualization: Mohamed LA; Data curation: Habib SA, Abd Elaziz OH; Formal analysis: Habib SA, Mohamed LA; Investigation: Habib SA, Abd Elaziz OH; Methodology: Hamdy RM, Mohamed LA, Abd Elaziz OH; Project administration: Hamdy RM; Resources: Mohamed LA, Abd Elaziz OH; Supervision: Hamdy RM; Validation: Habib SA, Abd Elaziz OH; Visualization: Abd Elaziz OH; Writing - original draft: Hamdy RM, Mohamed LA; Writing - review & editing: Hamdy RM, Mohamed LA.

### **INTRODUCTION**

One of the most common diseases in the population is hypertension (HTN). It's a well-known risk factor for cardiovascular disease that induces left ventricular (LV) pressure overload, which leads to a variety of changes in LV geometry, eventually leading to heart failure (HF) with preserved ejection fraction (EF) and/or HF with reduced EF.<sup>1)</sup>

The right ventricle (RV)'s function has been widely accepted as a significant predictor of detrimental outcomes in patients with cardiac diseases. In HF patients, RV function correlates more closely with exercise capability than LV function, according to studies.<sup>2)</sup>

Because of the intimate anatomic relationship of the two ventricles, the RV chamber is often involved in LV pathologies as a result of a direct injury extension, after load shifts, or ventricular interdependence.<sup>3)</sup>

The literature abounds with studies that have assessed LV function. However, studies on RV structure and function in hypertensive subjects are limited, and the majority of those that have been done have been on severely hypertensive patients.<sup>4)</sup> It is unclear if the RV is involved in milder types of HTN, and no research has looked into this yet.<sup>5)</sup>

On this basis, we compared RV and LV functions in a group of patients with essential HTN to normotensive healthy subjects using conventional and newer 4D-echocardiographic techniques.

## **METHODS**

#### **Study population**

We conducted an observational case-control study at the cardiology outpatient clinic, Al-Zahraa University Hospital, Cairo, Egypt, between January 2019 and February 2020. All participants provided their informed oral consent, and the study was approved by the ethical committee of Al-Azhar University's Faculty of Medicine for Girls.

The study included 150 patients with uncontrolled essential HTN on antihypertensive medications for > 6 months (GI) and 75 age- and sex-matched healthy subjects as the control group. We diagnosed uncontrolled HTN when systolic blood pressure in the office or clinic is 140 mmHg and/or diastolic blood pressure is 90 mmHg on two or more occasions according to the guidelines<sup>6</sup> while using antihypertensive therapy for > 6 months.

We excluded patients with secondary causes of HTN, major clinical illness (as liver cell failure, chronic pulmonary disease and renal failure), major arrhythmias (e.g. atrial fibrillation, sustained or non-sustained ventricular tachycardia), chronic obstructive pulmonary disease, interstitial pulmonary fibrosis, coronary artery disease, congenital heart disease, diabetes mellitus, rheumatic heart disease either moderate to severe valvular regurgitation or stenosis, HF, cardiomyopathies or other complications of HTN e.g. cerebrovascular stroke.

#### History taking and examination

All participants were subjected to history taking and thorough clinical examination. Anthropometric measures (height, weight) were obtained. Body mass index (BMI) and body surface area were calculated, as well as office blood pressure measurements and heart rate.

#### Laboratory investigations

Routine serum creatinine, serum electrolytes (Na<sup>+</sup> and K<sup>+</sup>), lipid profile in addition proteinuria were evaluated in both hypertensive and control groups.

#### Two-dimensional (2D) echocardiography

Two-dimensional echocardiography was performed on all study populations using Vivid E9 (GE Ultrasound, Horton, Norway) ultrasound machine. Cases were examined with a multi frequency (2.5MHz) matrix probe (M3S). Echocardiograms were digitally acquired using a standard protocol with additional RV-focused views in all subjects. All images were digitally stored for later off-line analysis at EchoPAC. GE VERSION 201.

LV parameters were assessed including LV dimensions, EF, LV mass index (LVMI), LV diastolic function using conventional Doppler across mitral valve and tissue Doppler imaging (TDI) at mitral annulus and 2D global longitudinal strain (2D-GLS). In addition, the left atrium (LA) was evaluated using both the diameter and LA volume index (LAVI).

RV functional measures were obtained from M-mode tricuspid annular plane systolic excursion (TAPSE), apical four chamber fractional area change (FAC), calculated as [(end-diastolic area) – (end-systolic area) / end-diastolic area] × 100, and the RV myocardial performance index was calculated by both conventional and TDI myocardial (RV-MPI and TDI-MPI).

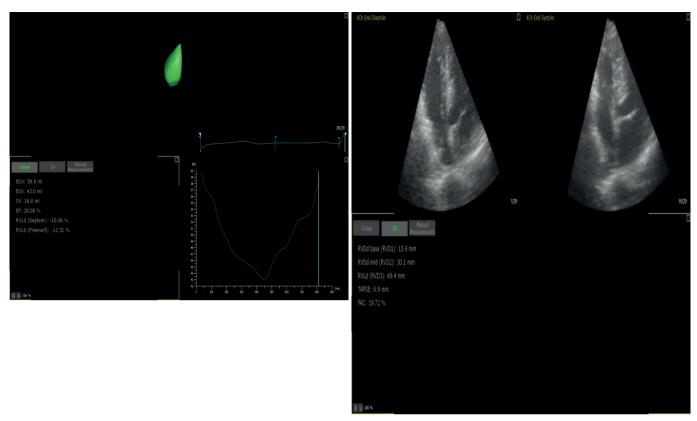
Tricuspid flow velocities were assessed by pulsed-wave Doppler in the apical four-chamber view. The following variables were determined: early diastolic peak flow velocity  $(E_{TV})$ ; late diastolic flow velocity  $(A_{TV})$ ; and their ratio  $(E/A)_{TV}$ <sup>7)</sup> as well as tricuspid regurgitation, maximum velocity and peak systolic gradient to obtain right ventricular systolic pressure (RVSP). TDI was used to obtain RV myocardial velocities in the apical four-chamber view at the lateral segment of the tricuspid annulus to obtain peak tricuspid annular systolic velocity  $(S_{RV})$ , early diastolic velocity  $(E_{RV})$  and late diastolic velocity  $(A_{RV})$ . 2D-RV strain imaging was performed by using 2D images in the apical four-chamber view to assess RV-GLS.<sup>7</sup>

#### 4D echocardiographic imaging of the RV

Using a Vivid E9 (GE Vivid Ultrasound, Horton, Norway) equipped with a 4V probe, six-beat fullvolume 3D data sets ( $\geq$  30 vol/s) were obtained during breath hold. During acquisition, the 12-slice display was used to ensure that the RV was fully included in the data set.<sup>8)</sup> The 4D data sets were exported to a separate workstation with the required software (EchoPAC. GE VERSION 201).

The longitudinal axes of the LV and RV were set in the reference end-diastolic frame to align with the 4D data set. The landmarks corresponding to the aortic annulus diameter was set on the LV apical long-axis view, and then the anterior and posterior junctions of the RV free wall (FW) with the interventricular septum, as well as the septum-to-RV FW distance were set on the RV short-axis view. The software algorithm analyses ultrasound backscatter intensities and adapts a static RV shape model to all the input data, which can be further optimized by the operator. Then, the RV contours are automatically tracked over the entire cardiac cycle using speckle-tracking technology, and automated measurements of RV volumes, EF and strain are provided. Manual corrections on end-systolic and end-diastolic frames are continuously updated on the RV 4D model and then propagated to all the other frames of the cardiac cycle using the derived tracking. RV volumes over time are computed from the dynamic surface model, and maximal and minimal volumes are used to calculate end diastolic volume (EDV), end systolic volume (ESV) and EF (**Figure 1**).

#### **RVP in Uncontrolled Hypertensive Patients**



**Figure 1.** 4D-RV quantification for one of the studies cases showing different RV parameters including RVEDV, RVESV, EF, RVSS, RVFWS, TAPSE and FAC. EF: ejection fraction, FAC: fractional area change, RVEDV: right ventricular end-diastolic volume, RVESV: right ventricular end-systolic volume, RVFWS: right ventricular free wall strain, RVSS: right ventricular septal strain, TAPSE: tricuspid annular plane systolic excursion.

#### **Studies of reproducibility**

For assessment of the obtained echocardiographic parameters reproducibility, images of randomly selected 50 patients from each group were evaluated by two experts in echocardiographic interpretation who were blinded to each other and to the patients' data. Evaluation was performed twice with at least one week interval.

#### **Statistical analysis**

Data obtained from the present study were statistically analyzed using SPSS 25 (IBM, Armonk, NY, USA). Numerical data were presented as mean and standard deviation (SD) and compared using t test, while categorical data were presented as number and percent and compared using  $\chi^2$  test. Pearson's correlation coefficient was used to identify correlations of numerical variables. Interobserver variability was evaluated by inter and intraclass correlation coefficient (ICCC), with ICCC > 0.9 being considered excellent agreement. Receiver operating characteristic (ROC) analysis was used to identify diagnostic power of the investigated parameter. The value of p less than 0.05 was considered statistically significant.

## RESULTS

Clinical characteristics and echocardiographic parameters of the studied cases are shown in **Tables 1** and **2**.

Variables	Group I (n = 150)	Group II (n = 75)	p-value
Male	84 (56)	41 (54.3)	0.171
Age (years)	46.0 ± 7.2	$45.2 \pm 3.8$	0.530
Weight (kg)	80.9 ± 10.8	$72.2 \pm 5.8$	0.010
Height (cm)	166.5 ± 7.1	$165.5 \pm 8.2$	0.612
BMI (kg/m²)	29.2 ± 8.9	$26.4 \pm 6.9$	0.030
SBP(mmHg)	149.3 ± 16.6	113.5 ± 5.9	0.003
DBP (mmHg)	89.4 ± 9.1	$74 \pm 5.9$	0.001
Mean BP (mmHg)	133.4 ± 14.6	111.8 ± 7.9	0.001
Heart rate (bpm)	77.6 ± 14.9	65.9 ± 7.5	0.001
Duration of HTN (months)	50.2 ± 20.1	-	-
Use of BB	45 (30)	-	-
Use of ACEI	120 (80)	-	-
Use of CCB	39 (26)	-	-
Use of diuretics	20 (12.5)	-	-
Hypercholestremia	30 (20)	-	-
Smoking	45 (30)	-	-
Na⁺ (mEq/L)	135.4 ± 6.2	134.8 ± 7.9	0.570
K⁺ (mEq/L)	4.1 ± 0.7	$4.0 \pm 0.2$	0.100
S. Creatinine (mg/dL)	1.1 ± 0.2	0.8 ± 0.2	0.001
Proteinuria (mg/dL)	7.5 ± 4.6	0 ± 0	0.001
S. Cholesterol (mg/dL)	287.9 ± 63.9	$158.1 \pm 34.2$	0.001
Triglycerides (mg/dL)	204.6 ± 53.2	141.8 ± 37.5	0.001
LDL (mg/dL)	110.1 ± 43.6	45.5 ± 14.4	0.001
Hb (gm/dL)	13.1 ± 8.5	13.0 ± 2.2	0.871

Table 1. Baseline clinical characteristics of study population

Values are presented as number (%) or mean  $\pm$  SD.

ACEI: angiotensin converting enzyme inhibitors, BB: beta blockers, BMI: body mass index, CCB: calcium channel blockers, DBP: diastolic blood pressure, Hb: hemoglobin, LDL: low density lipoprotein, SBP: systolic blood pressure.

Hypertensive patients had higher weight, BMI, heart rate and blood pressure measurements (systolic, diastolic and mean) compared to the control group. Moreover, hypertensive patients showed abnormal levels of lipid profile assessed by serum cholesterol, triglycerides, and LDL compared to the control group. Despite that hypertensive patients had higher levels of both serum creatinine and proteinuria relative to the normotensive group, both were within normal range. No significant difference regarding the age, sex, serum electrolytes, and Hb% between both groups (**Table 1**).

Hypertensive patients had significantly higher LVMI, LA diameter, LAVI and E/Ea<sub>LV</sub> compared to the control group while 2D-LV-GLS and average S-LV were significantly reduced in hypertensive group relative to normotensive group. Furthermore, hypertensive patients had significant impairment of 2D RV systolic and diastolic indices including 2D-TAPSE, 2D-RV-GLS, S-RV, RV-MPI (conventional and TDI), E/A<sub>TV</sub> and average E/Ea<sub>RV</sub> compared to the control group. Regarding 4D RV parameters; hypertensive patients showed significant decrease in 4D-right ventricular EF (RV-EF), 4D-FAC, 4D-RV-SS, 4D-FWS and 4D-TAPSE compared to the control group. We found that hypertensive patients had significantly higher 4D-RV-EDV, and RV-ESV in comparison to the control group (**Table 2**).

We demonstrated the incidence of RV systolic dysfunction among hypertensive patients defined by the following parameters: 1) 15% of them had 2D-TAPSE < 17 mm vs. 40% by 4D-TAPSE; 2) 25% of them had 2D-GLS < 19% vs. 42% by 4D septal strain and 35% by 4D FW strain; 3) 35% of hypertensive patients had 4D-EF < 45%; and finally; 4) 25% of hypertensive patients had 2D-FAC. ROC curve was plotted and analysis of the studied cases revealed that the cut-off value of 4D-RV FAC was 35.8% had 89% sensitivity and 88% specificity to define RV systolic dysfunction (**Table 2, Figure 2**).

Variables	Group I (n = 150)	Group II (n = 75)	p-value
IVSd (mm)	12.3 ± 2.4	7.9 ± 1.4	0.001
LVIDd (mm)	$45.5 \pm 4.5$	44.6 ± 3.9	0.111
LVIDs (mm)	29.6 ± 3.4	$28.0 \pm 2.9$	0.110
LVPWd(mm)	$12.0 \pm 2.2$	7.2 ± 1.2	0.001
EF (%)	$66.9 \pm 6.4$	67.4 ± 3.6	0.172
FS (%)	$36.9 \pm 4.2$	$36.7 \pm 2.9$	0.673
LVMI (g/m²)	$106.7 \pm 29.0$	64.6 ± 19.6	0.001
LV RWT	0.5 ± 0.1	0.3 ± 0.1	0.020
LA diameter (mm)	41.2 ± 4.2	34.0 ± 4.4	0.003
LAVI (mL/m²)	37.1 ± 4.8	26.7 ± 37	0.001
E/AMV ratio	$1.0 \pm 0.2$	1.4 ± 0.3	0.050
Average S-LV (cm/s)	5.8 ± 1.0	7.1 ± 0.9	0.002
Average E/Ea <sub>LV</sub>	11.1 ± 2.5	7.7 ± 1.9	0.004
2D-LV-GLS (%)	$18.0 \pm 2.8$	$22.7 \pm 2.5$	0.003
FAC (%)	4.0 ± 0.1	5.0 ± 0.1	0.050
2D-TAPSE (mm)	18.6 ± 3.8	23.9 ± 2.6	0.002
S-RV (cm/s)	9.4 ± 1.7	11.7 ± 1.6	0.003
RV-MPI	0.5 ± 0.1	$0.4 \pm 0.2$	0.040
RV-TD-MPI	0.6 ± 0.2	0.4 ± 0.1	0.002
E/A <sub>TV</sub> ratio	1.1 ± 0.3	1.3 ± 0.3	0.040
TR Vmax (m/s)	$1.0 \pm 0.5$	$0.9 \pm 0.4$	0.110
RVSP (mmHg)	25.1 ± 8.5	23.8 ± 4.3	0.110
Average E/Ea <sub>rv</sub>	6.3 ± 1.7	5.8 ± 1.9	0.050
2D-RV-GLS (%)	20.7 ± 3.2	24.8 ± 2.5	0.030
4D-RV-EDV (mL)	$58.8 \pm 23.4$	$47.2 \pm 10.6$	0.050
4D-RV-ESV (mL)	37.9 ± 17.7	$22.2\pm5.7$	0.010
4D-RV-EF (%)	33.6 ± 10.5	$50.6 \pm 5.0$	0.001
4D-FAC (%)	30.1 ± 11.9	48.3 ± 7.1	0.002
4D-RV-SS (%)	$10.7 \pm 3.3$	17.3 ± 4.0	0.050
4D-RV-FWS (%)	$15.1 \pm 5.6$	$20.9 \pm 4.3$	0.005
4D-TAPSE (mm)	11.4 ± 3.9	$13.5 \pm 2.4$	0.030

Table 2. Baseline echocardiographic parameters of all hypertensive patients and control group

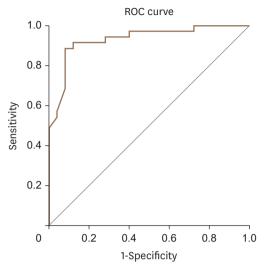
Values are presented as mean  $\pm$  SD.

E/Ea<sub>LV</sub>: early diastolic mitral velocity/average early diastolic velocities at 6 mitral annular sites derived from TDI, E/AMV: early to late diastolic mitral inflow velocities, Average E/Ea<sub>RV</sub>: early diastolic tricuspid velocity/early diastolic velocity at lateral tricuspid annulus by TDI, E/A<sub>TV</sub> ratio: early to late diastolic tricuspid inflow velocities, EF: ejection fraction, FAC: fractional area change, FS: fractional shortening, IVSd: diastolic interventricular septum, LA: left atrium, LAVI: left atrial volume index, LVIDd: end diastolic left ventricular internal diameter, LVIDs: end systolic left ventricular internal diameter, LVMI: left ventricular mass index, LVPWd: diastolic left ventricular posterior wall thickness, LV-RWT: left ventricular relative wall thickness, RV-EDV: right ventricular end-diastolic volume, RV-ESV: right ventricular end-systolic volume, RV-FWS: right ventricular free wall strain, RV-GLS: right ventricular global longitudinal strain, RV-MPI: right ventricular myocardial performance index, RVTD-MPI, RVSP: right ventricular septal wall strain, SLV: average of systolic velocities at 6 mitral annular sites derived from TDI, S-RV: peak systolic velocity of lateral tricuspid annulus by TDI, TAPSE: tricuspid annular plane systolic excursion.

Among the overall population of the study, we found a positive correlation between 4D-RV volumes (4D-EDV and 4D-ESV) and RV TD-MPI (r = 0.309, p = 0.02) and (r = 0.395, p < 0.01), respectively. 4D-RV-ESV was negatively correlated with 2D-FAC (r = -0.374, p = 0.01) and 2D-TAPSE (r = -0.345, p = 0.01). There was positive correlation between LVMI and both RV TD-MPI (r = 0.396, p = 0.01) and 4D-RV-ESV (r = 0.393, p = 0.01). Meanwhile, there was negative correlation between LVMI and 2D/4D-RV-FAC (r = -0.468, p = 0.01 and r = -0.368, p = 0.01 respectively), 2D/4D-TAPSE (r = -0.449, p = 0.01 and r = -0.313, p = 0.01 respectively), 2D-RV-GLS and 4D-RVEF (r = -0.357, p = 0.05 and r = -0.443, p = 0.01 respectively).

#### **Reproducibility of 4D-RV parameters**

The mean time between repeated measurements by two observers was  $10 \pm 2.6$  days. ICCC of different 4D-RV parameters between observers was evaluated with satisfactory agreement



Diagonal segments are produced by ties.

**Figure 2.** Sensitivity and specificity of 4D fractional area change in diagnosis of right ventricular systolic dysfunction in patients with hypertension (AUC = 0.931). AUC: area under the ROC curve, ROC: receiver operating characteristic.

## DISCUSSION

The present study revealed that hypertensive patients had RV systolic dysfunction defined by significant reduction of both 2D-TAPSE (15%) and 2D-FAC (25%). Moreover, hypertensive patients had significant reduction of RV annular systolic velocity (S-RV) using TDI and significant impairment of RV-GLS (25%) compared to the control group.

Our results were concordant to the findings from Hanboly,<sup>9)</sup> who compared 80 patients with mild to moderate untreated systemic HTN to 40 healthy controls. TAPSE was found to be lower in hypertensive patients (18 mm) than in the healthy group.

Our results, on the other hand, contradicted those of Cicala et al.,<sup>10)</sup> who concluded that the values of TAPSE were similar between both hypertensive and normotensive healthy persons.

The current findings were consistent with those of Pedrinelli et al.,<sup>5</sup> who found that TDI significantly reduced systolic velocities in hypertensive patients compared to healthy subjects.

In addition, Ayoub et al.,<sup>11</sup> reported that 2D-RV-GLS was considerably lower in patients with systemic HTN in comparison to the control group ( $19.5 \pm 2.4\%$  vs.  $20.8 \pm 1.6\%$ ).

As compared to the control group in the current study, hypertensive patients had RV diastolic dysfunction as measured by a significant reduction in E/A ratio (using pulsed Doppler at tricuspid inflow). Furthermore, as compared to healthy subjects, hypertensive patients had a substantial increase in RV E/Ea indicating RV diastolic dysfunction.

Our findings are consistent with those of Myslinski et al.,<sup>12)</sup> who mentioned that RV diastolic dysfunction had been observed in hypertensive patients compared to control volunteers (using conventional pulsed Doppler modality).

Unlike the LV multidirectional strain, which can be longitudinal, circumferential, or radial, the RV strain primarily refers to longitudinal strain evaluation. The majority of RV fibers in the subendocardial layer are directed longitudinally, and their shortening is primarily responsible for the RV EF. Due to circumferential fibers of the sub-epicardial layer, RV remodeling is characterized by gradual reduction of longitudinal function with preserved and even enhanced transversal function at an early stage. As a result, RV longitudinal strain can be a sensitive RV parameter that can detect subtle changes at subclinical levels. This also means that FAC remains within the normal range for a long time and deteriorates last in the cascade.<sup>13</sup>

Furthermore, our findings were consistent with those of previous studies by Cicala et al.,<sup>10</sup> and Hanboly.<sup>9)</sup> who observed a significant reduction in RV E/A ratio in hypertensive patients compared to control group.

In our research, impaired RV systolic function (defined by reduced RV-EF, TAPSE and RV-GLS values) was closely correlated to higher LVMI. Moreover, RV-MPI was positively correlated with LVMI in the overall population.

TAPSE was negatively correlated with LVMI (r = -0.34, p < 0.0001), according to Ojji et al.,<sup>14</sup> who investigated RV systolic function in 611 hypertensive HF patients.

The most common clinical imaging method for evaluating the RV function is 2D echocardiography. However, the RV had a complex geometric structure, which included a crescent shape and an outspread inflow and outflow tract, necessitating the use of several scan planes to estimate RV size and function. As a result, current echocardiographic techniques are insufficient for accurately measuring RV volumes and function.<sup>15)</sup> The 4D anatomy of the RV can be visualized using 4D echocardiography, which can display both longitudinal and transverse movements at the same time.<sup>16)</sup> The feasibility and precision of 4D echocardiography, on the other hand, have not been thoroughly investigated.<sup>17)</sup> The American Society of Echocardiography and the European Association of Cardiovascular Imaging recently revised their guidelines for cardiac chamber quantification, stating that 4D measurement of RV volumes is recommended when RV volumes are clinically significant in laboratories with experience in 4D echocardiography.<sup>18)</sup>

CMR is currently the most reliable tool for measuring RV structure, and it is used as a standard for every new imaging technique.<sup>19)</sup> While CMR is the gold standard for measuring RV volume, it is limited in its use for monitoring RV function due to cost, procedure length, and patients with implanted devices. Furthermore, CMR necessitates a long breath hold, which can be painful for patients with HF. Echocardiography, on the other hand, is easy, inexpensive, and tolerable for repeated exams, even in patients with implantable devices.<sup>20)</sup>

We found that hypertensive patients had higher incidence of RV systolic dysfunction when 4D-echocardoagphic indices were used. Forty percent of patients had 4D-TAPSE < 17 mm; 42% had impaired 4D septal strain and 35% had impaired 4D FW strain. A cut-off value of 35.8% was used to define impaired 4D-FAC with 89% sensitivity and 88% specificity among hypertensive patients in our study. Accordingly, 45% of hypertensive patients had RV systolic dysfunction measured by 4D-FAC.

We observed that hypertensive patients had increased 4D-RV volumes (both EDV and ESV) compared to the control group. 4D-RV-ESV was negatively correlated with either 2D-FAC or 2D-TAPSE. In other word, increased 4D-RV-ESV had been associated with more impaired RV

systolic function defined by 2D-FAC or TAPSE. Moreover, we noticed that LVMI was positively correlated with 4D-ESV but negatively correlated with either 2D/4D FAC or 2D/4D-TAPSE meaning that with higher LVMI, 4D-RV-ESV is increased while RV systolic function is reduced (both FAC and TAPSE) detected by both 2D and 4D modalities.

According to one study, 4D echocardiography may be used to image the RV in a significant proportion of adult patients with unselected pathology (85%).<sup>15)</sup> According to Tadic et al.,<sup>21)</sup> LV geometry has a major impact on RV structural, functional, and mechanical remodeling. Furthermore, they reported that eccentric and concentric LVH groups had significantly higher 3D-RV volumes. This is clinically significant since the Multi-Ethnic Analysis of Atherosclerosis analysis revealed that RV remodeling is negatively correlated with overall mortality in the general population for the first time.<sup>22)</sup>

Findings from Tadic et al.,<sup>21)</sup> revealed that 4D RV volumes increased gradually from normal LV geometry to concentric LVH, while RV systolic function, as measured by 4D RV EF, decreased in the same direction. RV enlargement, as measured by RV EDV derived from magnetic resonance imaging (MRI) and RV EF, were not predictors of HF or death, according to Kawut et al.<sup>22)</sup> RV-EDV was found to be only marginally significant as a predictor of a negative outcome.<sup>21)</sup>

Overstimulation of both the rennin-angiotensin aldosterone system (RAAS) and the sympathetic nervous system, increased development of growth factors, oxidative stress, or endothelial dysfunction are among the potential mechanisms that could explain the connection between arterial HTN and RV remodeling.<sup>21)</sup> These bio-humoral mechanisms (most notably RAAS) are related to eccentric and concentric LVH patterns<sup>23)</sup> as well as the major effect of RAAS on RV remodeling.<sup>24)</sup> The interaction of the sympathetic nervous system, the RAAS, and insulin sensitivity, which causes LV and RV hypertrophy, diastolic dysfunction, and deformation impairments, may explain the connection between LV geometry and RV remodeling. The interdependence of the ventricles is especially important in explaining this connection.<sup>25)</sup>

Four dimensional-modality trans-thoracic echocardiography (TTE) showed a higher incidence of RV affection than 2D-modality TTE. We suggested that 4D echocardiography with 4D-strain imaging would be more useful for assessing RV morphology and function in hypertensive patients, as 4D echocardiography could quantify RV volumes and function without making geometric assumptions compared to 2D modality.

#### Limitations

- Since the number of patients was relatively small, the number of patients in subsequent studies would need to be increased.
- Global strain was used to measure 2D-RV strain rather than FW strain, which may be affected by the sharing of interventricular septum fibers in both ventricles.
- In the case of the 4DSTE technique, the acquisition of 4D data sets was constrained by the acoustic windows. Furthermore, due to dropouts and translation artifacts, identifying the RV endocardial border in 4DSTE was difficult. During the study, several manual adjustments were made, reducing the reproducibility of the results.
- The lack of gold standards for 4D validation, such as cardiac MRI.
- Further studies are recommended to un-reveal the effect of structural and functional changes in RV in hypertensive patients on cardiovascular morbidity and mortality.

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