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Right atrial structure and function in patients with hypertension and with chronic heart failure

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Abstract

Background—Prior studies have shown that both heart failure (HF) and atrial fibrillation (AF) are factors that impact left atrial function and structure. However, right atrial (RA) function measured as RA emptying fraction (RAEF) on echocardiography has not been analyzed systematically in a chronic HF population. The aim of this study was to assess RA volume index (RAVI) and RAEF in patients with chronic HF and patients with hypertension (HTN) and to relate these findings to other cardiopulmonary ultrasound parameters and 12-month outcomes.

Methods and Results—In this prospective observational study, we identified 119 patients with chronic HF (64 patients without a history of AF [HF without AF], 55 with AF [HF with AF]), and 127 patients with HTN but without important cardiac disease who underwent routine outpatient transthoracic echocardiography. We found that RAEF was impaired in patients with HF without AF compared to patients with HTN (35% $\pm$ 2 vs 50% $\pm$ 1, $P < .001$), whereas RAVI did not differ between these two groups. Lower RAEF was associated with larger RAVI and higher estimated RA pressures but not with a higher degree of pulmonary congestion by lung ultrasound. Both lower RAEF and higher RAVI were associated with an increased risk of 12-month HF

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DISCLOSURES

None.

DISCLAIMER

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SUPPORTING INFORMATION

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hospitalizations or all-cause death (age, sex, and AF adjusted HR: 4.07, 95% CI: 1.69–9.79; $P = .002$, vs 2.74, 95% CI: 1.15–6.54, $P = .023$).

Conclusions—In an outpatient HF cohort, both lower RAEF and increased RAVI were associated with other markers of impaired cardiac function and 12-month adverse events.

Keywords

atrial fibrillation; echocardiography; heart failure; right atrium

1 | INTRODUCTION

Atrial remodeling is a common response to heart failure (HF) caused by elevated filling pressures due to pressure and/or volume overload. Along with structural adaptations, functional changes have also been observed in these patients.^{1–3} Similarly, atrial function deteriorates with increasing electrical burden of atrial fibrillation (AF).⁴ Prior reports have described left atrial (LA) structure and function in patients with and without HF.^{1,4–6} Both increased LA volumes (LAVI) and reduced LA emptying fractions (LAEF) have been identified as prognostically important markers for HF hospitalizations and AF.^{6–9}

In contrast to the LA, right atrial (RA) structure and function are not as well described in patients with chronic HF, although RA volumes have been identified as an independent predictor of adverse events in patients with HF with reduced ejection fraction (HFrEF) assessed on both MRI and echocardiography.^{10,11} An inverse association between increased RA volume index (RAVI) and impaired RA emptying fraction (RAEF) has been reported in patients with pulmonary arterial hypertension (PAH) assessed by either echocardiography or MRI.^{12,13} However, data on the association between RAVI and RAEF in patients with HF are lacking.

In this study, we assessed RA structure and function in patients with chronic HF stratified by AF and patients with hypertension (HTN) without HF. In addition, we related these findings to other echocardiographic parameters and signs of pulmonary congestion on lung ultrasound. In an exploratory analysis, we investigated the relationship between impaired RA structure and function in patients with HF on 12-month survival and HF hospitalization rate. We hypothesized that RAEF differs between patients with HTN without HF and patients with HF and that impaired RAEF is associated with adverse outcomes in patients with HF.

2 | METHODS

2.1 | Study population

We conducted a prospective, single-center observational study that enrolled adult patients referred for routine outpatient transthoracic echocardiograms (TTEs) at an academic hospital between February 2014 and October 2015. Inclusion criteria were as follows: adult patients with either HTN or HF scheduled for an elective outpatient echocardiogram. From this cohort, we excluded patients with a history of heart transplantation or significant lung disease (eg, pulmonary fibrosis, cancer involving the lungs or chest, pneumonia), liver

failure, with current pregnancy, who required hemodialysis or with same-day admission to the hospital. For the purpose of this analysis, we divided patients from this population into three groups:

HF without AF: Patients with a diagnosis of chronic HF independent of left ventricular ejection fraction (LVEF) according to Framingham criteria¹⁴ and without prior AF.

HF with AF: Patients with a diagnosis of chronic HF independent of LVEF according to Framingham Criteria with a history of AF or AF at time of echocardiography.

HTN: Patients with a diagnosis of HTN (blood pressure >140/90 mm Hg at time of echocardiography, a history of hypertension, or taking blood pressure-lowering medications) but without relevant cardiac disease as detailed below. We excluded patients with LVEF <50%, AF, pacemaker, implanted cardioverter-defibrillator (ICD), relevant valve disease (more than mild), or prior myocardial infarction. Detailed exclusion criteria are provided in the Data S1. For the lung ultrasound analysis, we further excluded all patients with postradiation changes on CT or chest radiography (n = 17).

This study complied with the Declaration of Helsinki and the Partners Institutional Review Board approved the research protocol. Written informed consent was obtained from all study subjects. We used the STROBE checklist to describe the data collection and to identify potential biases (see Data S1).

2.2 | Clinical and demographic data

Clinical, demographic, and laboratory data were extracted from the patients' hospital records by a trained research assistant. Dyspnea was assessed at time of enrollment using a questionnaire asking for shortness of breath while lying flat, and/or climbing a flight of stairs over the past 2 weeks. If patients answered one of the questions with yes, they were categorized as having any dyspnea or otherwise as having no dyspnea.

2.3 | Echocardiographic analysis

Transthoracic echocardiograms were performed with standard ultrasound equipment by three different manufacturers (General Electric, Milwaukee, WI, USA; Philips, Bothell, WA, USA; and Siemens, Erlangen, Germany) using 2–5 MHz phased array transducers. To assess cardiac structure and function, studies were analyzed off line using standard echocardiographic software (Syngo Dynamics, Siemens, Malvern, PA, USA). Image analysis for each component of the examination was performed by one of four investigators according to the current guidelines by the American Society of Echocardiography,¹⁵ blinded to lung ultrasound (LUS) and clinical data.

Right atrial pressures were estimated based on the diameter and inspiratory collapse of the IVC. Pulmonary arterial systolic pressures (PASP) were calculated from the maximal tricuspid regurgitation velocity (TRV) by adding the estimated RA pressure.¹⁵

Right atrial volumes were measured from the apical four-chamber view using the single plane area-length method at end-systole and end-diastole, defined by opening and closure of

the tricuspid valve and indexed to body surface area.^{16,17} RA length was measured from the middle of the tricuspid valve annulus and parallel to the interatrial septum (Figure 1). RA volume was calculated as follows: $0.85 \times (\text{RA four-chamber area}^2 \div \text{RA length})$. For all individuals without a history of AF, RAVI was measured over two representative cardiac cycles and then averaged.

For individuals with current AF (at the time of TTE) or a history of AF, RAVI measurements of three cardiac cycles were obtained and then averaged.

All RA measurements were performed by one investigator (MP). We assessed intra- and inter-rater agreement for RAEF and RAVI in a sample of 26 randomly selected patients using the Bland-Altman method.

For intra-rater agreement, the mean difference for RAEF was -0.7% (95% limits of agreement: -10.3 to 9.0). For inter-rater agreement of RAEF the mean difference was -4.3% (95% limits of agreement: -17.2 to 8.6) (Figure S1B).

For intra-rater agreement, the mean difference for RAVI was -2.0 mL/m^2 (95% limits of agreement: -6.3 to 2.3). For inter-rater agreement of RAVI, the mean difference was 0.6 mL/m^2 (95% limits of agreement: -7.5 to 8.6) (Figure S1A).

2.4 | Lung ultrasound analysis

At the time of TTE, LUS examinations were performed in 8 zones by two trained investigators using the same ultrasound equipment and transducers as for echocardiograms. The highest number of B-lines obtained in one intercostal space per zone was counted off line by a single investigator who was blinded to TTE data. The sum of B-lines in all 8 zones was considered as the total number of B-lines as previously described.^{18,19}

2.5 | Outcomes

We collected outcome data in the subset of patients with HF. HF hospitalizations were captured through follow-up phone calls, contacting the patients' primary care physicians or cardiologists and review of electronic medical records and adjudicated by a physician (see Data S1).²⁰ Time to first event was used for all outcome measures (composite of HF hospitalization or all-cause mortality) over 12 months. All-cause mortality was validated through the institution's electronic medical records, the social security death index, and obituaries.

2.6 | Statistical analyses

Descriptive statistics for continuous variables are expressed as either medians (IQR) (for Table 1) or estimated medians/means ($\pm$ standard error) to estimate and interpret adjusted predictions. Categorical variables are presented as counts and percentages unless otherwise noted. Between-group comparisons for baseline characteristics were assessed using Wilcoxon rank-sum tests for continuous variables and chi-square and Fisher's exact tests for categorical variables as appropriate.

To examine the association between RAEF and other echocardiographic and LUS variables, we divided all patients with HF irrespective of AF into two groups on the basis of the median value for RAEF due to the absence of an established cutoff value. For RAVI, we divided the HF cohort into two groups using the upper limit of normal (32 mL/m^2) as cutoff as suggested by the current ASE guideline.¹⁵ Quantile and linear regression were used to determine the association between the two RAEF and RAVI groups and other echocardiographic and LUS measures after adjusting for age, sex, and AF as possible confounders.^{21,22} Due to the high percentage of patients with cancer in the HTN cohort, a sensitivity analysis that excluded all patients with active cancer was performed investigating the differences of RAVI and RAEF between the three study groups. For the outcome analysis, we used unadjusted and adjusted Cox proportional hazard models (adjusting for age, sex, and AF) to investigate the effects of RAEF and RAVI in HF patients on event-free survival. Harrell's C-statistic was calculated for each of the models. All analyses were performed using Stata SE, version 14.1 (StataCorp., College Station, TX, USA, 2015) with P -values $<.05$ considered statistically significant.

3 | RESULTS

3.1 | Study population

We identified 127 patients with HTN and without important cardiac comorbidities, 64 patients with HF, and without a history of AF and 55 patients with HF and AF (Figure 2). Baseline characteristics of this study population are presented in Table 1. Patients with HF were older and more likely to have impaired renal function than patients with HTN. Patients with HF and AF were older than those without AF and more likely to be male. Compared with the HF groups, a higher proportion of patients had active cancer in the HTN cohort (48% vs 4%, $P < .001$).

Heart failure patients with a lower RAEF were older (median 74 vs 66 years, $P = .004$) and more likely to have had prior AF (66% vs 28%, $P < .001$) (see Data S1). Rates of prior stroke or transient ischemic attack (TIA) were similar in the two groups.

3.2 | Echocardiographic analyses by study group

Right atrial emptying fraction was impaired in patients with HF without AF compared to patients with HTN ($35\% \pm 2$ vs $50\% \pm 1$, $P < .001$), whereas RA structural measures were similar (Figure 3). RAVI of HF patients with AF were larger compared to RAVI of HF patients without AF ($40 \text{ mL/m}^2 \pm 2$ vs $26 \text{ mL/m}^2 \pm 2$, $P < .001$) and RAEF were lower ($18\% \pm 2$ vs $35\% \pm 2$, $P < .001$). The direction and significance of these results remained stable when patients with active cancer were excluded from the analyses. Results were similar when RAEF and RAVI were analyzed stratified by HFpEF and HFrEF (HFpEF $29\% \pm 3$ vs HFrEF $25\% \pm 2$, $P = .22$ and HFpEF $32 \text{ mL/m}^2 \pm 3$ vs HFrEF $36 \text{ mL/m}^2 \pm 2$, $P = .34$). Patients with HF without AF had larger LAVI and lower LAEF than the HTN patients ($25 \text{ mL/m}^2 \pm 2$ vs $20 \text{ mL/m}^2 \pm 1$, $P = .019$ and $44\% \pm 2$ vs $57\% \pm 1$, $P < .001$). LVEF was similar in HF patients with and without AF ($46\% \pm 2$ vs $43\% \pm 2$, $P = .35$).

By contrast, measures of RV systolic function were largely similar between the 3 groups, with the exception of RV S' which was lower in patients with HF without AF compared to the HTN patients ($9 \text{ cm/s} \pm 1$ vs $11 \text{ cm/s} \pm 1$, $P = .002$). TAPSE was only impaired in HF patients with AF compared to the HF without AF group ($16 \text{ mm} \pm 1$ vs $21 \text{ mm} \pm 1$, $P = .011$). While the number of patients with ≥ 3 B-lines was similar in the HF groups, a higher proportion of patients with HF had ≥ 3 B-lines on LUS than those with HTN (39% vs 12%, $P = .002$). Echocardiographic and LUS data by study group are presented in Table 2.

3.3 | Analyses by RAEF and RAVI group and association with ultrasound measures

The median RAEF in our HF cohort was 30% (IQR 14–38), and median RAVI was 31 mL/m^2 (IQR 23–45). Patients with RAEF $<30\%$ had larger RA volumes than patients with RAEF $\geq 30\%$ ($39 \text{ mL/m}^2 \pm 3$ vs $29 \text{ mL/m}^2 \pm 3$, $P = .032$). However, 28% of the patients with RAEF $<30\%$ had RAVI $<32 \text{ mL/m}^2$. Lower RAEF was also associated with larger IVC diameter ($2.0 \text{ cm} \pm 0.1$ vs $1.6 \text{ cm} \pm 0.1$, $P < .001$) and higher estimated RA pressure (10 ± 1 vs 6 ± 1 , $P < .001$).

In the HF population, lower RAEF was associated with impaired RV systolic function, including TAPSE and RV S' . Patients with lower RAEF also had larger LAVI ($35 \text{ mL/m}^2 \pm 2$ vs $29 \text{ mL/m}^2 \pm 2$, $P = .047$) and lower LAEF ($31\% \pm 3$ vs $41\% \pm 3$, $P = .010$) but similar LVEF. Larger RAVI was associated with larger LAVI ($37 \text{ mL/m}^2 \pm 3$ vs $26 \text{ mL/m}^2 \pm 3$, $P = .010$) and larger IVC diameters (2.1 ± 0.1 vs 1.6 ± 0.1 , $P = .002$). Measures of RV or LV function were comparable between the two RAVI groups.

Lung ultrasound findings were similar across the RAVI and RAEF groups. Echocardiographic and LUS data by RAEF group are shown in Table 3.

3.4 | Outcome analysis by RAEF and RAVI group

In the HF cohort, we observed primary outcome events in 30 patients (25%) during the 12-month follow-up period. The unadjusted and adjusted risk of the composite outcome of HF hospitalization and all-cause mortality for patients with HF is shown in Table 4.

Heart failure patients with RAVI $>32 \text{ mL/m}^2$ had a more than 2.5-fold risk of the primary outcome than patients with lower RAVI (adjusting for age, sex, and AF; HR: 2.74 (1.15–6.54), $P = .023$) (Figure 4A). Patients with a RAEF $<30\%$ had a fourfold risk of the primary outcome compared to patients with a RAEF $\geq 30\%$ (adjusting for age, sex, and AF; HR 4.07 (95% CI: 1.69–9.79; $P = .002$) (Figure 4B).

4 | DISCUSSION

In this prospective study, we observed three main findings. First, in contrast to RAVI, RAEF was impaired in patients with HF without AF compared to the HTN control group. Second, lower RAEF was associated with other markers of impaired cardiac function but not with LUS findings of pulmonary congestion. Finally, in an exploratory analysis both larger RAVI and lower RAEF were associated with 12-month HF hospitalizations or death irrespective of age, sex, and prior AF.

4.1 | Pathophysiologic considerations regarding RAVI and RAEF

Decreased LAEF and increased LAVI have been identified as useful parameters to evaluate cardiac performance especially in patients at risk for HF.^{1,5,9} In a larger epidemiologic study that analyzed LA structure and function in a spectrum of cardiovascular risk, HF patients demonstrated both higher LAVI and lower LAEF compared to HTN patients or patients free of cardiac risk factors.¹ However, the role of RAVI and RAEF in the pathophysiology of chronic HF has not been analyzed systematically. A small prior study compared RA systolic strain and strain rates of patients with HF with reduced LVEF to healthy adults and found that these parameters were impaired in patients with HF.²³

Similarly, in our analysis, RAEF was reduced in patients with HF compared to those with HTN, in contrast to RAVI; thus, changes in RA volume may reflect varying degrees of compensation whereas impairment of RA function as measured by RAEF may be a more specific early marker of right heart decompensation in ambulatory patients with HF. Conversely, both LAVI and LAEF were significantly different between patients with HTN and those with HF without AF, suggesting that in patients with predominantly left-sided HF, both increased LA volume and impaired LA function are sensitive markers of reduced cardiac reserve.

While we did not perform strain measurements of the RA in this study, this could provide further insights into RA function in patients with HF and warrants further investigation.

4.2 | RAVI and RAEF in patients with AF

Atrial fibrillation is a common finding especially in older patients with chronic HF.²⁴ Decreased LAEF has been identified as an independent risk factor for the occurrence of AF.⁸ In addition, larger RAVI and lower RAEF have been shown to be a predictor of recurrence of AF after direct current cardioversion and were superior to LA parameters in those studies.^{25,26}

In this analysis, RAVI of HF patients with AF was larger and RAEF was lower compared to the HF patients without AF. While there was no significant difference in the prevalence of cerebrovascular events between the HF groups and between the RAEF groups at baseline, we did not collect data on subsequent events. However, RAVI and RAEF are easy to measure with standard echocardiographic equipment and might provide important additional information regarding right heart function in patients with HF and those with AF.

Whether RAVI and RAEF could improve risk stratification in patients at risk for cerebrovascular events, including those with HF, beyond LA structure and function should be analyzed in future research investigations.

4.3 | Echocardiographic correlates of impaired RAEF

Right atrial emptying fraction has been investigated in patients with PAH in prior studies and was associated with other echocardiographic, hemodynamic, and laboratory parameters of cardiac function as well as 6-minute walk distance.^{12,13,27} In this current study, we were able to show that in patients with chronic HF, lower RAEF was associated with larger RAVI.

Interestingly, among the patients with RAEF <30%, 28% had RAVI <32 mL/m². This implies that measuring only RAVI might miss a decline in RA function in some patients.

The association of lower RAEF with lower TAPSE and RV S' as measures of RV systolic function in our HF cohort confirms and extends the reported relationship between reduced RA and RV systolic function that has been previously shown in patients with PAH.^{12,13} However, we did not observe an association between RAEF and RV fractional area change. This might be in part because the free wall of the RV is often obscured by the lung which complicates tracing the endocardial borders and could result in imprecise measurements.

Increased LAVI has been associated with more B-lines as a sign of pulmonary congestion on lung ultrasound in patients with chronic HF.¹⁸ Although we observed that lower RAEF was associated with lower LAEF and larger LAVI, as markers of impaired left-sided cardiac function, there was no significant relation of lower RAEF with a higher number of B-lines on lung ultrasound indicating that pulmonary congestion is primarily a symptom of impaired left heart function.

4.4 | Prognostic value of RAVI and RAEF

Prior studies of patients with HFrEF demonstrated that increasing RAVI is an independent predictor of HF hospitalizations and death.^{10,11} Moreover, increased RA sphericity indices assessed on 3D echocardiography were linked to adverse clinical outcomes in patients with PAH.²⁸ Additionally, studies in PAH cohorts showed an association between impaired RAEF and worse outcomes.^{12,13} Although the follow-up period was shorter with fewer events than in these studies, we observed the same trend for RAVI and RAEF in this chronic HF cohort. Our findings suggest that RAEF may provide prognostic information in HF patients with predominantly left heart disease. Whether RAEF provides incremental value over RAVI or established markers of decompensation, should be investigated in larger studies.

4.5 | Limitations

This was a single-center study with a relatively small sample size but well-defined study cohorts. Measures of RA structure and function were not compared to other imaging methods, such as cardiac MRI to further validate our results. As this was an outpatient cohort, patients did not undergo physical examination including assessment of NYHA class at the time of echocardiographic examination. However, patient-reported symptoms were prospectively collected. In addition, NT-proBNP values were only available in 49 patients because this parameter is not routinely assessed at our institution for outpatient visits. The HTN group had a high number of patients with active cancer. However, in a sensitivity analysis that excluded patients with cancer the results with respect to RAVI and RAEF in relation to the three study groups remained stable. Our measures of RAVI were larger than LAVI which might be explained by the fact that these two measures were assessed using two different techniques (monoplane area-length method vs biplane Simpson's method of disks) and that measurements of the LA were not averaged over 3 cardiac cycles in contrast to RA measurements. Nonetheless, RAVI demonstrated overall good reproducibility and inter-observer agreement was consistent with prior studies.¹²

However, inter-observer agreement was less robust for RAEF due to a small number of outliers.

5 | CONCLUSION

In this study of outpatient HF patients, both lower RAEF and increased RAVI were associated with other markers of impaired cardiac function by echocardiography and 12-month adverse events, but not with sonographic findings of pulmonary congestion. Whether RAEF provides incremental value over other markers of decompensation, should be evaluated in future studies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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FIGURE 1.
Example of right atrial area and right atrial length measured at end-systole

FIGURE 2.

Study flow diagram.

AF = atrial fibrillation; HF = heart failure; HTN = hypertension; LVEF = left ventricular ejection fraction; RAEF = right atrial emptying fraction; TTE = transthoracic echocardiogram;

*see Data S1

FIGURE 3.

A and B, Box plot comparing RAVI and RAEF by study group (n = 246). A, RAVI: $P = .70$ comparing HTN to HF without AF and $P < .001$ comparing HF without AF to HF with AF after adjusting for age and sex. B, RAEF: $P < .001$ between all groups after adjusting for age and sex. AF = Atrial fibrillation; HF = heart failure; HTN = hypertension; RAEF = right atrial emptying fraction; RAVI = right atrial volume index

FIGURE 4.

A and B, Cumulative incidence of HF hospitalization or all-cause mortality in patients with HF (n = 119) by RAVI and RAEF group. HF = heart failure; RAEF = right atrial emptying fraction; RAVI = right atrial volume index

TABLE 1

Baseline characteristics of the overall cohort (n = 246)

Clinical characteristics	N	Hypertension (n = 127)	Heart failure (n = 119)		P-value*	P-value**
		HTN without AF (n = 127)	HF without AF (n = 64)	HF with AF (n = 55)		
Age (years)	246	61 (52–70)	69 (57–76)	74 (64–81)	.002	.035
Men	246	55 (43%)	35 (55%)	42 (76%)	.14	.014
Race	246				.014	.46
White		85 (67%)	54 (84%)	49 (89%)	.009	.40
Black		13 (10%)	6 (9%)	2 (4%)	.73	.21
Other		29 (23%)	4 (6%)	4 (7%)	.004	.82
BMI (kg/m ²)	246	28 (25–31)	27 (25–32)	27 (24–30)	.77	.19
Heart rate at time of echo (beats/min)	246	68 (58–77)	67 (60–78)	70 (60–78)	.94	.78
Systolic BP at time of echo (mm Hg)	234	136 (122–151)	124 (113–141)	130 (115–141)	<.001	.63
Diastolic BP at time of echo (mm Hg)	234	76 (67–82)	71 (62–77)	72 (62–80)	.006	.65
Any dyspnea	230	58 (49%)	38 (63%)	35 (67%)	.07	.66
Medical history						
HFpEF (EF ≥ 50%)	246	N/A	23 (36%)	18 (33%)	–	.71
Hypertension	246	127 (100%)	56 (88%)	49 (89%)	–	.79
Diabetes mellitus	245	23 (18%)	19 (30%)	21 (38%)	.07	.33
Myocardial infarction	246	N/A	14 (22%)	13 (24%)	–	.81
CABG	246	N/A	9 (14%)	17 (31%)	–	.044
Stroke/TIA	246	3 (2%)	6 (9%)	4 (7%)	.06	.75

Clinical characteristics	N	Hypertension (n = 127)		Heart failure (n = 119)		P-value *	P-value **
		HTN without AF (n = 127)	HTN with AF (n = 55)	HF without AF (n = 64)	HF with AF (n = 55)		
Prior HF hospitalization	246	N/A		34 (53%)	26 (47%)	–	.52
COPD	246	5 (4%)		2 (3%)	6 (11%)	1.00	.14
Sleep apnea	246	11 (8%)		8 (13%)	13 (24%)	.44	.15
Active cancer	200	49 (48%)		2 (4%)	2 (4%)	<.001	1.00
Laboratory data							
Sodium (mmol/L)	194	139 (137–141)		140 (138–142)	140 (138–141)	.18	.83
eGFR (mL/min/1.73 m ²)	196	80 (63–107)		61 (41–86)	47 (40–60)	<.001	.041
Hemoglobin (g/L)	184	129 (115–143)		129 (125–145)	130 (104–136)	.17	.11
Albumin (g/L)	153	42 (40–44)		43 (38–44)	41 (39–42)	.79	.28
NT-proBNP 125 ng/L (n,%)	49	–		16 (80%)	28 (97%)	–	.08

Categorical variables are presented as count (%) and continuous variables as median (IQR) unless otherwise noted.

HTN = hypertension; HF = heart failure; AF = atrial fibrillation; BMI = body mass index; BP = blood pressure; HFpEF = HF with preserved ejection fraction; CABG = coronary artery bypass graft; TIA = transient ischemic attack; COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate.

* P-value comparing HF without AF and HTN.

** P-value comparing HF without AF and HF with AF.

TABLE 2

Echocardiographic and lung ultrasound measurements by study group (n = 246)

	Hypertension (n = 127)		Heart failure (n = 119)		P-value*	P-value**
	N	HTN without AF (n = 127)	HF without AF (n = 64)	HF with AF (n = 55)		
RA structure and function						
RA length (cm)	246	4.9 (0.1)	4.9 (0.1)	5.8 (0.1)	.87	<.001
RA width (cm)	246	3.9 (0.1)	4.0 (0.1)	4.5 (0.1)	.40	.003
RA area (cm ²)	246	16.7 (0.5)	17.0 (0.7)	22.4 (0.8)	.75	<.001
RA volume index (mL/m ²)	246	25 (2)	26 (2)	40 (2)	.70	<.001
RA emptying fraction (%)	246	50 (1)	35 (2)	18 (2)	<.001	<.001
IVC diameter (cm)	228	1.6 (0.1)	1.7 (0.1)	1.9 (0.1)	.57	.06
Estimated RA pressure (mm Hg) ^a	228	6 (1)	7 (1)	8 (1)	.013	.21
LA structure and function						
LA volume index (mL/m ²)	243	20 (1)	25 (2)	35 (2)	.019	<.001
LA emptying fraction (%)	243	57 (1)	44 (2)	30 (2)	<.001	<.001
LV structure and function						
Septal wall thickness (cm)	240	1.1 (0.1)	1.1 (0.1)	1.1 (0.1)	.63	.99
LV mass index (g/m ²)	240	85 (3)	119 (5)	110 (5)	<.001	.18
LVEF (%)	246	62 (1)	43 (2)	46 (2)	<.001	.35
E/e′	220	10 (1)	15 (1)	13 (1)	<.001	.12
RV structure and function						
RV S′ (cm/s)	216	11 (1)	9 (1)	7 (1)	.002	.010

	N	Hypertension (n = 127)		Heart failure (n = 119)		P-value *	P-value **
		HTN without AF (n = 127)		HF without AF (n = 64)	HF with AF (n = 55)		
RV FAC (%)	210	40 (1)		42 (2)	39 (2)	.54	.25
TAPSE (mm)	208	23 (1)		21 (1)	16 (1)	.10	.011
TR velocity (m/s)	192	2.3 (0.1)		2.4 (0.1)	2.4 (0.1)	.29	.62
Estimated PASP (mm Hg)	184	28 (1)		30 (2)	34 (2)	.37	.12
Lung ultrasound							
B-line number	3 (n, %)	13 (12%)		22 (39%)	25 (46%)	.002	.85

Continuous variables are presented as estimated medians (standard error) unless otherwise noted.

HTN = hypertension; HF = heart failure; AF = atrial fibrillation; IVC = inferior vena cava; RA = right atrial; LA = left atrial; LVEF = left ventricular ejection fraction; LV = left ventricular; E/e' = mitral inflow to mitral relaxation velocity ratio; RV = right ventricular; FAC = fractional area change; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation; PASP = pulmonary arterial systolic pressure.

^aVariables are presented as estimated means (standard error).

* P-value comparing HF without AF and HTN, adjusting for age and sex.

** P-value comparing HF without AF and HF with AF, adjusting for age and sex.

TABLE 3

Echocardiographic measurements by RAEF group in heart failure patients (n = 119)

Variable	N	RAEF	30% (n = 61)	RAEF < 30% (n = 58)	Unadjusted P-value	Adjusted P-value*
RA emptying fraction (%)	119	37 (2)	16 (2)	–	–	–
RA volume index (mL/m ²)	119	29 (3)	39 (3)	<.001	<.001	.032
IVC diameter (cm)	108	1.6 (0.1)	2.0 (0.1)	<.001	<.001	.003
Estimated RA pressure (mm Hg) ^a	108	6 (1)	10 (1)	<.001	<.001	<.001
LA volume index (mL/m ²)	116	29 (2)	35 (2)	<.001	<.001	.047
LA emptying fraction (%)	116	41 (3)	31 (3)	<.001	<.001	.010
LVEF (%)	119	47 (3)	42 (3)	.25	.25	.25
E/e'	97	14 (1)	16 (1)	.91	.91	.30
RV FAC	97	40 (2)	41 (2)	.27	.27	.66
RV S' (cm/s)	107	10 (1)	7 (1)	<.001	<.001	.003
TAPSE (mm)	100	22 (1)	17 (1)	<.001	<.001	<.001
TR velocity (m/s)	100	2.4 (0.1)	2.5 (0.1)	.029	.029	.28
>Moderate TR (%) ^b	116	0	6 (10%)	.027	.027	–
Estimated PASP (mm Hg)	90	31 (3)	37 (2)	.004	.004	.14
B-line number 3 (n, %)	110	19 (34%)	28 (52%)	.06	.06	.36

Continuous variables are presented as estimated medians (standard error).

RAEF = right atrial emptying fraction; IVC = inferior vena cava; RA = right atrial; LA = left atrial; LVEF = left ventricular ejection fraction; LV = left ventricular; E/e' = mitral inflow to mitral relaxation velocity ratio; RV = right ventricular; FAC = fractional area change; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitant; PASP = pulmonary arterial systolic pressure.

^aVariables are presented as estimated means (standard error).^bModerate to severe or severe TR.

* P-value adjusted for age, sex and atrial fibrillation.

TABLE 4

Primary outcome by RAEF and RAVI group in heart failure patients (n = 119)

Primary outcome	RAEF		RAVI	
	RAEF 30% (n = 61)	RAEF < 30% (n = 58)	RAVI 32 mL/m ² (n = 62)	RAVI > 32 mL/m ² (n = 57)
12-mo HF hospitalization (%)	5 (8%)	19 (34%)	8 (13%)	15 (27%)
Death (%)	3 (5%)	7 (12%)	2 (3%)	8 (14%)
Composite outcome (first event) (%)	8 (13%)	22 (38%)	10 (16%)	20 (35%)
Unadjusted HR (95% CI)	(ref)	3.43 (1.52–7.71) <i>P</i> = .003	(ref)	2.41 (1.13–5.17) <i>P</i> = .023
Model 1: Adjusted HR (95% CI)	(ref)	4.07 (1.69–9.79) <i>P</i> = .002	(ref)	2.74 (1.15–6.54) <i>P</i> = .023
Model 2 ^a : Adjusted HR (95% CI)	(ref)	3.84 (1.59–9.23) <i>P</i> = .003	(ref)	2.62 (1.12–6.14) <i>P</i> = .026

RAEF: Unadjusted model: C-statistic 0.65.

Model 1: Adjusted for age, sex and atrial fibrillation (C-statistic 0.67).

Model 2: Adjusted for age, atrial fibrillation and LVEF (C-statistic 0.68).

RAVI: Unadjusted model: C-statistic 0.61.

Model 1: Adjusted for age, sex and atrial fibrillation (C-statistic 0.64).

Model 2: Adjusted for age, atrial fibrillation and LVEF (C-statistic 0.64).

RAEF = right atrial emptying fraction; RAVI = right atrial volume index; HF = heart failure; HR = hazard ratio, CI = confidence interval.

^aFurther adjustment for sex in the Cox models produced no substantial changes in the strength or significance of the reported associations.