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Original Article

Right ventricular outflow tract function in chronic heart failure

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ABSTRACT

Background: Heart failure (HF) is a common, progressive, complex clinical syndrome and a subset of HF patients has symptoms out of proportion to the resting hemodynamics and left ventricular ejection fraction (LVEF). Right ventricular (RV) function is a powerful prognostic factor in HF, but assessing it is a challenge because of the right ventricle's complex geometry.
Objective: The aim of this study was to investigate the clinical application value of RV outflow tract (RVOT) function measured by transthoracic echocardiography in HF patients.
Method: We prospectively investigated 36 chronic HF patients with dilated heart and LV systolic dysfunction and 21 healthy control subjects (normal ventricular function and ECG, and no cardiac risk factors). In addition to clinical and conventional echocardiographic parameters, RVOT size and fractional shortening (RVOT-FS) parameters were analyzed.
Results: The RVOT-FS was less in HF patients than healthy controls (18.8 ± 15.7 vs 55.8 ± 6.7, $p < 0.001$) and correlated positively with TAPSE ($r = 0.814$, $p < 0.001$) and inversely with SPAP ($r = -0.728$, $p < 0.001$) and functional capacity ($r = -0.842$, $p < 0.001$). There was a statistically significant difference in RVOT-FS among the HF subgroups with regard to NYHA functional capacity ($p < 0.001$), although there was no statistically significant difference with regard to LVEF.
Conclusion: Although the apparent discordance between LVEF and the degree of functional impairment in HF is not well understood, it may be explained in part by alterations in RV function. We found that the RVOT-FS was a noninvasive and easily applicable measure of RV function and might be used for a comprehensive evaluation and follow-up of HF patients with a combined assessment of RV by other RV parameters.

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1. Introduction

Heart failure (HF) is a common, progressive, complex clinical syndrome with high morbidity and mortality.[1] Decreased exercise capacity is the main symptom in HF patients; therefore, the physician should provide an estimation of the functional class of the patient based on an assessment of the patient's daily activity and the limitations imposed by the patient's symptoms of HF. Although imperfect, the New York Heart Association (NYHA) classification has long been used to categorize HF patients, and this classification provides important prognostic information. Although HF is generally regarded as a hemodynamic disorder, many studies have indicated that there is a poor relation between measures of cardiac performance and the symptoms produced by the disease. However, a subset of patients with HF has symptoms out of proportion to the resting hemodynamics. Patients with a very low left ventricular ejection fraction (LVEF) may be asymptomatic, whereas patients with preserved LVEF may have severe disability. The apparent discordance between LVEF and the degree of functional impairment is not well understood but may be explained in part by alterations in ventricular distensibility, valvular regurgitation, pericardial restraint, cardiac rhythm abnormalities, and left atrial or right ventricular (RV) function.[1–3]

For many years, cardiologists were not interested in studying RV function and the role of the RV in HF. In recent years, RV function has been found to be a powerful prognostic factor in HF and pulmonary hypertension (PH),[4] but assessing it is a challenge because of the right ventricle's complex geometry, its interrelationship with the left ventricle (LV), its extreme sensitivity to loading conditions and to alterations in pulmonary pressure, and a limited understanding of underlying mechanisms of right HF.[5–7] Due to its widespread availability, echocardiography is used as the first line imaging modality for assessment of RV size and function; however, a single widely accepted and generally applicable index of RV function is not available.[5,7] The RV has 3 distinct features, i.e., the ''inflow'', ''trabeculated apical'', and ''outflow tract'' (infundibulum or conus) compartments, with different extent of contribution to the overall systolic function.[8–10] There are some data to suggest that the myocardium of the RV itself is intrinsically different to that of the LV.[11–13] The RV shortens in a circumferential direction during the isovolumic contraction controlled by subepicardial fibers and longitudinally during the ejection phase controlled by subendocardial fibers. The RV outflow tract (RVOT) has superficial circumferential muscle fibers, which causes radial RVOT contraction during systole.[11] It starts with a short contraction of the inlet region and ends with the contraction of the RVOT that is of longer duration. Since the onset of the RV ejection at RVOT occurs 25–50 ms after the contraction of the inflow tract, these result in overall peristalsis-like ventricular motion.[2,14–16] The RVOT function has been found to correlate closely with other anatomical, long axis as well as functional parameters and transtricuspid retrograde pressure gradient.[11–13]

Although the inlet part of the RV has a greater contribution to overall RV function compared with the infundibulum,[17–19] some studies have reported a possibility of using RVOT movement or contraction as a marker of RV systolic function.[11–13,20] Therefore, we aimed to evaluate the clinical and functional significance of RVOT in patients with HF.

2. Methods

We prospectively included HF patients. Inclusion criteria included a diagnosis of chronic HF for at least 12 months. All patients gave their written consent to participate in this study. All patients with arrhythmia, infectious disorders, malignant tumor, previous history of right heart failure or diagnosis of Group 1 PH (e.g., pulmonary arterial hypertension), Group 3 PH (PH associated with lung respiratory diseases and/or hypoxia), Group 4 PH (PH due to chronic thrombotic and/or embolic disease), and Group 5 PH (PH associated with a miscellaneous of rare diseases), and poor echocardiographic window were excluded. In keeping with current guidelines,[21] PH was defined using the pre-specified cut-off of PASP >50 mmHg at rest. In the present study, the term PH refers to an increased PASP associated with left heart diseases (Group 2 PH).

The study patients had a clinical diagnosis of HF made on the basis of compatible clinical presentation and history combined with documented systolic LV dysfunction (LVEF <50%) and dilation by transthoracic echocardiography. All patients were on standard HF therapy. Patients were divided into 3 groups according to their NYHA functional class (I, no symptoms with ordinary activity; II, mild limitation of physical activity and symptoms with ordinary physical activity; III, marked limitation of physical activity and symptoms with less than ordinary physical activity; and IV, symptoms with any physical activity or at rest). The patient groups were compared to a control group consisting of 21 age- and sex-matched, healthy control group.

Transthoracic echocardiography was performed by using a GE Vivid S5 with a 3.0 MHz phased-array transducer. Patients were examined in the left lateral decubitus position.

The SPAP was estimated by continuous wave Doppler evaluation of tricuspid regurgitation.[22,23]

RV long axis function via the tricuspid annular systolic excursion (TAPSE) was recorded from the apical four-chamber view with the M-mode cursor positioned at the free wall angle of the tricuspid valve. The distance between the tricuspid annulus and the RV apex was measured at end diastole and end systole of the same cardiac cycle, and TAPSE was calculated (in millimeters) as the difference between end-diastolic and end-systolic measurements.[24]

Two-dimensional echocardiograms of the parasternal short axis view at the level of the aortic root were obtained for the RVOT sizes and fractional shortening (RVOT-FS) values. M-mode recordings of the RVOT were obtained and dimensions were measured at end diastole (onset of the Q wave) and end systole (end of T-wave) using endocardial leading edge methodology. RVOT-FS was calculated as the percentage fall in RVOT diameter in systole with respect to that in diastole using the same M-mode images, as reported by Lindqvist et al.[13] (Fig. 1).

Data were analyzed by SPSS 16.0 (SPSS Inc., Chicago, IL, USA) software. Continuous variables were expressed as

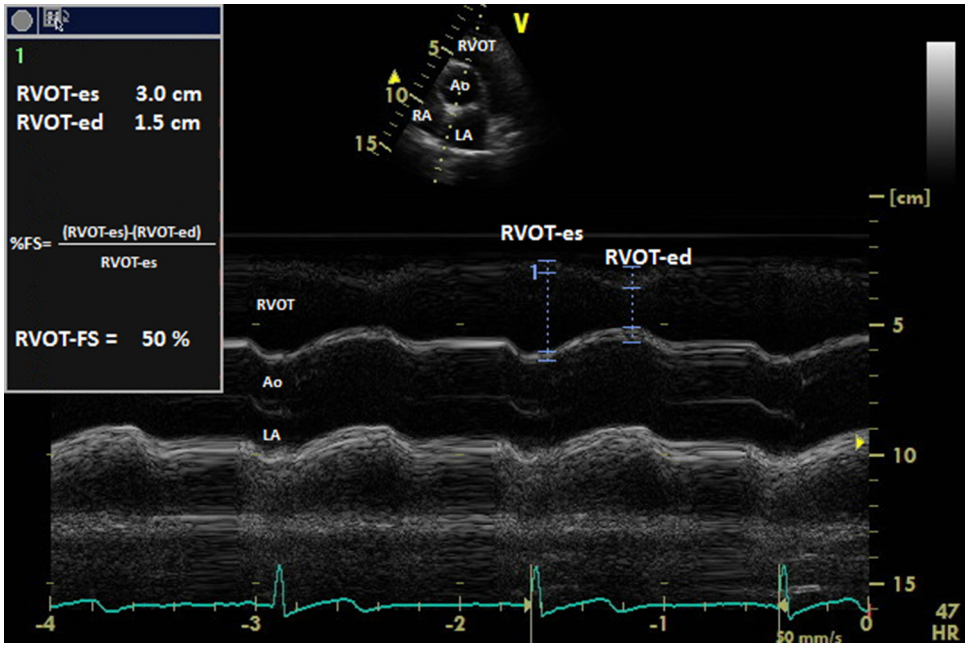

Fig. 1 – Two-dimensional echocardiogram of the parasternal short axis view at the level of the aortic root showing the right ventricular outflow tract (RVOT) maximal ("RVOT-es" at end systole) and minimal ("RVOT-ed" at end diastole) sizes, and RVOT-FS value using the M-mode images. RVOT, right ventricular outflow tract; RVOT-es, the maximal RVOT size at end systole; RVOT-ed, the minimal RVOT size at end-diastole; RVOT-FS, RVOT fractional shortening; Ao, aorta; LA, left atrium; RA, right atrium.

mean ± standard deviation and categorical variables as numbers and percentages. Two group comparisons were performed using an unpaired *t*-test or Mann–Whitney *U*-test according to normality test results, and an analysis of variance (ANOVA) test with Tukey's Honestly Significant Difference (HSD) post hoc test was used for comparison of three groups. Nonparametric methods were applied when the distribution was skewed or the number in a group was below 30. Chi-square analyses were conducted to compare categorical variables. Pearson or Spearman correlation coefficients were calculated in order to assess the associations between the two continuous variables. *p*-value less than 0.05 was defined as statistically significant.

3. Results

Thirty-six HF patients (81% men; mean age, 62 ± 8 years) participated in the study. The subject group was compared to a control group consisting of 21 asymptomatic healthy control subjects with a mean age of 56 ± 11 years (Table 1). All 36 patients had undergone coronary angiography and 16 had unobstructed coronary arteries and no identifiable secondary cause (including no documented infarction by history or the presence of Q waves satisfying standard ECG criteria of infarction) and were being treated with a clinical diagnosis of dilated cardiomyopathy. 20 subjects had angiographically documented CAD (>50% stenosis in ≥1 coronary arteries) and had a history of anterior myocardial infarction. The patient characteristics are detailed in Table 1.

The RVOT-FS was less in HF patients than healthy controls (18.8 ± 15.7 vs 55.8 ± 6.7, $p < 0.001$) and correlated positively with TAPSE ($r = 0.814$, $p < 0.001$) and inversely with SPAP ($r = -0.728$, $p < 0.001$) and functional capacity ($r = -0.842$, $p < 0.001$) (Table 2). There was a statistically significant difference in RVOT-FS among the HF subgroups with regard to NYHA functional capacity ($p < 0.001$), although there was no statistically significant difference with regard to LVEF (Table 3).

Table 1 – Comparison of echocardiographic parameters in patients with and without heart failure. BMI, body-mass index; TAPSE, tricuspid annular plane systolic excursion; SPAP, systolic pulmonary artery pressure; LVEF, left ventricular ejection fraction; LVEDD; left ventricular end-diastolic diameter; RVOT, right ventricular outflow tract; RVOT-FS, right ventricular outflow tract fractional shortening.

Patients	Heart failure ($n = 36$)	Control ($n = 21$)	p value
Age (years)	60.5 ± 7.7	56.3 ± 10.6	0.086
Sex (male, %)	80.6%	81.0%	0.971
BMI (kg/m^2)	28.8 ± 4.0	28.6 ± 3.7	0.892
TAPSE (mm)	15.7 ± 6.0	27.5 ± 3.3	<0.001
SPAP (mmHg)	37.1 ± 8.2	19.1 ± 1.9	<0.001
LVEF (%)	21.5 ± 4.8	66.9 ± 2.8	<0.001
LVEDD (mm)	62.5 ± 4.9	46.9 ± 2.7	<0.001
Diastolic RVOT size (mm)	39.7 ± 4.9	30.2 ± 3.5	<0.001
RVOT-FS (%)	18.8 ± 15.7	55.8 ± 6.7	<0.001

Table 2 – Correlation analysis of RVOT-FS with other right ventricular echocardiographic parameters and functional capacity. RVOT-FS, right ventricular outflow tract fractional shortening; TAPSE, tricuspid annular plane systolic excursion; SPAP, systolic pulmonary artery pressure; RVOT, right ventricular outflow tract; LVEDD; left ventricular end-diastolic diameter; NYHA; New York Heart Association functional classification.

RVOT-FS	*r* value	*p* value
TAPSE	0.814	<0.001
SPAP	−0.728	<0.001
Diastolic RVOT size	−0.788	<0.001
LVEDD	−0.508	<0.001
NYHA functional capacity	−0.842	<0.001
LVEF	0.888	<0.001

Table 3 – Comparison of echocardiographic parameters in subgroups of heart failure patients with regard to functional capacity. NYHA, New York Heart Association functional classification; LVEF, left ventricular ejection fraction; TAPSE, tricuspid annular plane systolic excursion; SPAP, systolic pulmonary artery pressure; LVEDD, left ventricular end-diastolic diameter; RVOT, right ventricular outflow tract; RVOT-FS, right ventricular outflow tract fractional shortening.

Heart failure subgroups	NYHA I & II (*n* = 14)	NYHA III (*n* = 14)	NYHA IV (*n* = 8)	*p* value
Age (years)	62.4 ± 7.0	56.9 ± 7.6	63.5 ± 7.1	0.072
LVEF (%)	24.6 ± 5.9	20.0 ± 4.2	20.7 ± 3.5	0.072
TAPSE (mm)	21.9 ± 5.2	13.6 ± 3.7	10.9 ± 2.0	<0.001
SPAP (mmHg)	26.4 ± 3.9	35.5 ± 10.2	47.1 ± 16.4	0.016
LVEDD (mm)	59.3 ± 2.8	64.3 ± 4.1	65.3 ± 6.3	0.003
Diastolic RVOT size (mm)	36.4 ± 3.3	40.2 ± 4.8	44.5 ± 3.5	<0.001
RVOT-FS (%)	34.9 ± 3.3	9.1 ± 2.4	7.6 ± 2.4	<0.001

4. Discussion

We found that the RVOT systolic function assessed by RVOT-FS decreased in HF patients compared to healthy controls, and more interestingly, RVOT-FS was correlated inversely with NYHA functional capacity despite LVEF being similar in HF subgroups.

The majority of the proposed methods of echocardiographic assessment of RV function are based on volumetric approximations of the RV. Such approaches have inherent limitations: (1) because volume-related measures such as ejection fraction are load dependent and (2) because of the complex geometry of the RV. The issue of RV geometry is usually overcome using geometry-independent parameters such as TAPSE and the Tei index.[2,25] However, RVOT-FS has been shown to be correlated with PH more than TAPSE.[13] In the current study, RVOT size and contraction were correlated with functional capacity and TAPSE in HF.

Recently, there has been an increasing interest in the RV, particularly with regard to LV failure.[20,26,27] Several studies have shown that exercise capacity, as measured by peak VO_2, is more closely associated with RV ejection fraction than with LVEF.[26] It has also shown that RV function is an important predictor of both response to CRT and long-term clinical outcome of HF patients,[28,29] and recommended that routine assessment of the RV should be considered in the evaluation of HF patients for CRT. In the current study, we found that RVOT-FS decreased in HF patients and correlated inversely with NYHA functional capacity despite similar LVEF in HF subgroups. Although the inlet part of the RV has a greater contribution to overall RV function compared with the infundibulum,[17–19] some studies have reported a possibility of using RVOT movement or contraction as a marker of RV systolic function.[11–13,22] Lindqvist et al.[13] reported that RVOT-FS moderately correlated with TAPSE, and moderately and inversely correlated with transtricuspidal Doppler gradient. Similar to RVOT-FS, Asmer et al.[11] reported that RVOT systolic excursion, which is actually a component of RVOT-FS, is novel, simple, and promising parameter for assessing RV function. They speculated that separation of RVOT systolic excursion values were better compared to RVOT-FS values, due to the fact that RVOT-FS is affected by LV function as well, whereas LV function has no effect on RVOT systolic excursion.[11] In patients with good LV function, the aorta is pushed anteriorly in systole, contributing to RVOT-FS even in the presence of reduced RV function; however, this effect also might provide positive effect on RV function.

There were a number of limitations to our study. Firstly, the window for measurement of RVOT size has not been standardized, and oblique imaging of the RVOT may underestimate the fractional shorting value or overestimate its size echocardiographically. The diameters of RVOT are different at different sites, when using different methods and in different body position.[5] Again, the endocardial definition of the anterior wall is often suboptimal. Secondly, there is lack of a comparative gold standard technique for assessing global RV function, such as cardiac catheterization and/or cine magnetic resonance imaging. Therefore, the association of RVOT-FS with left-sided filling pressures and PVR by echo parameters was not addressed, and absence of measurement of RV fractional area change remains a major issue. Thirdly, we did not evaluate the diastolic HF patients. Finally, despite the NYHA functional classification system providing a rapid assessment of the functional status during physical exertion in HF patients, it is often heavily reliant on subjective measurements made by both the clinician and the patient. Therefore, the other noninvasive tests such as the 6-min walking test would serve as a benchmark to assess the functional capacity.[30]

In conclusion, although the apparent discordance between LVEF and the degree of functional impairment in HF is not well understood in some patients, it may be explained in part by alterations in RV and RVOT function. We demonstrated that the RVOT-FS was a noninvasive and easily applicable measure of RV function and might be used for a comprehensive evaluation and follow-up of HF patients.

Conflicts of interest

The authors have none to declare.

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