Right ventricular function in patients with preserved and reduced ejection fraction heart failure

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Aims To determine the prevalence of right ventricular (RV) dysfunction in patients with preserved left ventricular (LV) ejection fraction (EF) heart failure (HF) and to compare RV function between patients with preserved EF HF and those with reduced EF HF.

Methods and results Hundred patients (72 ± 14 years, 59% male) with HF were prospectively enrolled. Fifty-one had preserved EF HF (LVEF > 50%). The prevalence of RV systolic dysfunction in patients with preserved EF HF was 33, 40, and 50%, by using RV fractional area change (FAC), tricuspid annular motion (TAM), and peak systolic tricuspid annular tissue velocity (S0) criteria, respectively. Tricuspid S0 and TAM correlated the best with LVEF (r = 0.48, P < 0.01). Patients with preserved EF HF had higher RV FAC (54 ± 18 vs. 36 ± 20%, P < 0.01), TAM (17 ± 1 vs. 11 ± 1 mm, P < 0.01), and tricuspid S0 (14 ± 6 vs. 9 ± 4 cm/s, P < 0.01) compared with those with reduced EF HF. Of those 51 patients, 34% had tricuspid E/e' suggestive of elevated RV filling pressures. Early tricuspid inflow (E), early diastolic tricuspid annular tissue (e'), tricuspid E/e', and hepatic vein systolic velocities were also higher in patients with preserved EF HF.

Conclusion The prevalence of RV systolic and diastolic dysfunctions was not uncommon in patients with preserved EF HF. However, patients with preserved EF HF had milder degree of RV systolic and diastolic dysfunctions compared with those with reduced EF HF.

Keywords Right ventricle; Heart failure; Dysfunction; Preserved ejection fraction; Echocardiography

Introduction

Heart failure (HF) with preserved ejection fraction (EF) has recently become an important health problem.1,2 The mortality of this clinical syndrome is similar to that of reduced left ventricular (LV) EF HF, previously called systolic HF.3 Previous studies have demonstrated that right ventricular (RV) dysfunction in patients with reduced EF HF is common and associated with an increased mortality.4–8 However, the prevalence of RV dysfunction in patients with preserved EF HF presenting with symptoms of HF has not been investigated. The aims of this study were to determine the prevalence of RV dysfunction in patients with preserved EF HF and to compare RV systolic and diastolic functions between patients with preserved EF HF and those with reduced EF HF.

Methods

Patients

Detailed transthoracic echocardiographic data were prospectively collected from 100 consecutive adult patients who were hospitalized with HF. Clinical data were abstracted from the medical record by two physicians. The study protocol was approved by our institution’s Investigational Review Board.

Echocardiographic study and analysis

In addition to standard LV assessment,9,10 quantitative echocardiographic parameters to assess RV systolic and diastolic functions were obtained and analysed. RV systolic parameters included RV fractional area change (FAC), tricuspid annular motion (TAM), and tricuspid peak systolic annular tissue velocity (S0). RV FAC was calculated as: (RV end-diastolic area − RV end-systolic area)/RV end-diastolic area × 100. TAM was measured in the apical four-chamber view using two-dimensional maximal amplitude of lateral tricuspid annular movement from end-diastolic frame to end-systolic frame.12,15–17 Tricuspid S0 was measured at peak systolic velocity obtained by TDI of lateral tricuspid annulus. RV diastolic parameters included right atrial volume (RAV) index, tricuspid inflow velocities, tricuspid annular tissue velocities, and hepatic venous velocity. RAV
was measured in the apical four-chamber view by using single plane area-length method\textsuperscript{18,19} and indexed to body surface area. Tricuspid early diastolic (E) and late diastolic (A) inflow velocities obtained by pulse wave Doppler at the tricuspid leaflet tip\textsuperscript{20–22} as previously described. Tricuspid annular early (e') and late (a') diastolic velocities were obtained by TDI of the lateral tricuspid annulus as previously described.\textsuperscript{23} Global RV function included RV Tei index that was calculated by measuring two intervals: ‘a’ representing the interval between cessation and onset of tricuspid inflow which can be substituted by the duration of tricuspid valve regurgitation (TR) and ‘b’ representing the ejection time of RV outflow tract. RV Tei index=\( \frac{a-b}{b} \).\textsuperscript{24} Pulmonary artery systolic pressure (PASP) was estimated by adding the pressure gradient between the RV and the right atrium by the peak continuous-wave Doppler velocity of the TR jet using the modified Bernoulli equation to the estimated right atrial pressure as estimated from inferior vena caval size and collapsibility with respiration, as previously described and validated.\textsuperscript{25–28} The echocardiographic data were digitally stored for off-line analysis by an experienced cardiologist. All measurements represent an average of five consecutive cardiac cycles.

### Echocardiographic criteria

Preserved EF HF was defined as symptomatic HF with LVEF ≥ 50%.

The criteria for RV systolic and diastolic dysfunctions were based on previously validated studies. RV systolic dysfunction was defined as one of the following criteria: (i) RV FAC < 45\%;\textsuperscript{11–14} (ii) TAM < 1.5 cm;\textsuperscript{12,29} or (iii) tricuspid S’ < 11.5 cm/s\textsuperscript{4}. RV diastolic dysfunction or elevated estimated RV filling pressure was defined as tricuspid E/e’ > 6.\textsuperscript{30}

### Statistical analysis

Categorical data were expressed as frequencies and percentages and continuous data were expressed as means and standard deviations. Comparison of categorical variables was performed using a \( \chi^2 \) test. Correlation between echocardiographic parameters and LVEF was analysed with linear regression analysis and Spearman’s correlation coefficients. Statistical significance was defined as \( P < 0.05 \). Statistical analysis was performed by using JMP statistics package.

### Results

Of 100 study patients (72 ± 14 years, 59% men), 51 patients had preserved EF HF. Patient characteristics are shown in Table 1. Seventy-five percent of patients with preserved EF HF (37 of 49) and reduced EF HF (38 of 51) had NYHA class III or IV symptoms. Pulmonary oedema was present more frequently in patients with preserved EF HF compared with those with reduced EF HF. Age, gender, and a history of diabetes, hypertension, chronic obstructive lung disease (COPD), and obstructive sleep apnea were similar between patients with preserved and reduced EF HF. However, a history of coronary artery diseases and cardiomyopathy was more common in patients with reduced EF HF.

### Right ventricular systolic dysfunction in patients with preserved and reduced ejection fraction heart failure

The prevalence of RV systolic dysfunction in patients with preserved EF HF was 33, 40, and 50%, by using RV FAC, TAM, and tricuspid S’ criteria, respectively. The prevalence of RV systolic dysfunction was higher in patients with reduced EF HF 63, 76, and 73%, by using RV FAC, TAM, and tricuspid S’ criteria, respectively. The prevalence of RV systolic dysfunction significantly increased with lower LVEF (Figure 1). Patients with preserved EF HF had higher RV FAC (54 ± 18 vs. 36 ± 20\%, \( P < 0.01 \)), TAM (17 ± 1 vs. 11 ± 1 mm, \( P < 0.01 \)), and tricuspid S’ (14 ± 6 vs. 9 ± 4 cm/s, \( P < 0.01 \)) compared with those with reduced EF HF (Table 2). PASP significantly correlated with RV FAC (\( r = 0.46, P < 0.01 \)), TAM (\( r = 0.48, P < 0.01 \)), and tricuspid S’ (\( r = 0.48, P < 0.01 \)) (Table 3).

### Right ventricular diastolic dysfunction in patients with preserved and reduced ejection fraction heart failure

Elevated RV filling pressures suggestive of RV diastolic dysfunction was present 34 and 63% in patients with preserved and reduced EF HF, respectively. Patients with preserved EF HF had significantly higher tricuspid E velocity (64 ± 21 vs. 56 ± 23 cm/s, \( P = 0.02 \)), tricuspid e’ velocity (13.2 ± 5.9 vs. 7.6 ± 4.0 cm/s, \( P < 0.01 \)), tricuspid a’ velocity (12.3 ± 7.3 vs. 9.2 ± 8.8 cm/s, \( P < 0.01 \)), and hepatic vein systolic forward velocity (34 ± 19 vs. 24 ± 21 cm/s, \( P < 0.01 \)) compared with those with reduced EF HF (Table 2). PASP significantly correlated with tricuspid e’ velocity (\( r = 0.46, P < 0.01 \)), tricuspid a’ velocity (\( r = 0.23, P = 0.04 \)), tricuspid E/e’ (\( r = -0.32, P < 0.01 \)), and hepatic vein systolic forward velocity (\( r = 0.25, P = 0.02 \)) (Table 3).

### Right ventricular function and pulmonary hypertension

In the overall study population, estimated PASP significantly correlated with RV systolic and diastolic measurements, including FAC (\( r = -0.40, P < 0.01 \)), TAM (\( r = -0.29, P < 0.01 \)), RAV index (\( r = 0.30, P < 0.01 \)), tricuspid E

### Table 1 Baseline characteristics of patients with reduced and preserved left ventricular ejection fraction heart failure

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Reduced EF HF (n = 49)</th>
<th>Preserved EF HF (n = 51)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (%)</td>
<td>31 (63%)</td>
<td>28 (55%)</td>
<td>0.39</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>123 ± 24</td>
<td>125 ± 21</td>
<td>0.54</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>69 ± 17</td>
<td>64 ± 13</td>
<td>0.13</td>
</tr>
<tr>
<td>Heart rate (b.p.m.)</td>
<td>78 ± 18</td>
<td>72 ± 13</td>
<td>0.12</td>
</tr>
<tr>
<td>NYHA, n (%)</td>
<td>12 (24%)</td>
<td>13 (26%)</td>
<td>0.81</td>
</tr>
<tr>
<td>Class II</td>
<td>13 (24%)</td>
<td>13 (26%)</td>
<td>0.81</td>
</tr>
<tr>
<td>Class III</td>
<td>19 (39%)</td>
<td>23 (45%)</td>
<td>0.81</td>
</tr>
<tr>
<td>Class IV</td>
<td>18 (37%)</td>
<td>15 (29%)</td>
<td>0.81</td>
</tr>
<tr>
<td>Pulmonary oedema, n (%)</td>
<td>39 (49%)</td>
<td>30 (52%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Diabetes (n)</td>
<td>22 (45%)</td>
<td>15 (29%)</td>
<td>0.10</td>
</tr>
<tr>
<td>Coronary artery disease (n)*</td>
<td>30 (61%)</td>
<td>21 (41%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Cardiomyopathy (n)*</td>
<td>27 (55%)</td>
<td>5 (10%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Obstructive sleep apnea (n)</td>
<td>6 (12%)</td>
<td>4 (8%)</td>
<td>0.46</td>
</tr>
<tr>
<td>COPD (n)</td>
<td>11 (22%)</td>
<td>13 (25%)</td>
<td>0.72</td>
</tr>
</tbody>
</table>

EF, ejection fraction; HF, heart failure; COPD, chronic obstructive pulmonary disease; NYHA, New York Heart Association.

*\( P < 0.05 \).


Discussion

The major findings of our study are: (i) the prevalence of RV systolic dysfunction in patients with preserved EF HF was 33–50%, whereas the prevalence in patients with reduced EF HF was higher, 63–76%; (ii) the prevalence of RV systolic dysfunction increased with an increasing severity of LV systolic function; (iii) the prevalence of RV diastolic dysfunction was 34 and 63% in patients with preserved and reduced EF HF, respectively; (iv) the severity of RV systolic and diastolic dysfunctions was increased in patients with reduced EF HF compared with patients with preserved EF HF, although the PASPs were similar between two groups; and (v) most, but not all, RV systolic and diastolic variables correlated with PASP. The aforementioned findings also held true in patients without COPD or significant pulmonary disease.

Table 2 Right ventricular systolic and diastolic functions in patients with reduced and preserved left ventricular ejection fraction heart failure

<table>
<thead>
<tr>
<th></th>
<th>Reduced EF HF (n = 49)</th>
<th>Preserved EF HF (n = 51)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV systolic function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV fractional area change (%)*</td>
<td>36 ± 20</td>
<td>54 ± 18</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Tricuspid annular motion (mm)*</td>
<td>11 ± 1</td>
<td>17 ± 1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peak systolic tricuspid annular tissue velocity (S) (cm/s)*</td>
<td>9 ± 4</td>
<td>14 ± 6</td>
<td>0.0004</td>
</tr>
<tr>
<td>RV diastolic function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right atrial volume index (mL/m²)</td>
<td>41 ± 24</td>
<td>36 ± 17</td>
<td>0.366</td>
</tr>
<tr>
<td>Tricuspid E’ velocity (cm/s)*</td>
<td>56 ± 23</td>
<td>64 ± 21</td>
<td>0.018</td>
</tr>
<tr>
<td>Tricuspid A velocity (cm/s)</td>
<td>37 ± 25</td>
<td>45 ± 27</td>
<td>0.064</td>
</tr>
<tr>
<td>Tricuspid E DT (ms)</td>
<td>129 ± 97</td>
<td>152 ± 189</td>
<td>0.687</td>
</tr>
<tr>
<td>Tricuspid e’ (cm/s)*</td>
<td>7.6 ± 4.0</td>
<td>12.3 ± 5.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Tricuspid a’ (cm/s)*</td>
<td>9.2 ± 8.8</td>
<td>12.3 ± 7.3</td>
<td>0.020</td>
</tr>
<tr>
<td>Tricuspid E/e’*</td>
<td>8.2 ± 4.9</td>
<td>5.3 ± 3.7</td>
<td>0.0007</td>
</tr>
<tr>
<td>Hepatic vein S velocity (cm/s)*</td>
<td>24 ± 21</td>
<td>34 ± 19</td>
<td>0.0065</td>
</tr>
<tr>
<td>Hepatic vein D velocity (cm/s)</td>
<td>42 ± 24</td>
<td>40 ± 22</td>
<td>0.815</td>
</tr>
<tr>
<td>Hepatic vein DR velocity (cm/s)</td>
<td>25 ± 16</td>
<td>28 ± 13</td>
<td>0.137</td>
</tr>
<tr>
<td>RV global function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV Tei index*</td>
<td>0.53 ± 0.24</td>
<td>0.43 ± 0.22</td>
<td>0.017</td>
</tr>
<tr>
<td>Estimated PA systolic pressure (mmHg)</td>
<td>52 ± 12</td>
<td>53 ± 18</td>
<td>0.951</td>
</tr>
</tbody>
</table>

*P < 0.05.

Figure 1 The prevalence of right ventricular systolic and diastolic dysfunctions stratified by left ventricular ejection fraction E, early inflow velocity; e’, early tissue annular velocity; EF, ejection fraction; FAC, fractional area change; HF, heart failure; LV, left ventricular; RV, right ventricular; S’, peak systolic tricuspid annular velocity; TV, tricuspid; TAM, tricuspid annular motion.
Right ventricular systolic dysfunction

The prevalence of RV systolic dysfunction in patients with preserved EF HF was ~1/3 to 1/2 of our patient population and, not surprisingly, was more common in patients with reduced EF HF. The prevalence of RV systolic dysfunction in reduced EF HF patients (63–76%) is higher compared with a study by de Groote et al, who found that RV systolic dysfunction was present in 52% (107 of 205 patients) in systolic HF patients with LVEF ≤ 45%. The potential explanation of higher prevalence in our study was the fact that we used the higher cut-off LVEF (≥ 50%) to define reduced EF HF.

In our study, we also demonstrated that not only the prevalence but also the severity of RV systolic dysfunction increased with increasing severity of LV systolic dysfunction. Interestingly, estimated PASP was similar in patients with reduced and preserved EF HF. Furthermore, LVEF did not significantly correlate with PASP in our study. This suggests that the mechanism of RV systolic dysfunction in at least some of our patients with reduced EF HF was not solely pulmonary venous hypertension which can lead to an increase in pulmonary vascular resistance and RV systolic failure, but it may be partly attributed to primary RV diseases and/or ventricular interdependence. In our study, a history of coronary artery diseases and cardiomyopathy was more common in patients with reduced EF HF. These findings also suggest that coronary artery diseases and cardiomyopathy may have contributed to the mechanism of RV dysfunction in these patients. The mechanism of RV systolic dysfunction in patients with preserved EF HF has not been established.

On the basis of chart review for the patients with preserved LV HF and reduced RV systolic function, the majority had LV diastolic dysfunction. We believe that pathophysiological basis is mainly similar to the causes of RV dysfunction in patients with reduced EF HF, which is that RV failure is a result of diastolic failure on the left and systolic failure on the right. The contribution of primary RV disease or cardiomyopathy in patients with preserved EF HF is less compared with those with reduced HF.

Right ventricular diastolic dysfunction

The prevalence of RV diastolic dysfunction in our study was 34 and 63% in patients with preserved and reduced EF HF, respectively. Yu et al.21 has previously demonstrated that RV diastolic dysfunction is common in patients with HF as nearly 60% of patients had prolonged tricuspid isovolumic relaxation time and 55% of patients had reversed tricuspid E–A ratio. However, the study reported the prevalence in overall HF patients irrespective of reduced or preserved EF HF. In our study, we did not use those tricuspid inflow parameters as markers for RV diastolic dysfunction, since tricuspid inflow is relatively preload, age, and heart rate dependent. Instead, we used tricuspid E/e’ which has been demonstrated by Nageh et al.30 that it significantly correlated with invasive mean right atrial pressure. Additionally,
tricuspid \( E/e' > 6 \) correlated well with mean right atrial pressure > 10 mmHg.\(^{30}\) In the majority of patients, we believed that one of the essential mechanisms for impaired RV diastolic function in preserved EF HF patients is pulmonary hypertension secondary to elevated LV filling pressures from chronic LV diastolic dysfunction.

**Study limitations**

First, we included only hospitalized patients with symptoms of HF referred for echocardiography. These patients may be sicker than the outpatients with HF. Hence, the overall prevalence of right heart dysfunction both systolic and diastolic may be lower in an outpatient HF population. A second limitation in our study is the lack of invasive right heart haemodynamic data, especially in the determination of RV diastolic dysfunction. However, right heart haemodynamics as assessed by non-invasive echocardiographic methods are both reliable and validated.\(^{30}\) We used echocardiographic parameters (tricuspid \( E/e' \) and cut-off values (>6) similar to those reported by Nageh et al.\(^{30}\) who demonstrated good correlation between Doppler echocardiographic data and invasive haemodynamics. Finally, our study population was small. A larger prospective study with greater external validity including non-hospitalized HF population or a community-based study is needed to verify this data.

**Conclusions**

Right ventricular systolic and diastolic dysfunctions are common in patients with preserved EF HF. The severity of RV dysfunction in patients with preserved EF HF was less compared with those with reduced EF HF. Not only the prevalence but also the severity of RV systolic dysfunction increased with increasing severity of LV systolic function. Further studies defining the relationship between RV dysfunction and clinical outcomes in patients with preserved EF HF are needed.

**Conflict of interest:** none declared.

**References**


