Right ventricle Tei-index: A tool to increase the accuracy of non-invasive detection of pulmonary arterial hypertension in connective tissue diseases


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Received 6 March 2006; received in revised form 4 May 2006; accepted 2 June 2006
Available online 17 July 2006

Abstract

Objective: To assess the accuracy of echocardiography for predicting pulmonary arterial hypertension (PAH) in a cohort of patients with systemic sclerosis and other connective tissue diseases, and to evaluate whether addition of the right ventricular (RV) Tei-index contributes to the non-invasive diagnosis of PAH in this patient group.

Patients and methods: Ninety-eight patients with systemic sclerosis and other connective tissue diseases in whom an echocardiography was performed in the period from January 1st 2004 to July 1st 2005 were included. Echocardiographic systolic pulmonary arterial pressure (PAP), end-diastolic PAP and RV Tei-index were calculated. In cases with a high suspicion of PAH right heart catheterization was performed and systolic, diastolic and mean PAP as well as pulmonary wedge pressure, cardiac output and pulmonary vascular resistance were obtained. These results were compared to the echocardiographic measurements.

Results: The average RV Tei-index of our patients was substantially above normal values. In 35 (36%) patients a right heart catheterization was performed and PAH was confirmed in 28 patients. In 6 of 7 patients without PAH, the RV Tei-index was below the upper limit of normal. A significant correlation was found between the RV Tei-index and the catheterization parameters such as systolic PAP, diastolic PAP and mean PAP.
Conclusion: The accuracy of echocardiography for the detection of PAH increases when the echocardiographic systolic PAP is combined with an elevated RV Tei-index. As a result, by applying the Tei-index, the number of negative catheterizations can be minimized.

Introduction

Pulmonary arterial hypertension (PAH) is a life-threatening complication of autoimmune disorders, especially systemic sclerosis (SSc). PAH is defined as a mean pulmonary artery pressure (PAP) of >25 mmHg at rest or >30 mmHg during exercise, measured during right heart catheterization (RHC). The symptoms of PAH are non-specific, and are therefore often overlooked. This is especially true in patients with SSc, who are already limited in their activities by fatigue and other complications of their conditions. The prevalence of PAH in SSc patients is estimated between 12% and 29% in catheterization-based studies. Since effective treatments have become available, screening for PAH in patients with SSc on a yearly basis is recommended. PAH is suspected when a patient reports dyspnea at exertion, when pulmonary function testing reveals an isolated decrease in diffusion capacity of the lungs, and/or the echocardiographic criteria for PAH are met. These criteria consist of an estimated PAP systolic >35 mmHg and/or an estimated mean PAP ≥ 25 mmHg. Because echocardiographic results are flawed by both false positive and false negative results RHC is necessary to confirm the diagnosis of PAH and to exclude other forms of pulmonary hypertension. To avoid unnecessary RHCs, the diagnostic potentials of echocardiography must be fully utilized. As shown in Fig. 1, the myocardial performance index, also known as Tei-index, is defined as the sum of the isovolumic contraction and the isovolumic relaxation time divided by ejection time, and thus incorporates elements of both systolic and diastolic phases in the assessment of global ventricular function. The Tei-index can be estimated for both the left ventricle (LV) and the right ventricle (RV). An increased Tei-index results from ventricular dysfunction and provides prognostic information for a variety of myocardial conditions. The RV Tei-index is a candidate to increase the non-invasive diagnosis of PAH because it reflects the RV function, is easy to assess, and can be estimated in the same session as the echocardiographic PAP. The normal value of the RV Tei-index is 0.28 ± 0.04. An increased RV Tei-index is associated with either LV diastolic abnormalities or pulmonary hypertension. In this study we assessed the accuracy of echocardiography for predicting PAH in a cohort of patients with SSc and other connective tissue diseases (CTD), and determined whether the RV Tei-index can be used as a tool to increase the accuracy of echocardiographic measurements for the detection of PAH in these patients.

Patients and methods

Ninety-eight patients with CTD, in whom echocardiography was performed from January 1st 2004 to July 1st 2005, were included in this study. The majority of the patients had SSc (n = 91; 93%), the other diagnoses were mixed connective tissue disease (n = 3; 3%), systemic lupus erythematosus (n = 2; 2%), and undifferentiated connective tissue disease (n = 2; 2%). Echocardiography is part of the yearly screening protocol for PAH in our cohort of patients with SSc. The characteristics of the patients are shown in Table 1.

Echocardiography

All echocardiographic analyses were performed by the same cardiologist who was only aware of the
diagnosis of CTD, but not of other clinical aspects of the patients. Using the GE Vivid 7.0 (second harmonic imaging; 1.7/3.4 MHz), the RV Tei-index was calculated with Doppler-echocardiography in all patients as previously described. Using the GE Vivid 7.0 (second harmonic imaging; 1.7/3.4 MHz), the RV Tei-index was calculated with Doppler-echocardiography in all patients as previously described.7 Echocardiographic systolic PAP was calculated from the tricuspid regurgitation velocity and right atrial pressure estimate.12 End-diastolic PAP was estimated by using end-diastolic pulmonary regurgitation velocity and right atrial pressure estimate. By applying a regression equation the mean PAP was calculated from the RV acceleration time and ejection time ratio.13

Right heart catheterization

In 35 cases, all with an echocardiographic systolic PAP ≥35 mmHg, an RHC was performed. During RHC systolic, diastolic and mean PAP and pulmonary wedge pressure were measured. Thermo dilution cardiac output was established, and pulmonary vascular resistance was calculated. The latest echocardiography available before the RHC was used for comparison of the PAP values.

Statistical analysis

For descriptive statistics the mean ± SD was calculated. Prevalence for the echocardiographic diagnosis of PAH based on the systolic threshold, elevated RV Tei-index, and a combination of these two were calculated. We compared continuous variables using Student’s t-test. The correlation between hemodynamic variables, echocardiographic estimates of hemodynamics and the RV Tei-index was calculated using Spearman’s rho. p-Values < 0.05 were considered statistically significant.

Results

Echocardiography versus right heart catheterization

Thirty-five of 98 patients (36%) met the echocardiographic threshold of systolic PAP ≥35 mmHg; in these patients an RHC was performed. The echocardiographically calculated systolic PAP values appeared to be significantly higher than the values measured during RHC (60.7 mmHg ± 18.2 mmHg vs. 55.1 mmHg ± 21.3 mmHg; mean ± SD; p < 0.001)). However, the diastolic PAP values of RHC were significantly higher than the values of echocardiography (19.9 mmHg ± 8.2 mmHg vs. 23.5 mmHg ± 9.2 mmHg; p = 0.04).

Tei-index

In 2 of 98 patients the RV Tei-index could not be determined for technical reasons. The RV Tei-index in our patient population was 0.33 ± 0.20 (mean ± SD), which differs substantially from the normal value: 0.28 ± 0.04. The RV Tei-index was above the upper limit of normal (95% CI of normal value 0.20–0.36) in 41 of 96 (43%) of our patients.

Tei-index and echocardiographic systolic PAP

RHC confirmed the echocardiographic suspected PAH in 28 of the 35 (80%) examined patients. Using the systolic threshold of ≥35 mmHg the correlation of the systolic PAP with the RV Tei-index was significant (r = 0.46; p = 0.01). When raising the systolic threshold, this did not change.

Tei-index and catheterization variables

The mean RV Tei-index of the catheterized patients was 0.41 (±0.21). In an attempt to improve the accuracy of the echocardiography for PAH in patients with SSC an RV Tei-index > 0.36 was combined with the systolic threshold. Table 2 shows

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Patient characteristics of study population (N = 98)</th>
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<tbody>
<tr>
<td>Mean age (±SD) years</td>
<td>58 (±13)</td>
</tr>
<tr>
<td>Male:female</td>
<td>31:67</td>
</tr>
<tr>
<td>Mean duration (±SD) of CTD (years)</td>
<td>8.5 (±7.1)</td>
</tr>
<tr>
<td>%SSc:other CTD</td>
<td>93:7</td>
</tr>
<tr>
<td>%dcSSc:lcSSc</td>
<td>21:79</td>
</tr>
<tr>
<td>Mean echo systolic PAP (±SD) (min–max)</td>
<td>55.7 mmHg (±20.9) (21–106)</td>
</tr>
<tr>
<td>Mean echo diastolic PAP (±SD) (min–max)</td>
<td>17.7 mmHg (±9.0) (2–39)</td>
</tr>
<tr>
<td>Mean echo mean PAP (±SD) (min–max)</td>
<td>30.7 mmHg (±11.0) (10–53)</td>
</tr>
<tr>
<td>Mean % predicted vital capacity (±SD) (min–max)</td>
<td>87.5 (±24.8) (11–37)</td>
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<tr>
<td>Mean % predicted CO diffusion capacity (±SD) (min–max)</td>
<td>51.6 (±19.4) (17–116)</td>
</tr>
<tr>
<td>%NYHA class 1–2:3–4</td>
<td>67:33</td>
</tr>
</tbody>
</table>

CTD: connective tissue disease; dcSSc: diffuse cutaneous systemic sclerosis; lcSSc: limited cutaneous systemic sclerosis; NYHA class: the degree of functional disability, based on exercise performance, according to the New York Heart Association (NYHA) criteria; and PAP: pulmonary artery pressure.
that by doing so the prevalence of PAH as confirmed by RHC was raised to 95% (19/20 patients). However, in 9 patients with PAH at RHC, the RV Tei-index was >0.36. In 6 of 7 patients with a negative RHC, the RV Tei-index was ≤0.36. Therefore, a combination of RV Tei-index and echocardiographically systolic PAP has a higher predictive value for diagnosing PAH at RHC than the systolic threshold alone. When comparing the RV Tei-index with other parameters such as the systolic, diastolic, and mean PAP measured during catheterization, the correlation is constantly significant. However, no correlation was found with pulmonary vascular resistance measured during catheterization (r = 0.33; p = 0.08). In the 35 patients with RHC, the correlation of the mean PAP measured during RHC and RV Tei-index was the strongest (r = 0.46; p = 0.01) (Fig. 2).

**Table 2** Combination of echocardiographic estimated systolic PAP ≥35 mmHg and RV Tei-index with PAH diagnosis at RHC

<table>
<thead>
<tr>
<th></th>
<th>PAH confirmed</th>
<th>PAH not confirmed</th>
<th>Total (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tei &gt; 0.36 (N)</td>
<td>19</td>
<td>1</td>
<td>20</td>
</tr>
<tr>
<td>Tei ≤ 0.36 (N)</td>
<td>9</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>Total (N)</td>
<td>28</td>
<td>7</td>
<td>35</td>
</tr>
</tbody>
</table>

**Discussion**

This study shows that the mean RV Tei-index in a cohort with CTD differs substantially from the normal value in literature. The RV Tei-index was elevated in 43% of the patients, suggesting RV dysfunction. This finding confirms earlier findings of asymptomatic diastolic RV dysfunction in 40% of patients with SSC. The RV Tei-index is elevated due to an increased pulmonary vascular resistance, and a decreased myocardial contraction. Thus, in patients with PAH the RV Tei-index is expected to be above the normal range. In our patients with an RV Tei-index >0.36 PAH was confirmed by RHC in all but one case. This case provided a diagnostic dilemma, an RHC, also during exercise, was negative twice in a 6-month period.

When combining the systolic threshold with the RV Tei-index >0.36, the predictive value of echocardiography for PAH increases. Using the echocardiographic systolic PAP ≥35 mmHg we found a prevalence of PAH of 80%. This result confirms earlier findings. In daily clinical practice an echocardiographic systolic PAP ≥35 mmHg is used as a preliminary diagnosis of PAH. As shown before, we found that the echocardiographically systolic PAP is significantly higher than the values found by RHC. For the diastolic PAP we found the opposite. So, echocardiography overestimates the systolic PAP and underestimates the diastolic PAP, which results in an overestimation of the mean PAP. This leads to unnecessary RHCs. As accuracy of echocardiography alone is not optimal, the combination of clinical evaluation, calculated systolic and mean PAP should determine whether or not an RHC has to be performed. Also in our study negative catheterizations occurred in 7 of 35 patients (20%), underlining the necessity of increasing the diagnostic potential of echocardiography to select patients at risk without increasing the number of undiagnosed patients. The RV Tei-index is easy to assess and has a low inter- and intra-observer variability. It could therefore be used as an additional screening tool for PAH. Other promising echocardiographic techniques, such as tissue Doppler-echocardiography and contrast echocardiography, can perhaps contribute to the accuracy of echocardiography, but their values have yet to be established. The RV Tei-index correlated significantly with hemodynamics, but no significant correlation was found with the pulmonary vascular resistance. In theory, an elevated RV Tei-index should be the result of either diastolic dysfunction of the LV, or RV dysfunction, or elevated pulmonary vascular resistance. The fact that the correlation was not

![Figure 2](image-url)  
**Figure 2** Correlation of mean PAP measured during right heart catheterization and RV Tei-index.
significant might be caused by the small number of patients with an RHC. We did not analyze the influence of medication but in previous studies we found no impact of calcium channel blockers or immunosuppressive agents for the occurrence of PAH.\textsuperscript{15,16}

In total 9 patients had an RV Tei-index $\leq 0.36$ but a positive echocardiogram and catheterization for pulmonary hypertension. The patients’ characteristics of this group were not different from the patients with a positive echocardiogram, catheterization and RV Tei-index $> 0.36$. The results of this study might be biased by the fact that we only performed RHC in cases when the echocardiographic criteria for pulmonary hypertension were met. This resulted in small numbers. Furthermore, the echocardiography and RHC were not performed simultaneously. As the natural variability of PAP and pulmonary vascular resistance can be as high as 13%,\textsuperscript{17} some blurring of the findings could be the result.

**Conclusion**

Echocardiography is a useful screening tool for PAH. The accuracy of echocardiography for predicting PAH might increase when the systolic PAP threshold of $\geq 35$ mmHg is combined with an RV Tei-index $> 0.36$. Thus, in patients with SSc the combination of an increased systolic PAP and an increased RV Tei-index should prompt RHC. Further development of a combination of reliable, non-invasive tests to improve the pretest probability of PAH should be investigated in order to reduce the number of negative RHCs without missing cases of PAH.

**Acknowledgements**

We thank Prof. Dr. P.C. Sander and Mrs. A.I. Smetsers, M.A. for their technical supports.

**References**


