Utility of TEI index in patients with pulmonary arterial hypertension: prognostic parameter and correlation with treatment, clinical parameters and right heart catheterization

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Abstract: Objectives – We set to evaluate the potential utility of right ventricle (RV) TEI-index as a prognostic parameter in patients with pulmonary arterial hypertension (PAH). We investigated its correlation with the clinical status, current treatment, a series of paraclinical parameters, as well as established determinants of prognosis in patients with PAH.

Methods – We enrolled in our study 24 patients with PAH confirmed by right heart catheterization (RHC) over a period of 4 years (2012-2016). We performed complete transthoracic echocardiography and six minute walk distance in all subjects.

Results – The RV TEI index correlated with the World Health Organization functional class (WHO FC) (p=0.05) and right atrial pressure determined by RHC (p=0.01). Patients undergoing diuretic treatment had a statistically significant lower TEI Index (p=0.017). There was also a trend of association between treatment with bosentan and a lower TEI index (p=0.0727).

Conclusions – In PAH patients, the RV TEI Index correlates with clinical parameters (WHO FC, 6MWD) and hemodynamic variables (right atrial pressure). RV TEI Index could improve under treatment with diuretics and possibly bosentan in these patients.

Keywords: pulmonary arterial hypertension, TEI index

INTRODUCTION

Pulmonary arterial hypertension (PAH) is a rare but life-threatening disease. PAH is defined as an increase in pulmonary arterial pressure \( \geq 25 \) mmHg as assessed by right heart catheterization (RHC) associated with a pulmonary artery wedge pressure (PAWP) \( \leq 15 \) mmHg and a pulmonary vascular resistance (PVR) >3 Wood units in the absence of other causes of precapillary PH\textsuperscript{1}.

Echocardiography is currently the most useful method of screening and monitoring for patients diagnosed with PAH, regardless of whether they are undergoing treatment or not. In this category of patients, right ventricular function is a major determinant...
of effort capacity and clinical evolution. Echocardiography is also a non-invasive method for establishing the causes and consequences of elevated pulmonary artery pressures. The measured parameters include estimation of pulmonary artery systolic pressure (sPAP), right ventricle (RV) to right atrium (RA) gradient, RV areas and fractional area change (FAC), tricuspid annular plane systolic excursion (TAPSE), and RV Tei-index. Current guidelines acknowledge measurement of RA area and the presence of pericardial effusion as echocardiographic prognostic markers in PAH. The TEI index also known as the RIMP is a global estimate of both systolic and diastolic function of the RV and it is based on the relationship between ejection and non-ejection work of the RV.

**OBJECTIVE**

We sought to evaluate the potential utility of RV TEI-index as a prognostic parameter in patients with PAH. We investigated its correlation with the clinical status, current treatment, a series of paraclinical parameters, as well as established determinants of prognosis in patients with PAH.

**MATERIAL AND METHOD**

We enrolled in our study 24 patients with PAH confirmed by right heart catheterization (RHC) over a period of 4 years (2012-2016). Patients were referred to our cardiology ward from the “Marius Nasta” Institute of Pneumology, and were all included in the National Program for Arterial Pulmonary Hypertension Management. Mean age of the study group was 53.5 +/- 14.7 years, range 26-82 years, with 29 % women.

All subjects underwent complete transthoracic echocardiography using a Vivid 7 system within maximum 6 months before or after the RHC (medium interval 2 months). We measured TAPSE, RA, RV, S wave, acceleration time (AT), mean pulmonary artery pressure (mPAP), right ventricle to right atrium pressure gradient, right ventricle ejection fraction, pulmonary artery systolic pressure (sPAP), E wave, A wave, E/E', inferior vena cava dimension and TEI index, all according to the current guidelines for RV echocardiographic evaluation.

Thus, the TEI index was defined as the ratio of isovolumic time (IVT) divided by ejection time (ET), or 

\[
\frac{\text{IVT}}{\text{ET}} = \frac{(\text{IVCT} + \text{IVRT})}{\text{ET}}
\]

Spectral Doppler recordings of CW of the tricuspid regurgitation jet in order to measure the interval “a” between the start and end of trans tricuspid flow (Figure 1), and PW of right ventricular outflow in order to measure interval “b”, the right ventricular ejection time (Figure 2).

Intervals a and b are used to calculate myocardial performance index (MPI) for the right and left ventricle as per the formula: 

\[
\text{MPI} = \frac{a - b}{b}
\]

bpm = beats/min; CW = continuous-wave Doppler; HR = heart rate; PW = pulsed-wave Doppler.

In order to measure the isovolumic time and ejection time, the formula is using 2 time intervals a and b as shown in the figures 1 and 2, isovolumic time = a-b and ejection time = b. The interval a includes the IVCT, the ejection time (ET) and the IVRT, and the TEI index may also be expressed by the formula a-b/b. For the evaluation of the right ventricular (RV) TEI index the a interval, from the end to the start of trans-tricuspid flow (the interval from the end of the A wave to the start of the E wave), is obtained from the apical 4-chamber view with the Doppler sample volume located betwe-
RESULTS

Mean TEI index was 0.652 +/-0.356. TR was moderate in 22 patients and severe in 2 patients. Mean distance in the 6MWD was 440 m (range 200 m – 700 m). Mean RA volume was 90.8 mL (range 39 – 205 mL). Clinically, 1 patient presented in WHO FC I, 6 patients in WHO FC II, 16 in WHO FC III and 1 in WHO FC IV. Mean right atrial pressure (RAP) was 7 mmHg (range 1-14 mmHg).

The TEI index correlated with WHO FC and RAP determined by RHC, but not with other echocardiographic markers of RV function, such as TAPSE, RV ejection fraction or right cavities dimensions (Table 1).

Possible implications of the different treatments for PAH on the value of TEI index were also investigated (Table 2). Patients undergoing diuretic treatment had a statistically significant lower TEI Index (p=0.017). There was also a trend of association between treatment with Bosentan and a lower TEI index (p=0.0727).

When considering TEI index as normal when <0.4 and high when >0.4, a correlation was documented between normal TEI index and longer than 440 m distance of the tips of the tricuspid valve leaflets. The b interval (right ventricular ejection time) is measured from the parasternal long-axis view, with the sample volume located just below the pulmonary valve.

The upper reference limit used for the right-sided MPI is 0.40 using the pulsed Doppler method, according to current recommendations1.

Tricuspid regurgitation (TR) was functional in all patients in terms of mechanism and was evaluated by means of quantitative (PISA measurements), qualitative (tricuspid valve morphology, color flow TR jet) and semi-quantitative parameters (vena contracta width, hepatic vein flow).

All patients underwent a six-minute walk distance (6MWD) test within 6 months before or after the RHC. The 6MWD test was performed by a trained pneumologist on a 20 m corridor with no prior practice walks in accordance with the American Thoracic Society guidelines. The World Health Organization (WHO) functional class (FC) was determined in accordance with current PAH guidelines1.
DISCUSSION
The most relevant findings of our study were: (1) the TEI index correlated with clinical parameters used in the assessment of PAH severity such as WHO FC and 6MWD; (2) the TEI index was associated strongly with diuretic treatment and had a trend towards association with Bosentan treatment; (3) the TEI index correlated strongly with RA pressure determined invasively.

Several studies tested the utility of RV TEI index in the evaluation of RV function and as a marker of adverse outcome in patients with pulmonary hypertension. The advantages of using the TEI Index are that it avoids the geometric assumptions and limitations of complex RV geometry. The WHO FC class, despite its interobserver variability, remains one of the most powerful predictors of survival, as a worsening FC class is one of the most alarming markers of disease progression. The correlation between the TEI index and the WHO class (p=0.052) supports the potential of the TEI index as an indicator of RV function and overall prognosis. The TEI index also correlated with the 6MWD. This strengthens the association between the TEI index and clinical parameters assessing the severity of the disease. In our study group the correlation was present at a threshold of the 6MWD of 440 m. Consequently, patients with a TEI index >0.4 had a odds ratio of 2.602 (borderline statistical significance, p=0.059) for a shorter than 440 m walking distance and conversely, patients with a TEI index <0.4 were associated with longer than 440 m 6MWD. For the lower threshold of the 6MWD, those with a TEI index <0.4 were associated with shorter than 440 m walking distance and conversely, patients with a TEI index >0.4 had an odds ratio of 2.602 (borderline statistical significance, p=0.059) for a shorter than 440 m walking distance and conversely, patients with a TEI index <0.4 were associated with longer than 440 m 6MWD.

A surprising finding is the lack of correlation among the TEI index and other echocardiographic parameters used in the global assessment of RV function, such as: RV EF, TAPSE or S wave. This comes in contradiction with previous studies, such as the one conducted by Forfia et al. which reported that TAPSE strongly reflects RV function and prognosis in PAH.

Regarding the association between TEI Index and hemodynamic variables, Dyer et al. and Ogihara et al demonstrated that RV Tei-index correlated with mean PAP as well as pulmonary vascular resistance (PVR). In our study, the TEI index correlated with the right atrial pressure (p=0.0178), but no other associations with hemodynamic measurements were possible. This correlation contradicts the assumption formulated by other studies, namely that TEI index measurement is unreliable when RA pressure is elevated.

Another finding of our study was that TEI Index was strongly associated with diuretic treatment, being lower in patients on furosemide or furosemide/spironolactone (p=0.017) compared to patients without diuretic treatment. These findings are similar to previous results, leading to the conclusion that the RV TEI index is in part preload-dependent. Since our study was observational, no evaluation was performed before versus after diuretic therapy in the same patient.

STUDY LIMITATIONS
The relatively long timespan (6 months) from the right heart catheterization to the moment of the echocardiography and clinical assessment (WHO FC, 6MWD) in some patients is one of the main limitations of our study. Patients in atrial fibrillation were excluded from the study as differing R-R intervals make TEI Index measurement unreliable. Absence of long-term follow-up and the relatively small patients group represent other limitations.

CONCLUSION
In PAH patients, the RV TEI Index correlates with clinical parameters (WHO FC, 6MWD) and hemodynamic variables (right atrial pressure). RV TEI Index could improve under treatment with diuretics and possibly Bosentan in these patients. The strong association with the clinical status of the patient warrants further studies to confirm the potential of the RV TEI Index as a prognostic parameter in patients with PAH.

Conflict of interest: none declared.

References:


