

Utility of Right Ventricular Tei Index in the Noninvasive Evaluation of Chronic Thromboembolic Pulmonary Hypertension Before and After Pulmonary Thromboendarterectomy

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OBJECTIVES We evaluated the utility of tissue Doppler-derived right ventricular (RV) Tei (or myocardial performance) index in patients with chronic thromboembolic pulmonary hypertension (CTEPH) before and after pulmonary thromboendarterectomy (PTE) and assessed correlations with mean pulmonary artery pressure (mPAP), pulmonary vascular resistance (PVR), and cardiac output (CO).

BACKGROUND The assessment of RV function is limited with 2-dimensional echocardiography. The RV Tei index, an indicator of RV myocardial performance, is derived by Doppler measurements and is unaffected by RV geometry. The use of tissue Doppler imaging (at the lateral tricuspid annulus) for RV Tei index calculation is simple and eliminates the need for pulsed-wave Doppler recordings of both RV inflow and outflow.

METHODS Ninety-three patients with CTEPH were prospectively studied along with 13 control patients. Right ventricular tissue Doppler imaging and right heart catheterization were performed before and after PTE. Right ventricular Tei index was compared with values of mPAP, PVR, and CO with the use of linear regression.

RESULTS Right ventricular Tei index was 0.52 ± 0.19 in patients with CTEPH and 0.27 ± 0.09 in control patients ($p < 0.0001$). After PTE, RV Tei index decreased to 0.33 ± 0.10 ($p < 0.0001$). Pulmonary vascular resistance correlated well with RV Tei index before ($r = 0.78$, $p < 0.0001$) and after ($r = 0.67$, $p < 0.0001$) surgery. Also, the absolute change in Tei index in each patient after PTE correlated well with the concomitant change in PVR ($r = 0.75$, $p < 0.0001$). RV Tei index did not correlate as well with mPAP (pre-operatively: $r = 0.55$, $p < 0.0001$; post-operatively: $r = 0.26$, $p = 0.03$) or CO (pre-operatively: $r = 0.57$, $p < 0.0001$; post-operatively: $r = 0.43$, $p < 0.0001$).

CONCLUSIONS These results demonstrate a correlation between RV Tei index and right heart hemodynamics (particularly PVR) in CTEPH. Because PVR is difficult to estimate noninvasively—and yet correlates with disease severity—the RV Tei index may be a valuable noninvasive parameter for monitoring disease severity in CTEPH and outcome after PTE. (J Am Coll Cardiol Img 2009;2:143–9) © 2009 by the American College of Cardiology Foundation

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ABBREVIATIONS AND ACRONYMS

- CO** = cardiac output
- CSA** = cross-sectional area
- CTEPH** = chronic thromboembolic pulmonary hypertension
- mPAP** = mean pulmonary artery pressure
- PTE** = pulmonary thromboendarterectomy
- PVR** = pulmonary vascular resistance
- RV** = right ventricular

Evaluating right ventricular (RV) function with 2-dimensional echocardiography is a troublesome endeavor. This problem affects the clinical assessment and management of patients with RV dysfunction, including those with chronic thromboembolic pulmonary hypertension (CTEPH). Although peak pulmonary artery pressure (PAP) can be estimated accurately with the use of continuous-wave Doppler (1), conventional 2-dimensional echocardiographic measurements cannot be extrapolated into accurate assessments of RV volume or global function. In addition, noninvasive estimation of pulmonary vascular resistance has its limitations (2,3).

See page 150

The Tei (or myocardial performance) index is a measurement of global myocardial function that has been used to evaluate both left ventricular and RV function (4-9). Derived from Doppler echocardiography, the Tei index is independent of ventricular geometry (4). Traditionally, the Tei index has been calculated with the use of sequential pulsed-wave Doppler recordings of ventricular inflow and out-

flow. More recently, the index has been calculated with tissue Doppler recordings from the lateral mitral annulus (10); this eliminates the need for sequential recordings and thereby reduces error from fluctuations in heart rate (11). Similarly, measurement of RV Tei index from tricuspid annular tissue Doppler recordings correlate well with calculations using pulsed-wave Doppler of RV inflow and outflow (12). The RV Tei index is defined as $(A - B)/B$, where A is time interval between the end and onset of tricuspid annular diastolic velocity and B is the duration of tricuspid annular systolic velocity (or RV ejection time) (Fig. 1) (4).

The RV Tei index has been useful in patients with RV dysfunction and congenital heart disease (4,6,7) and correlates well with RV ejection fraction in patients whose RV is their systemic ventricle (13). In individuals with idiopathic pulmonary arterial hypertension (IPAH), RV Tei index corresponds well with clinical status and predicts survival (8). Additionally, the RV Tei index correlates with mean PAP (mPAP) and response to therapy in children with idiopathic pulmonary arterial hypertension (14).

The goals of this study were to (1) measure tissue Doppler-derived RV Tei index in patients with CTEPH and assess changes after pulmonary thromboendarterectomy (PTE) and (2) compare RV Tei index values with hemodynamic measurements from invasive right heart catheterization, including mPAP, pulmonary vascular resistance (PVR), and cardiac output (CO) in patients with CTEPH before and after PTE.

METHODS

We prospectively studied 93 consecutive consenting patients with CTEPH who underwent PTE. Patients included 33 men and 60 women ages 18 to 83 years (mean age of 53 years). Fifteen healthy volunteers were also studied to determine normal RV Tei index. The study design was reviewed and approved by the UCSD Human Research Protection Program/Institutional Review Board. After patient consent was obtained, complete 2D and Doppler echocardiographic examinations were performed (along with TDI of the lateral tricuspid annulus) 13 ± 4 days before PTE and 9 ± 4 days after PTE. Examinations were performed on Philips ultrasound units (Bothell, Washington) with data stored digitally for off-line analysis. Lateral tricuspid annular TDI recordings were obtained from the apical 4-chamber view at end-expiration,

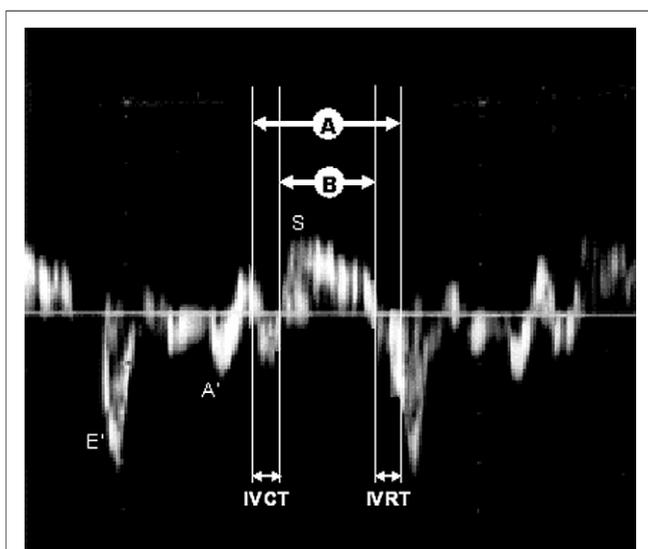


Figure 1. Example of Tissue Doppler Recording of Lateral Tricuspid Annular Velocity

Right ventricular Tei index is defined as $(A - B)/B$, where A is the period including the isovolumetric contraction time (IVCT), systolic contraction (S), and the isovolumetric relaxation time (IVRT). B is defined as the time period of systolic contraction alone. E' = early diastolic tissue velocity; A' = late diastolic tissue velocity.

and the results of 3 consecutive cardiac cycles were averaged. Measurements were made before and after PTE and analyzed in a blinded fashion. Assessment of RV size was performed both qualitatively and quantitatively. In the apical 4-chamber view, RV size was judged as (1) normal if the RV end-diastolic cross-sectional area (CSA) was less than the LV area, (2) mildly enlarged if the RV and LV cavity end-diastolic areas were approximately equal, (3) moderately enlarged if the RV area was clearly larger than the LV area, and (4) severely enlarged if the RV area was markedly larger than the LV area. Also in the apical 4-chamber view, RV end-diastolic CSA was measured on off-line analysis.

All study subjects underwent cardiac catheterization 9 ± 4 days before surgery, and mPAP, PVR, CO, and mean arterial pressure were measured. These values were measured again after PTE. Differences between mean values for mPAP, PVR, CO, mean arterial pressure, and RV Tei index before and after surgery were compared with the Student paired *t* test. Linear regression analysis and Pearson's correlations were used to compare the Tei index with mPAP, PVR, and CO before and after surgery. Differences in Tei index and PVR by RV size were also compared with the Student paired *t* test. Ten percent of study evaluations were repeated by the same and a second interpreter to assess intra- and interobserver variability. Statistical analyses were performed with Statview statistical software (SAS Institute, Cary, North Carolina). Data are expressed as mean value ± standard deviation. A *p* value of < 0.05 was considered statistically significant.

RESULTS

The RV Tei index for 15 healthy adults was 0.27 ± 0.09, which was similar to previously reported results (6,13). The RV Tei index in patients with CTEPH was 0.52 ± 0.19 (*p* < 0.0001 compared with control patients), which is similar to the findings of a smaller previous study of patients with CTEPH (0.55 ± 0.22) (15). Interobserver and intraobserver variabilities in the measurement of RV Tei index were both <5%.

Comparison of RV Tei index and hemodynamic measurements before and after surgery are shown in Table 1 and Figure 2. After PTE, mPAP decreased from 45.9 ± 10.5 mm Hg to 30.4 ± 8.3 mm Hg; cardiac output increased from 4.0 ± 1.3 l/min to 5.6 ± 1.6 l/min; PVR decreased from 831 ± 441

Table 1. Pre- and Post-Operative RV Tei Index and Right Heart Hemodynamic Measurements

Parameter	Pre	Post	p Value
PVR (dyne·s/cm ⁵)	831 ± 441	324 ± 149	<0.001
mPAP (mm Hg)	45.9 ± 10.5	30.4 ± 8.3	<0.001
CO (l/min)	4.0 ± 1.3	5.6 ± 1.6	<0.001
Heart rate (beats/min)	86 ± 10	84 ± 8	NS
Stroke volume (ml)	47 ± 8	66 ± 23	<0.001
Mean arterial BP (mm Hg)	92 ± 6	97 ± 10	0.03
RV Tei index	0.52 ± 0.19	0.33 ± 0.10	<0.0001
A interval	0.44 ± 0.08	0.40 ± 0.06	<0.001
B interval	0.29 ± .05	0.30 ± 0.06	NS

Pre- and post-operative values of PVR, mPAP, CO, heart rate, stroke volume, mean arterial BP, and RV Tei index (with A and B intervals; see Fig. 1) in patients with chronic thromboembolic pulmonary hypertension before and after pulmonary thromboendarterectomy.

BP = blood pressure; CO = cardiac output; mPAP = mean pulmonary artery pressure; PVR = pulmonary vascular resistance; RV = right ventricular.

dyne·s/cm⁵ to 324 ± 149 dyne·s/cm⁵ (*p* < 0.001 for all). The RV Tei index decreased from 0.52 ± 0.19 to 0.33 ± 0.10 (*p* < 0.0001). The “A” portion of the Tei index decreased significantly after PTE, whereas the “B” portion was unchanged (Table 1). This finding indicates a significant decrease in isovolumetric times after surgery but no significant change in RV ejection time. The post-operative Tei

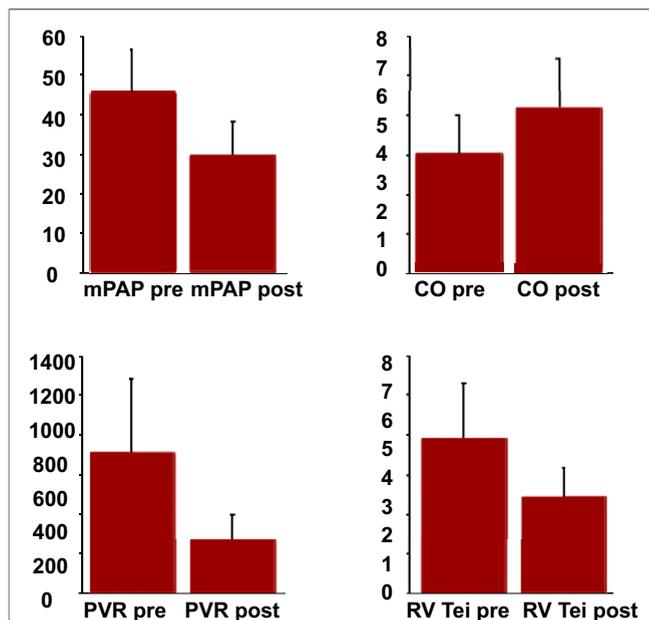


Figure 2. Pre- and Post-Operative Hemodynamic Indexes and RV Tei Index

Mean values (± SD) of hemodynamic parameters, including mean pulmonary artery pressure (mPAP) (mm Hg), cardiac output (CO) (l/min), pulmonary vascular resistance (PVR) (dyne·s/cm⁵), and right ventricular (RV) Tei index are shown before and after pulmonary thromboendarterectomy. mPAP, PVR, and RV Tei index all decreased markedly, whereas CO increased significantly. *p* < 0.001 for all comparisons.

Table 2. Pre- and Post-Operative Correlations Between Hemodynamic Values and RV Tei Index

Parameter	Pre-Operative		Post-Operative	
	r	p Value	r	p Value
PVR	0.78	<0.0001	0.67	<0.0001
mPAP	0.55	<0.0001	0.26	0.03
CO	0.57	<0.0001	0.43	<0.0001

Correlation coefficients (with p values) comparing pre- and post-operative hemodynamic values with RV Tei index.
Abbreviations as in Table 1.

index was much improved, but was still higher than the normal value of 0.27 ± 0.09 ($p < 0.01$).

Linear regression analysis results of RV Tei index with PVR, mPAP, and CO before and after surgery are shown in Table 2. Of these hemodynamic variables, RV Tei index correlated best with PVR pre-operatively ($r = 0.78$, $p < 0.0001$) (Fig. 3). Post-operatively, RV Tei index again correlated best with PVR ($r = 0.67$, $p < 0.0001$) (Fig. 4). Finally, analysis of the absolute change in RV Tei index versus absolute change in PVR for each patient was performed (Fig. 5). This relationship was highly significant as well ($r = 0.75$, $p < 0.0001$). RV Tei index correlated directly with mPAP and PVR and inversely with CO.

The RV Tei index and PVR also varied significantly with degree of RV enlargement. Table 3 shows the distribution of degrees of RV enlargement and corresponding mean Tei indexes and

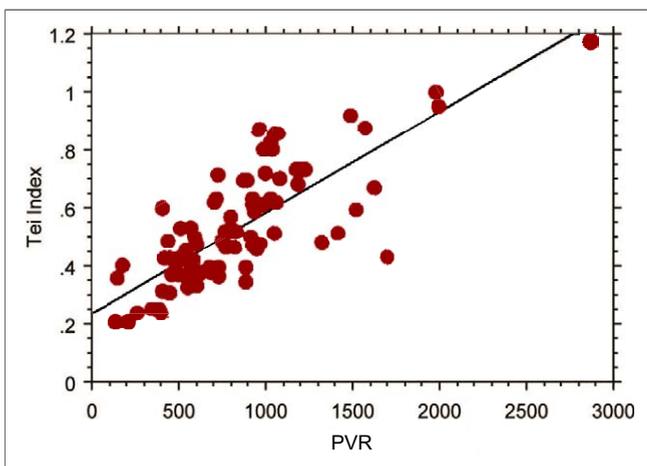
PVR. Differences in RV Tei index and PVR were not statistically significant between the groups with normal RV size versus mild RV enlargement ($p = 0.28$ and $p = 0.07$, respectively). However, differences in the 2 parameters were highly significant between the mild versus moderate RVE groups and the moderate versus severe RVE groups ($p = 0.025$ and $p = 0.002$ for RV Tei index, respectively; $p = 0.001$ and $p = 0.007$ for PVR). Quantitative measurements of RV size also are included in Table 3. In the group with normal RV size, RV CSA was 15.0 ± 2.3 cm². Right ventricular CSA was 24.7 ± 5.2 cm², 28.6 ± 5.0 cm², and 37.3 ± 7.7 cm² in the groups with mild, moderate, and severe RVE, respectively. Differences between these groups were all statistically significant ($p = 0.04$ for the difference between the normal vs. mild RVE groups, $p = 0.02$ for mild vs. moderate RVE, and $p = 0.001$ for moderate vs. severe RVE).

Six patients with CTEPH had mid-systolic partial closure of the pulmonic valve on m-mode imaging (the “flying W” sign): mean Tei index for this group was 0.71 ± 0.20 versus 0.50 ± 0.16 in patients without this finding ($p = 0.04$). Those with the flying W sign had a mean PVR of $1,081 \pm 457$ dyne·s/cm⁵, whereas the mean PVR of those without was 793 ± 329 dyne·s/cm⁵ ($p = 0.04$).

DISCUSSION

The Tei (or myocardial performance) index has been investigated extensively in the assessment of LV function (5,9,11,16). There is now a growing body of literature evaluating the utility of tissue Doppler imaging and the RV Tei index in patients with RV dysfunction and pulmonary hypertension (4,6–8,12,17,18). The Tei index is derived solely by Doppler measurements and thus is not affected by RV geometry. Initially, the RV Tei index was calculated using pulsed-wave Doppler recordings of RV inflow and outflow (4,6,7), but more recent studies have shown that tissue Doppler imaging of the lateral tricuspid annulus allows simpler (and equally accurate) measurements of RV Tei index (10,12). This method eliminates the need for 2 separate Doppler interrogations (RV inflow and RV outflow) and therefore negates the effect of heart rate variability.

RV dysfunction is associated with an increase in RV Tei index (7), and work in animal models has shown a graded response of the Tei index to increases in RV afterload and pulmonary artery pressure (19,20). Reports of acute RV overload in

**Figure 3. RV Tei Index Versus Pre-Operative PVR**

Linear regression analysis of pre-operative PVR (dyne·s/cm⁵) assessed by cardiac catheterization and tissue Doppler-derived RV Tei index in patients with CTEPH. The graph demonstrates the significant association between increasing values of PVR and RV Tei index before pulmonary thromboendarterectomy ($r = 0.78$, $p < 0.0001$). The regression equation is $y = 0.25 + 0.00034x$. CTEPH = chronic thromboembolic pulmonary hypertension; PVR = pulmonary vascular resistance; RV = right ventricular.

humans (during acute pulmonary embolism) have demonstrated a marked increase in RV Tei index compared with control patients, as well as a return toward normal after chronic anticoagulation therapy (21,22). Studies of chronic RV overload and pulmonary hypertension also have shown abnormally increased values of RV Tei index. The index is useful for predicting prognosis in adults with idiopathic pulmonary hypertension (8) and correlates well with mean PA pressure (and response to therapy) in children with idiopathic pulmonary hypertension (14).

Literature addressing the utility of the RV Tei index in CTEPH, however, is scarce. Previously, Menzel et al. (15) evaluated 24 patients with CTEPH who underwent PTE. They found that the RV Tei index decreased significantly after PTE (from 0.55 to 0.37, $p < 0.05$). This decrease is similar to that of the present study (0.52 to 0.33, $p < 0.0001$). Despite this, they did not find a correlation between RV Tei index and mPAP or PVR. This may have been due to the relatively small number of subjects. In this current study of 93 patients (which, to our knowledge, is the largest population evaluated to date), we found significant correlations between RV Tei index and mPAP, CO, and PVR. Although all of these relationships were statistically significant, the r value and strength of correlation was highest between RV Tei index and PVR.

One may ask why the RV Tei index is increased in CTEPH. Right ventricular systolic function is especially afterload-dependent, and the combination of pulmonary hypertension and RV dysfunction in CTEPH leads to an increase in isovolumetric contraction time and a decrease in RV ejection time. This results in an abnormally high Tei index. After PTE, RV afterload decreases dramatically and the time spent in isovolumetric contraction and relaxation decreases. We found that the RV ejection time did not change significantly immediately after surgery (Table 1), possibly because of persistent RV dysfunction and stunning in the perioperative period. The combination of these changes, however, led to a decrease in RV Tei index toward normal.

Is there an incremental value in measuring RV Tei index in patients with known or suspected CTEPH? We believe the answer is yes, for several reasons. First, the finding of a normal RV Tei index in a patient referred for possible CTEPH makes the diagnosis very unlikely. This conclusion could be especially useful when trivial or no TR is present and PAP cannot be estimated noninvasively. Second, the equations from the regression analyses

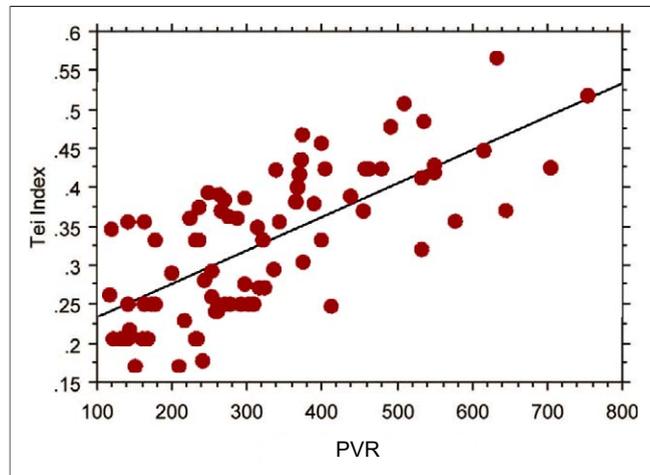


Figure 4. RV Tei Index Versus Post-Operative PVR

Linear regression analysis of post-operative PVR (dyne-s/cm⁵) assessed by cardiac catheterization and RV Tei index in patients with CTEPH. Similar to Figure 3, the graph demonstrates the significant association between increasing values of PVR and RV Tei index after pulmonary thromboendarterectomy ($r = 0.67$, $p < 0.0001$). The regression equation is $y = 0.19 + 0.00043x$. Abbreviations as in Figure 3.

provide a reasonable noninvasive estimate of pre- and post-operative PVR (which could be useful when a right heart catheter is not in place). Finally (and speculatively), post-operative RV Tei index and the change in Tei index after surgery could be useful markers of medium- and long-term prognosis after PTE. This is an area of ongoing research. **Study limitations.** Pre-operative transthoracic echocardiography and right heart catheterization were not

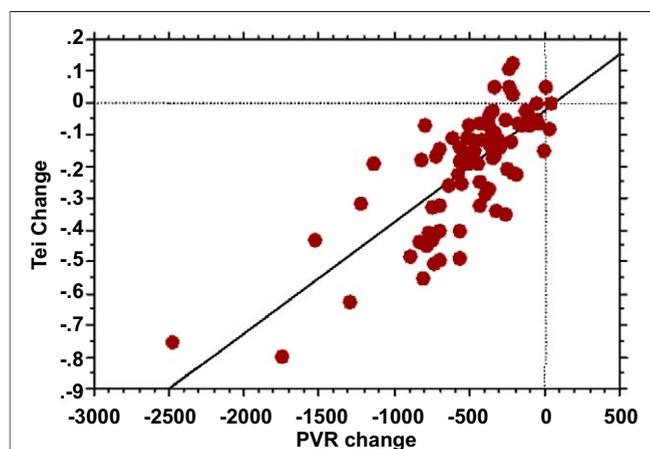


Figure 5. Change in RV Tei Index Versus Change in PVR

Linear regression analysis of change in PVR and RV Tei index for each patient after PTE. Although the absolute values of RV Tei index correlated with PVR before and after PTE, this graph demonstrates that the change in RV Tei index after surgery correlated significantly with the corresponding decrease in PVR ($r = 0.75$, $p < 0.0001$). The regression equation is $y = -0.023 + 0.00035x$. Abbreviations as in Figure 3.

Table 3. Comparison of RV Tei Index, PVR, and RV Enlargement

Extent of RV Enlargement	No. of Patients (n = 93)	RV Tei Index	PVR (dyne-s/cm ⁵)	RV CSA (cm ²)
1. None (normal)	5	0.33 ± 0.17	214 ± 112	15.0 ± 2.3
2. Mild	20	0.40 ± 0.12	546 ± 198	24.7 ± 5.9
3. Moderate	28	0.49 ± 0.14	776 ± 208	28.6 ± 5.0
4. Severe	40	0.63 ± 0.19	1081 ± 489	37.3 ± 7.7

Comparison of RV Tei index, PVR, and CSA in patients with differing severities of right ventricular (RV) enlargement. p values for differences between RV Tei index, PVR, and RV CSA comparing groups 2 versus 3 and 3 versus 4 are all significant. p values for RV CSA comparing groups 1 versus 2 also are significant (see text for details). CSA = cross-sectional area; other abbreviations as in Table 1.

performed simultaneously in this study, and up to 48 h elapsed between the 2 procedures. Because the nature of pulmonary hypertension was chronic in this patient population, we do not believe that simultaneous measurement would have yielded substantially different results. After PTE, the time between hemodynamic measurements and echocardiography was longer (mean of 9 days), and it is possible that hemodynamic and Doppler parameters fluctuated during this period. In general, however, patients in this study remained stable after PTE. As with previous studies from our institution, echocardiography was delayed until patients left the surgical intensive care unit and could be positioned properly for examination in the noninvasive cardiac laboratory (2,23).

CONCLUSIONS

The results of this study demonstrate a clear and significant correlation between RV Tei index and

right heart hemodynamics (especially PVR) in CTEPH. The RV Tei index is abnormally increased in these patients and decreases dramatically after PTE. The extent of change in Tei index after PTE accurately predicts the change in PVR ($r = 0.75$, $p < 0.0001$). Because PVR is difficult to measure noninvasively (and yet correlates with disease severity), the RV Tei index appears to be a useful parameter for estimating PVR and monitoring disease severity in CTEPH before and after PTE. Its independence of ventricular geometry and straightforward measurement make the RV Tei index particularly attractive in this population.

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Key Words: chronic thromboembolic pulmonary hypertension ■ right ventricle ■ Tei (myocardial performance) index ■ pulmonary vascular resistance ■ pulmonary thromboendarterectomy.