The use of the right ventricular diameter and tricuspid annular tissue Doppler velocity parameter to predict the presence of pulmonary hypertension

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KEYWORDS
Echocardiography; Pulmonary hypertension; Pulmonary artery systolic pressure; Tissue Doppler; Right ventricular diameter

Abstract  Aims: Detecting the presence of pulmonary hypertension (PH) is important especially with unexplained dyspnoea and suspected thromboembolism. Although PH can be detected invasively by right ventricular (RV) catheterisation, accurate non-invasive assessment by echocardiography has many advantages. This however relies on the presence of tricuspid regurgitation (TR). We examined if the presence of PH can be predicted echocardiographically without relying on TR.

Methods and results: Seventy-six consecutive patients with TR were recruited, and another 32 were used for prediction study. RV end-diastolic diameter (RVD) was measured in the apical view and tissue Doppler imaging (TDI) parameters were obtained from the lateral tricuspid annulus motion. Pulmonary artery systolic pressures (PASP) were estimated from TR. The RVD, and the TDI duration from start of isovolumic contraction to peak systole, $T_{\text{peak}}$, correlated with PASP. However, the RVD/$T_{\text{peak}}$ ratio offered the best correlation and, at a cutoff of 22 cm/s, predicted the presence of PH with 80% sensitivity and 83% specificity. The same results were obtained even if the study was confined to patients with or without RV dysfunction. The ratio displayed a good correlation with catheter-derived PASP in nine separate patients.

Conclusion: While RVD and $T_{\text{peak}}$ can adequately detect the presence of PH, RVD/$T_{\text{peak}}$ acted as the best predictor for PH. The results apply regardless of the presence or absence of RV dysfunction.

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Introduction

Pulmonary hypertension (PH) refers commonly to elevation of pulmonary artery pressures (PAP) above normal, and is defined as having a PA systolic pressure (PASP) of greater than 35 mmHg or a mean PAP of greater than 25 mmHg. PH is present in a number of conditions, e.g. chronic obstructive pulmonary disease, and pulmonary embolism. It may also reflect the presence of underlying pulmonary vascular disease which can be progressive and fatal, or the presence of elevated pressures in the left heart.

Traditionally, PAP is measured invasively by means of the pulmonary artery catheter (PAC), mostly in the intensive care setting. However, the use of PACs has declined in recent years due to the findings that the use of PAC with all the attendant risks did not confer any benefit to management nor did it improve patient outcomes.1,2 Indeed, the sales of PAC in Europe, the United States, and Japan has fallen by almost 9% since 2002.3 In contrast, echocardiography is widely used to estimate the PAP non-invasively if tricuspid regurgitation (TR) is present.4

Echocardiography provides an easy and non-invasive way of estimating PAP. The measurement relies entirely on the presence of adequate TR Doppler signal, which are not always present in every patient. Jet direction may add further frustrations to the measurements. In this study, we examined the predictive value of a new index, based on the right ventricular dimension and tricuspid annular tissue Doppler imaging (TDI), for the presence of PH. The detection of PH is particularly important in the acute situation because rapid diagnosis is often essential to improve patient outcome.

Methods

Patients

This study was carried out in the Cardiovascular Ultrasound Laboratory in a tertiary referral teaching hospital. The laboratory received both in-patient and out-patient referrals. The most common referral reasons were assessment of left ventricular function, presence of heart murmur, unexplained dyspnea and pulmonary embolism. Patients with (1) inadequate Doppler signal, (2) eccentric TR jet, and/or (3) suboptimal two-dimensional images were not recruited for the study. Altogether 108 patients were recruited for the non-invasive study. They were divided into two groups: (1) the first 76 consecutive patients for investigational study, and (2) the next 32 patients for prediction study. Another nine patients with indwelling PAC were recruited for invasive study. The PAP were obtained from the PAC recordings. The study protocol was approved by the institute’s ethics committee and written informed consent was obtained from each patient.

Echocardiography

Standard two-dimensional (2-D) and Doppler trans-thoracic echocardiographic (TTE) studies were performed using the Vivid 7 (GE Vingmed Ultrasound, Horton, Norway). All 2-D and Doppler images were acquired and recorded digitally, and analysed offline. The internal medio-lateral dimension of the right ventricular end-diastolic diameter (RVD) was measured along the minor axis in the apical four-chamber view, at a level of approximately one-third from the base of the ventricle. The peak-to-peak TAD were measured in the M-mode, which was obtained by placing the cursor through the lateral tricuspid annuls in the apical four-chamber view.5

The maximal TR velocity was recorded by continuous-wave Doppler from any standard views that yielded the highest peak velocity during expiration. The right ventricle-to-right atrium peak pressure gradient (ΔP_{RV-RA}) was calculated using the modified Bernoulli equation, \( ΔP_{RV-RA} = 4V^2 \) where \( V \) is the peak regurgitant velocity. PASP was estimated by using the equation \( PASP = ΔP_{RV-RA} + RAP \), where RAP is the right atrial pressure and was inferred from the inferior vena cava diameter (IVCd) and the caval respiratory index (IVCd during inspiration/IVCd during expiration).6,7 Briefly, the following RAP values were assigned: 5 mmHg for IVCd <2 cm with inspiratory collapse by >50%, 10 mmHg for non-collapsing IVCd of <2 cm; 15 mmHg for collapsing but dilated IVC (>2 cm) and 20 mmHg for fixed dilated IVC. PH was defined in this study as PASP >35 mmHg.

TDI parameters were measured offline using EchoPac software (v. 4 GE Vingmed Ultrasound, Horton, Norway). Briefly, the RV tricuspid annular (TA) motion (three cardiac cycles) was captured in the tissue velocity imaging mode in the apical view to display the myocardial tissue velocity (colour mapping). During offline analysis, the cursors were placed at the lateral TA and the TA velocity (TAV) profiles were displayed (Fig. 1A). The TAV profiles consisted of two distinct peaks during systole: the isovolumic contraction (IC) phase and the systolic phase (Sm). The Sm peak was followed by a gradual return to the baseline in most patients.
(Fig. 1B), but Sm might sometimes be followed by another smaller peak in some patients (Fig. 1C). The following parameters were measured: (1) $T_{\text{peak}}$, time duration as measured from the beginning of IC to the first systolic peak (Sm or Sm1); (2) $T_{\text{end}}$, time duration as measured from the beginning of IC to the end of Sm; and (3) Sm, the peak systolic velocity (Fig. 1).

**Prediction study**

The predictive values of the parameters were tested non-invasively using a group of 32 patients. Two investigators (IT and SJH, both accredited echocardiographers) were blinded during the prediction study and from each other. Each of them...
was randomly assigned to measure either the PASP or the $T_{\text{peak}}$ and RVD parameters separately offline.

In another group of nine patients, the predictive values of the RVD/$T_{\text{peak}}$ ratio were tested against the PAC derived PASP. The PAC derived PASP was obtained at the time of the echocardiography procedure by a non-investigator physician. The echocardiographers were blinded from the readings.

### Statistics

Results, unless stated otherwise, are expressed as mean ± SD. Where appropriate, the median values are also given. Group comparisons were made using Student’s t-test. Chi-square test was used instead for nominal data. Kruskal–Wallis one-way ANOVA was used when comparisons for more than two groups were needed. Post-hoc pairwise comparisons were made using Wilcoxon rank-sum test with downward adjustment of significance level to compensate for multiple comparisons. Correlations were made using linear regression (Pearson product–moment correlation). Receiver-operating characteristic curves were constructed using PASP = 35 mmHg as response variable. A confidence level of $P < 0.05$ was taken as significant.

### Results

The patients’ characteristics and the TTE data for the investigational study (76 patients) are depicted in Table 1. There were no significant differences in age and TTE data between the male and female groups. Out of the 76 patients, 37 displayed some degree of reduced right ventricular (RV) function as denoted by a reduction in lateral tricuspid annular displacement (TAD) (<2.14 cm). The echocardiographic parameters for patients with (TAD < 2.14 cm) and without (TAD ≥ 2.14 cm) RV dysfunction are shown in Table 2. The group with reduced RV function demonstrated a higher PASP but a reduced Sm. As there were no significant differences in the other echocardiographic parameters (except Sm) and in the correlations between PASP and RVD or $T_{\text{peak}}$, the data from both groups were pooled together in the analysis.

### RVD and PASP

The RVD was significantly larger in patients with PH (3.82 ± 0.68 cm vs 3.30 ± 0.62 cm, $P < 0.001$) (Fig. 2A). When using RVD as a predictor for the presence of PH (PASP > 35 mmHg), a cutoff 3.60 cm provided a sensitivity and specificity of 65% and 67%, respectively (accuracy of ROC = 72%) (Fig. 5). The positive (PPV) and negative (NPV) predictive values were 75% and 56%, respectively. The mean PASP for patients with RVD ≥ 3.6 cm was 47.2 ± 13.5 mmHg (Fig. 2B). The mean PASP for patients with RVD

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### Table 1 Patients’ characteristics and TTE data

<table>
<thead>
<tr>
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<th>All</th>
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<th>Female</th>
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<tr>
<td>Number</td>
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<td>33</td>
<td>43</td>
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<tr>
<td>Age</td>
<td>67.8 ± 17.8</td>
<td>65.4 ± 18.4</td>
<td>69.6 ± 17.3</td>
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<tr>
<td>Heart rate (bpm)</td>
<td>78.4 ± 17.7</td>
<td>77.7 ± 18.4</td>
<td>79.0 ± 17.3</td>
<td>0.762</td>
</tr>
<tr>
<td>RVD (cm)</td>
<td>3.6 ± 0.7</td>
<td>3.7 ± 0.6</td>
<td>3.6 ± 0.8</td>
<td>0.419</td>
</tr>
<tr>
<td>$\Delta P_{\text{RV-RA}}$ (mmHg)</td>
<td>35.0 ± 12.0</td>
<td>33.4 ± 11.9</td>
<td>36.2 ± 12.2</td>
<td>0.316</td>
</tr>
<tr>
<td>PASP (mmHg)</td>
<td>43.0 ± 14.0</td>
<td>40.5 ± 13.4</td>
<td>45.0 ± 14.2</td>
<td>0.164</td>
</tr>
<tr>
<td>Sm (cm/s)</td>
<td>8.8 ± 2.4</td>
<td>9.0 ± 2.3</td>
<td>8.6 ± 2.6</td>
<td>0.552</td>
</tr>
<tr>
<td>$T_{\text{peak}}$ (s)</td>
<td>0.155 ± 0.034</td>
<td>0.152 ± 0.033</td>
<td>0.157 ± 0.036</td>
<td>0.541</td>
</tr>
<tr>
<td>$T_{\text{end}}$ (s)</td>
<td>0.340 ± 0.065</td>
<td>0.330 ± 0.064</td>
<td>0.346 ± 0.067</td>
<td>0.297</td>
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</tbody>
</table>

TTE, transthoracic echocardiography; RVD, RV end-diastolic diameter; $\Delta P_{\text{RV-RA}}$, peak RV-RA pressure gradient; PASP, pulmonary artery systolic pressure; Sm, peak systolic tissue Doppler velocity of the lateral tricuspid annulus; $T_{\text{peak}}$, time duration between start of isovolumic contraction and peak systolic velocity; $T_{\text{end}}$, time duration between start of isovolumic contraction and end-systole. $P$, the significance level between male and female groups.

### Table 2 TTE data for patients with normal (TAD ≥ 2.14 cm) or reduced (TAD < 2.14 cm) RV systolic function

<table>
<thead>
<tr>
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<th>TAD ≥ 2.14 cm</th>
<th>TAD &lt; 2.14 cm</th>
<th>$P$</th>
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<tr>
<td>Number</td>
<td>39</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>63.3 ± 19.7</td>
<td>72.5 ± 14.3</td>
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<tr>
<td>TAD</td>
<td>2.30 ± 0.25</td>
<td>1.42 ± 0.27</td>
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<tr>
<td>Sm (cm/s)</td>
<td>10.5 ± 1.7</td>
<td>7.0 ± 1.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PASP (mmHg)</td>
<td>39.4 ± 12.2</td>
<td>46.9 ± 14.8</td>
<td>0.018</td>
</tr>
<tr>
<td>RVD (cm)</td>
<td>3.6 ± 0.7</td>
<td>3.7 ± 0.7</td>
<td>0.46</td>
</tr>
<tr>
<td>$T_{\text{peak}}$ (s)</td>
<td>0.163 ± 0.033</td>
<td>0.150 ± 0.032</td>
<td>0.08</td>
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<tr>
<td>$T_{\text{end}}$ (s)</td>
<td>0.356 ± 0.062</td>
<td>0.322 ± 0.060</td>
<td>0.03</td>
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</table>
3.6 cm was not significantly different from 35 mmHg ($P = 0.163$).

### TDV parameters and PASP

A significant difference was observed in $T_{\text{peak}}$ between the PH and the non-PH groups, with the former displaying a shorter mean $T_{\text{peak}}$ duration ($0.144 \pm 0.028$ vs $0.174 \pm 0.03 s$, $P < 0.001$) (Fig. 3A). There was no difference in $T_{\text{end}}$ durations between the PH and non-PH groups ($0.332 \pm 0.071$ vs $0.350 \pm 0.056 s$, $P = 0.254$). Sm were also similar in both groups ($8.4 \pm 1.9$ vs $9.0 \pm 2.7 cm/s$, $P = 0.32$).

A $T_{\text{peak}}$ value of $\geq 0.190$ s offered a high sensitivity (98%) and negative predictive value (90%) for excluding PH (specificity = 30%, PPV = 68%; accuracy of ROC = 76%) (Fig. 5A). On the other hand, a $T_{\text{peak}}$ of $\leq 0.130$ s predicted PH with high specificity (93%) and PPV (92.9%) (sensitivity 28% and NPV 47%) (Fig. 5). When the $T_{\text{peak}}$ was stratified into three groups, viz. $< 0.13$ s (group A), $> 0.13$ to $< 0.19$ s (group B), and $\geq 0.19$ s (group C), there were significant differences in PASP between group A and group C ($P < 0.001$), as well as between group B and group C ($P = 0.003$) (Fig. 3B).

### RVD/$T_{\text{peak}}$ ratio and PASP

There was no correlation between RVD and $T_{\text{peak}}$ ($r = -0.05$, $P = 0.65$). A significant association was found between PASP and the RVD/$T_{\text{peak}}$ ratio ($r = 0.60$, $P < 0.001$). A cutoff RVD/$T_{\text{peak}}$ ratio of 22.0 cm/s offered a sensitivity and specificity of 80% and 83% in predicting a PASP of $> 35$ mmHg, respectively (accuracy 84%) (Figs. 4 and 5A). The PPV and NPV were 88% and 74%, respectively. Similar ROCs and cutoffs were obtained even when the patients were stratified according to the presence or absence of RV dysfunction (Fig. 5B). There was no significant correlation between the RVD/$T_{\text{peak}}$ ratio and heart rate ($P = 0.052$).
Predicting the presence of PH using RVD, Tpeak and RVD/Tpeak ratio

A total of 32 patients were used for the prediction and the results are depicted in Table 2. RVD correctly identified 20 patients (62.5%), 6 without and 14 with PH (Table 3). Tpeak ≥0.190 s were used to exclude PH, whereas Tpeak ≤0.130 s were used to confirm PH. Out of the 32 patients, Tpeak correctly identified 19 patients (59.3%) with or without PH, but 12 were inconclusive (37.5%). The Tpeak values for the inconclusive patients ranged from 0.135 to 0.185 s. RVD/Tpeak ratio, on the other hand, correctly identified 29 out of 32 patients (i.e. overall 90.6% accuracy).

RVD/Tpeak and PAC derived PASP

The RVD/Tpeak ratio demonstrated a good correlation with the PAC obtained PASP in nine separate patients (r = 0.87, P = 0.002) (Fig. 6). Five of these patients did not have any demonstrable TR jet, and four had suboptimal TR signals. Out of the nine patients, four had PASP >35 mmHg. Only three of these four patients had a RVD/Tpeak ratio <22 cm/s (i.e. 75%). The other five patients had RVD/Tpeak ratio of >22 cm/s and had PASP >35 mmHg.

Intraobserver and interobserver variability

The mean of differences between two measurements made by the same examiner were 0.002 ± 0.022 s (from -0.04 to 0.08 sec) for Tpeak and -0.004 ± 0.292 cm (from -0.62 to 0.45 cm) for RVD. Interobserver values for Tpeak and RVD by two independent observers were in good agreement (r = 0.975 and slope = 0.99 for Tpeak, and r = 0.780 and slope = 1.18 for RVD).

Discussion

The detection of the presence of PH is important in certain clinical scenarios, such as in suspected thromboembolic disease, ascites and peripheral...
oedema of unknown origin, and unexplained dyspnea. The use of PAC is often not recommended after balancing the risks and benefits in many of these situations. Echocardiography, on the other hand, has for a long time provided an alternative for the determination of PASP.4,8 However, the requirement of the presence of TR has made echocardiography nugatory in some situations. The present study demonstrated that the RVD/T peak ratio can predict the presence of PH with high accuracy without relying on TR.

The determination of PASP based on TR is the most common echocardiographic method. Although TR can be found in normal subjects, it is not invariably present. The prevalence of TR increases with the severity of PH, with TR most commonly seen where PASP >50 mmHg. The prevalence may reach as high as 84—96%.4,8,9 In patients with mild to moderate PH, the prevalence was lower at only 40—50%.4 In a recent retrospective cohort database examination in more than 7000 patients underwent echocardiography, only 91 (1.2%) were identified to have moderate-severe to severe TR.10 Whether or not the same proportion applies to other geographical locations awaits further research.

In the absence of TR, other echocardiographic methods involving blood flow Doppler can be used to estimate PAP. For example, pulmonary regurgitant velocity can be used to estimate MPAP and end-diastolic PAP.11 Derived regression models, though not widely used, have also been proposed.12—14 Similar to other Doppler velocity measurements, these methods are subjected to various limitations and errors, such as requiring the presence of adequate Doppler signals and an optimal angle of incidence parallel to the jet, and exposing to inaccurate or biased measurements due to poor signal/noise ratio and/or tachycardia. Other sources of errors include respiratory variation and loading conditions.

Measurements which were not reliant on blood flow Doppler were suggested, including the use of the changes in respiratory variation in superior vena cave, which was found to correlate with ΔP RV,RA in COPD patients (r = 0.61).15 Some pulmonary valve motion features has been shown to be associated with PH, but the same authors nevertheless pointed out that none of these features is sufficiently sensitive or specific to be considered diagnostic.16,17 With the advent of technology, tissue Doppler imaging (TDI) has also been used to differentiate different levels of PASP.18

Based on the pulsed Doppler principle, TDI is used in echocardiography to measure the motion (velocity) of the myocardial tissue.19 TDI is superior to blood flow Doppler as it reflects the functional status of the myocardium directly, and is less subject to background noise and preload. Alignment of the sampling beam with the tissue motion does not usually constitute a problem. Extensive works have been carried out in using the technique for assessing of left ventricular systolic and diastolic functions.20 On the contrary, only a limited number of TDI studies were performed on the RV, mostly on RV systolic and diastolic function.21—23 Caso et al. used the technique to stratify severity of PASP in COPD patients.18 By measuring the tissue Doppler velocity of the lateral tricuspid annulus, they found that the relaxation time was proportional to the severity of PH. In patients with mitral stenosis, Ozdemir et al. demonstrated that the RV myocardial performance index

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<tr>
<td>Number of patients</td>
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<tr>
<td>≤0.130</td>
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<tr>
<td>&gt;0.130—&lt;0.190 s</td>
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<td>9</td>
<td>12</td>
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<tr>
<td>≥22</td>
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</table>

Table 3 Results for using RVD, T peak and the RVD/T peak in predicting PH

Figure 6 Correlation between RVD/T peak and PAC derived PASP.
obtained by TDI correlated with PASP. Unfortunately, the diagnostic or prediction data was not available in these studies, and the application of the results in this aspect has not been pursued further.

The present study tested the usefulness of a morphological parameter, RVD, and a physiological parameter, $T_{peak}$, and the ratio of these two parameters, $RVD/T_{peak}$, in predicting the presence of PH. Although RVD is known to be increased with PASP, it is a relatively poor predictor of PH itself. $T_{peak}$, on the other hand, displayed an inverse relationship with PASP, and could rule-in and rule-out PH when two separate cutoffs were used. That said, there was still a range of $T_{peak}$ (between 0.130 and 0.190 s) where the presence or absence of PH could not be ascertained. When these two parameters were combined, the $RVD/T_{peak}$ ratio displayed a good positive correlation with PASP. The predictive value of the ratio for detecting the presence of PH was better than using RVD or $T_{peak}$ alone. Also, this ratio seems to be independent of RV systolic function.

The validity of the ratio was further studied in a group of nine patients with PAC inserted for various clinical reasons. The results demonstrated that the $RVD/T_{peak}$ ratio bore a good correlation with the PA catheter obtained PASP. The cutoff of 22 cm/s acted as a good predictor for PASP $>35$ mmHg. However, the correlation of this ratio with catheter-derived PASP requires further confirmation using a larger sample size.

**Limitation**

The major source of error in using the Doppler estimates was the estimation of RAP which might not be as certain as the $\Delta P_{RV-RA}$. While many studies used a fixed value of 5 or 10 mmHg, we preferred RAP estimates based on the IVC diameter and its changes during respiration. This method provides the closest correlation with the catheter-derived PASP measurements.

Although we can readily explain the relation between RVD and PASP, we are unable to explain why $T_{peak}$ correlates with PASP. This is mainly because the physiology of RV contraction is not as well studied as the LV. The different patterns of $3m$ observed in the study, e.g. some with one peak and others with two peaks, confirms the complexity and heterogeneity of RV contractile function in response to increased afterload. Although we speculate the change in mechanical property might be responsible for the shortening of $T_{peak}$, further research into this area is definitely required.

**Conclusions**

To our knowledge, this is the first study to have derived an index, the $RVD/T_{peak}$ ratio, which is based on both morphological and functional data, to predict the presence of PH. This index appears to be independent of the RV systolic function. When used as a diagnostic tool, a cutoff of 22 cm/s predicts PH with good accuracy, sensitivity and specificity. Further applications of this index, for example in specific disease and to stratify severity of PH, require additional investigations.

**References**