Descriptive patterns of severe chronic pulmonary hypertension by chest radiography

Toru Satoh*, Shingo Kyotani, Yoshiaki Okano, Norifumi Nakanishi, Takeyoshi Kunieda

Department of Medicine, Division of Cardiology and Pulmonary Circulation, National Cardiovascular Center, 5-7-1 Fujishirodai, Suita, Osaka 565-8565, Japan

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Summary  Background: To find chest roentgenographic (CXR) features to help differentiate two representative diseases with severe chronic pulmonary hypertension (PH).

Study subjects: Thirty-six consecutive patients with chronic thromboembolic PH (CTEPH), 38 with primary PH (PPH), and 37 with left heart disease and PH.

Methods: CXRs were reviewed about 6 features (left 2nd arc protrusion, right descending pulmonary artery diameter (rPAD), cardiothoracic ratio (CTR), right 2nd arc width, avascular area and pleural abnormality). Hemodynamic data and the degree of tricuspid regurgitation (TR) on echocardiography were compared with CXR findings.

Results: The diagnostic pattern of CTEPH was the presence of one of two findings, an avascular area or marked rPAD (>20 mm) together with pleuritic change. The diagnostic pattern of PPH was one of the two features; without pleuritic abnormality, marked left 2nd arc protrusion (>10 mm) or moderate left 2nd arc protrusion (5–10 mm) with marked rPAD (<20 mm). The sensitivity for the diagnosis of CTEPH among the three diseases was 78% and specificity was 92%. The sensitivity for the diagnosis of PPH was 45% and specificity was 88%. CTR and right 2nd arc width were related to the degree of TR in CTEPH and PPH.

Conclusions: Characteristic roentgenographic findings can help differentiate two frequent diseases associated with chronic pulmonary hypertension and reflect the severity of disease.

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Introduction

Primary and chronic thromboembolic pulmonary hypertension (PH) are two major diseases
associated with severe chronic PH. These two representative diseases have very similar clinical presentation and results of various laboratory tests, but are very different in their treatment. Patients with primary pulmonary hypertension (PPH) are beginning to have a better prognosis with the introduction of continuous epoprostenol infusion\textsuperscript{1,2} and many patients with chronic thromboembolic pulmonary hypertension (CTEPH) can be cured by pulmonary thromboendarterectomy.\textsuperscript{3} In view of their different pathologic processes, there may be characteristic chest radiographic findings in each entity that can be used to help differentiate them, though some features are shared. Simple radiographic recognition would lead to early diagnostic deduction of the disease, reducing the cost and relieving the burden on the patients from unnecessary examinations.

Chest radiographic findings characteristic in primary\textsuperscript{4,5} and thromboembolic\textsuperscript{6} PH have been reported in detail separately. Differentiation of the two entities by chest roentgenography was thought difficult in several series\textsuperscript{7,8} but was pursued vigorously with somewhat satisfactory results by Anderson et al.\textsuperscript{9} They, however, included acute and chronic varieties in their cases of thromboembolic PH, and failed to pick up important features such as proximal pulmonary arterial dilatation caused by severe intimal thickening in the chronic cases.

We, therefore, evaluated chest roentgenograms to identify characteristic findings in 38 consecutive patients with PPH and 36 with CTEPH with definite final diagnosis and hemodynamic measurement. We also evaluated chest roentgenograms in patients with left heart disease and PH to differentiate PPH, CTEPH and secondary PH due to left heart disease. We then compared the findings in these three categories and defined the diagnostic patterns for the former two PH diseases. In addition, the variables measured in roentgenograms were quantified and compared with hemodynamic parameters to relate the roentgenographic findings to the severity of disease.

### Methods

#### Study patients

Patients from the three categories were studied retrospectively. Patients with CTEPH consisted of 36 consecutive patients who were diagnosed by radionuclide perfusion lung scan, computed tomography and pulmonary angiography with hemodynamic measurement.\textsuperscript{9} All patients had more than moderate hypoxia and multiple perfusion defects on radionuclide perfusion lung scan, suggesting central type pulmonary embolism. Patients with PPH were 38 consecutive patients with hemodynamic measurement by right heart catheterization who were defined as having PH unexplained by any secondary causes, based on the criteria of the National Institutes of Health registry on PPH.\textsuperscript{10} The third group consisted of patients with left heart disease and PH who had equivalent age, sex and pulmonary pressure as the group of patients with CTEPH. They included 23 patients with valvular heart disease and 12 with idiopathic cardiomyopathy, which were diagnosed by echocardiography and cardiac catheterization. Detailed patient characteristics are presented in Table 1. Patients with PPH were younger, had a larger proportion of female patients and had higher pulmonary artery pressure.

#### Chest roentgenographic evaluation

The radiographs were taken by computed radiography (FCR AC-3, Fuji Medical Systems, Co., Ltd., Tokyo, Japan). Tube voltage was 120 kV, tube current was 200 mA and phototimer was 30–40 ms. Films were exposed during suspension of respiration at deep inspiration. The focus-film distance in the PA projection was 1.8 m with the patient upright.

Two of the authors (T. S. and S. K.) evaluated the chest roentgenographs retrospectively without knowing the patient names. The measured

<table>
<thead>
<tr>
<th>Disease</th>
<th>Number</th>
<th>Age \text{ (y/o)}</th>
<th>Sex \text{ (m/f)}</th>
<th>Weight \text{ (kg)}</th>
<th>MPA \text{ (mm Hg)}</th>
<th>PVR \text{ (unit)}</th>
<th>PCWP \text{ (mm Hg)}</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTEPH</td>
<td>36</td>
<td>52 ± 14</td>
<td>19/17</td>
<td>55 ± 9</td>
<td>45 ± 14</td>
<td>13 ± 8</td>
<td>8 ± 3</td>
</tr>
<tr>
<td>PPH</td>
<td>38</td>
<td>35 ± 15</td>
<td>13/25</td>
<td>54 ± 9</td>
<td>61 ± 12</td>
<td>17 ± 9</td>
<td>9 ± 6</td>
</tr>
<tr>
<td>LHD</td>
<td>37</td>
<td>56 ± 15</td>
<td>21/16</td>
<td>56 ± 10</td>
<td>38 ± 14</td>
<td>4 ± 2</td>
<td>21 ± 8</td>
</tr>
</tbody>
</table>

CTEPH: chronic thromboembolic pulmonary hypertension; LHD: left heart disease; m/f: male/female; mPA: mean pulmonary artery pressure; Number: number of patients; PCWP: pulmonary capillary wedge pressure; PPH: primary pulmonary hypertension; PVR: pulmonary vascular resistance; y/o: years old. Some values are presented as mean ± SD.
variables in study patients were compared between the two authors by Student’s t-test. There were no significant differences between the two for all the measured variables. Therefore, the two measured values were averaged and used for the following evaluation. The chest roentgenographs evaluated were taken within one week of cardiac catheterization and hemodynamic measurement. The measured variables are demonstrated in Fig. 1: (1) The degree of left 2nd arc protrusion. (2) Right descending pulmonary artery diameter. (3) Cardi thoracic ratio. (4) Width of right 2nd arc. (5) Avascular area. (6) Pleural sign. For details see text.

Statistical analysis

Chest roentgenographic features were compared among the three groups by Scheffe’s multiple comparison analysis or $\chi^2$-test. Sensitivity was calculated by dividing the number of true positive cases by the number of positive cases. Specificity was calculated as dividing the number of true negative cases by the number of negative cases among the three groups.

Results

Average values of and frequency of presence of each roentgenographic finding

Detailed results are presented in Table 2. (1) The degree of left 2nd arc protrusion was greater in PPH. (2) The right descending pulmonary artery was wider in chronic thromboembolic and primary PH than in left heart disease. (3) Pleural sign was recognized more frequently in CTEPH and left heart disease. (4) The cardiothoracic ratio (CTR) was not different among the three. (5) An avascular area was only found in CTEPH. (6) The width of the right 2nd arc was not statistically significantly different among the three groups.

Differential diagnosis of chronic thromboembolic and primary pulmonary hypertension

1. **CTEPH**: The presence of avascular area (Fig. 2) was only found in this entity and in 15 out of the 36 patients. It was decided as the first diagnostic pattern. As the right descending pulmonary artery was more prominent in diameter and the pleuritic signs were seen more frequently in this group, the next diagnostic pattern for CTEPH was the width of the right descending pulmonary artery diameter more than 20 mm together with pleuritic abnormality (Fig. 3). It was seen in 13 out of the remaining 21 patients without avascular area in the thromboembolic group, 5 out of 38 patients with PPH and
1 out of 37 patients with left heart disease. If we define owning one of these 2 roentgenographic patterns as the diagnostic features for CTEPH, the sensitivity among these 3 diseases was 78% and the specificity was 92%. The positive predictive value was 82% and the negative predictive value was 97% (Table 3).

2. PPH: Left second arc protrusion of more than 10 mm (Fig. 4) was found in 3 patients in CTEPH, 7 in PPH and 3 in left ventricular disease. Left second arc protrusion of more than 5 mm with right descending pulmonary arterial diameter more than 20 mm without pleural abnormality was found 3 in thromboembolism, 10 in PPH and no patient in left ventricular disease and pulmonary hypertension. When the presence of one of these two roentgenographic findings was defined as the diagnostic pattern for PPH, the sensitivity among these three disease groups was 45% and the specificity 88%. The positive predictive value was 65% and the negative predictive value 88%.

Table 2 Chest roentgenographic findings.

<table>
<thead>
<tr>
<th></th>
<th>CTEPH</th>
<th>PPH</th>
<th>LHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>lt2ndArc (mm)</td>
<td>4.8 ± 3.6</td>
<td>6.6 ± 3.4*</td>
<td>3.4 ± 5.1</td>
</tr>
<tr>
<td>rtPA (mm)</td>
<td>21 ± 6*</td>
<td>20 ± 4*</td>
<td>16 ± 3</td>
</tr>
<tr>
<td>CTR (%)</td>
<td>54 ± 6</td>
<td>58 ± 13</td>
<td>59 ± 9</td>
</tr>
<tr>
<td>rt2ndArc (mm)</td>
<td>28 ± 12</td>
<td>30 ± 15</td>
<td>34 ± 17</td>
</tr>
<tr>
<td>Avascular area</td>
<td>15/36*</td>
<td>0/38</td>
<td>0/37</td>
</tr>
<tr>
<td>Pleuritic scar</td>
<td>21/36*</td>
<td>12/38</td>
<td>19/37*</td>
</tr>
</tbody>
</table>

CTEPH: chronic thromboembolic pulmonary hypertension; CTR: cardiothoracic ratio; LHD: left heart disease; lt2ndArc: degree of left second arc protrusion; PPH: primary pulmonary hypertension; rtPA: diameter of right descending pulmonary artery; rt2ndArc: width of right 2nd arc. Values for first 4 items are presented as mean ± SD. Avascular area and pleuritic scar are presented as the frequency of the presence of each finding. See text for details.

*P<0.05.
Mean pulmonary artery pressure and roentgenographic findings

The relations of mean pulmonary artery pressure with left 2nd arc protrusion, and with cardiothoracic ratio, among the three groups are depicted in Fig. 6. The degree of left 2nd arc protrusion was significantly correlated with mean pulmonary artery pressure only in the left heart disease group. The cardiothoracic ratio showed significant correlations with mean pulmonary artery pressure in the CTEPH and left heart disease group (Fig. 5).

Discussion

The authors tried to identify characteristic patterns in chest roentgenograms to differentiate two representative diseases associated with severe chronic pulmonary hypertension (PH); chronic thromboembolic pulmonary hypertension (CTEPH) and primary pulmonary hypertension (PPH). CTEPH was associated with a pathognomonic avascular area, pleuritic scarring and right descending pulmonary arterial dilatation. PPH cases showed more prominent left 2nd arc protrusion and moderate right descending pulmonary arterial dilatation. By combining these findings, the authors have selected new roentgenographic diagnostic patterns for chronic PH. The pattern of CTEPH is the existence of one of two findings; an avascular area or right descending pulmonary artery diameter more than 20 mm together with pleural abnormality. The diagnostic pattern of PPH is the existence of one of the following 2 features; left 2nd arc protrusion more than 10 mm or left 2nd arc protrusion of more than 5 mm with right descending pulmonary artery diameter more than 20 mm without pleural abnormality. Using these features, sensitivity and specificity for CTEPH between the two precapillary PH diseases even with left heart disease was satisfactory, and for PPH specificity was good and sensitivity fair.

Diseases associated with severe chronic PH are usually detected and diagnosed by history taking, physical examination and electrocardiography. Then the cause of PH will be sought and determined after careful differential diagnosis. Frequently encountered diseases associated with PH are left heart disease, PPH, pulmonary parenchymal disease, Eisenmenger syndrome, CTEPH,

### Table 3 Roentgenographic diagnostic criteria.

<table>
<thead>
<tr>
<th>Findings</th>
<th>CTEPH</th>
<th>PPH</th>
<th>LHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avascular area or rtPA ≥ 20 mm and pleuritic scar</td>
<td>28/36</td>
<td>5/38</td>
<td>1/37</td>
</tr>
<tr>
<td>Without pleural change, lt2ndArc ≥ 10 mm or lt2ndArc ≥ 5 mm and rtPA ≥ 20 mm</td>
<td>6/36</td>
<td>17/38</td>
<td>3/37</td>
</tr>
</tbody>
</table>

CTEPH: chronic thromboembolic pulmonary hypertension; LHD: left heart disease; lt2ndArc: degree of left second arc protrusion; PPH: primary pulmonary hypertension; rtPA: diameter of right descending pulmonary artery; Frequency in presence of each finding is shown.

Degree of TR and roentgenographic findings

The degree of TR was significantly correlated with cardiothoracic ratio and right second arc diameter in CTEPH and PPH (Fig. 6).
hypoventilation syndrome, high output cardiac failure and other rare diseases. Among the first five common etiologies, pulmonary parenchymal disease can be differentiated by chest roentgenography. Left heart disease and Eisenmenger syndrome can ordinarily be diagnosed by echocardiography. The differential diagnosis of CTEPH and PPH is rather difficult and requires further studies such as perfusion lung scan, which is available only at certain institutions. If chest X-ray, which is performed in most clinics, can help differentiate the cause of severe chronic PH, it will make further scrutiny more smooth and efficient.

There have been many studies concerning chest X-ray findings in patients with PH in general, but very few reports have documented the roentgenographic features of respective PH diseases or compared the findings. Kanemoto et al. performed a pioneering study on the roentgenographic findings in patients with PPH, claiming that main pulmonary artery protrusion was marked and had a rough correlation with pulmonary arterial pressure, and that CTR correlated with right atrial pressure and right heart failure in PPH. However, in our study, left 2nd arc protrusion was prominent but did not correlate with pulmonary arterial pressure, and CTR did not correlate with right atrial pressure but with tricuspid regurgitation. The correlation coefficients between the main pulmonary artery dilatation and mean pulmonary arterial pressure and between CTR and right atrial pressure that Kanemoto et al. reported were 0.31 and 0.37, barely significant. Anderson et al. classified PH patients according to pulmonary arterial dilatation and cardiomegaly, and revealed that patients with normal pulmonary arterial and cardiac configuration had the worst prognosis. Our roentgenographic patterns demonstrated high specificity for diagnosis of PPH but low sensitivity, suggesting that the existence of main pulmonary artery protrusion and a large CTR signifies severe PPH, but less marked protrusion or a normal CTR does not rule out PPH. CTR and right atrial pressure were correlated in patients with CTEPH in our study.

The roentgenographic findings found in CTEPH patients were studied in detail by Woodruff et al.
They reported that the signs frequently found in CTEPH were cardiomegaly (86%), oligemia (68%), right descending pulmonary artery enlargement (55%), effusion (23%) and pleural thickening (14%). We recognized similar findings with almost the same frequency. We showed that oligemia was very pathognomonic to differentiate CTEPH from any other PH diseases and that right descending pulmonary artery enlargement was prominent in CTEPH compared to PH due to left heart disease. Pleuritic change was more frequent in CTEPH than in PPH. By combining these findings, CTEPH can be diagnosed with good sensitivity and specificity. In two representative precapillary PH diseases, CTR and right 2nd arc width correlated with the degree of tricuspid regurgitation. In CTEPH in particular, CTR correlated with mean pulmonary arterial pressure and right atrial pressure, indicating that cardiomegaly well reflects the severity of the disease.

Anderson et al. evaluated and compared the characteristic roentgenographic findings demonstrated in PPH and CTEPH and reported that patients with PPH had an enlarged pulmonary artery but those with CTEPH had pathognomonic oligemia without pulmonary arterial dilatation. Their study patients had less severe PH and seemed to include patients with acute pulmonary embolism with less intimal thickening of the pulmonary artery, resulting in failure to demonstrate dilatation of the right descending pulmonary artery as an important finding in CTEPH. Patients with PPH had greater left 2nd arc protrusion owing to greater pulmonary hypertension, and those with CTEPH showed a wider branched pulmonary artery resulting from thickened pulmonary intima. They also reported that some of the PPH patients with the worst prognosis had normal pulmonary artery diameter and CTR on chest roentgenography, indicating the lower sensitivity of roentgenographic diagnosis of PPH, consistent with our results.

CTR and mPA were significantly correlated in CTEPH and LHD, but not in PPH. This is partly because pulmonary artery pressures in patients with CTEPH and LHD were distributed over a wide range, but those in patients with PPH were...
distributed within in a higher range, leading to the different statistical significance among those disease states. Essentially, CTR may be weakly correlated with the degree of PH regardless of the etiology.

CTR was well correlated with the degree of TR but not the mean right atrial pressure, although TR and right atrial pressure had a weak significant correlation. Right atrial pressure is sometimes elevated in right heart failure but TR is not prominent when pulmonary hypertension is rapidly progressive. CTR is more influenced by chronic dilatation of right atrium and ventricle.

As a study limitation, the radiographic findings cannot lead to a definitive diagnosis, though they may be helpful for reaching a tentative diagnosis and to direct further diagnostic plans. When CTEPH is suspected from the radiographic findings, then CT scanning is preferred for the next diagnostic method, because CT is now the most accurate and non-invasive diagnostic tool.14

**Conclusion**

Characteristic chest roentgenographic features were sought to help differentiate two chronic pulmonary hypertension. Chronic thromboembolic pulmonary hypertension had a pathognomonic avascular area, pleuritic scarring and right descending pulmonary artery dilatation. Primary pulmonary hypertension had more prominent left 2nd arc protrusion and moderate right descending pulmonary artery dilatation. By combining these findings, new roentgenographic diagnostic patterns for chronic pulmonary hypertension were determined. The former had good specificity and fair sensitivity and the latter had satisfactory sensitivity and specificity among them and PH due to left heart disease. Cardiac dilatation associated with pulmonary hypertension reflected the degree of tricuspid dilatation.

**References**