Scintigraphic Evaluation of Regional Pulmonary Circulation and Ventilation Abnormalities in Mitral Valvular Disease and Congestive Heart Failure

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Regional pulmonary mean transit time, MTT (RV-Lung) was measured by radionuclide angiography using $^{99m}$Tc-pertechnetate or $^{99m}$Tc-HSA.

In 8 normal subjects, MTT (RV-Lung) in upper (U) and lower (L) lung fields averaged 2.48 and 2.81 sec, respectively. In MS and CHF groups, MTT (RV-Lung) in L was markedly prolonged (5.04 and 5.10 sec, respectively) and after appropriate medical or surgical treatment, MTT in L markedly reduced.

Pulmonary ventilation perfusion scintigraphy with $^{133}$Xe was performed in 18 patients with MS. Both $\text{Vv}_U / \text{L}$ and $\text{Qu}_U / \text{L}$ increased in accordance with the severity of disease, however, $\text{Vv}_U / \text{L}$ had never exceeded unity.

The estimation of regional MTT in the lung field is to be useful way in evaluating the severity of pulmonary circulatory disturbance in MS or in congestive heart failure.

A variety of techniques for estimation of pulmonary blood flow distribution in patients with mitral valvular disease have been reported, including cardiac catheterization, pulmonary arteriography and external pulmonary scintillation scanning techniques using both radioactive gases and intravenous administration of macroaggregates of $^{131}$I-labeled human serum albumin ($^{131}$I-MAA).

It has become clear from physiological and radiological studies that in normal erect subjects, blood flow is greater at the dependent zones of the lung at the apices and that this pattern may be reversed in patients with mitral valvular disease.

The purpose of this study is to estimate the regional pulmonary circulatory disturbance in mitral valvular disease and in left heart failure with special reference to its change before and after medical or surgical treatment using radionuclide angiography with technetium-99m ($^{99m}$Tc) and pulmonary ventilation perfusion scanning with Xe-133 ($^{133}$Xe).

### TABLE 1 MATERIALS

<table>
<thead>
<tr>
<th>Pt. Group</th>
<th>No. of Pt.</th>
<th>Age (yrs.)</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>8</td>
<td>11 – 62</td>
<td>32.9</td>
</tr>
<tr>
<td>Mild MS</td>
<td>14</td>
<td>24 – 63</td>
<td>42.9</td>
</tr>
<tr>
<td>Severe MS</td>
<td>22</td>
<td>25 – 71</td>
<td>45.9</td>
</tr>
<tr>
<td>MI</td>
<td>6</td>
<td>21 – 57</td>
<td>44.5</td>
</tr>
<tr>
<td>CHF</td>
<td>12</td>
<td>28 – 78</td>
<td>49.6</td>
</tr>
</tbody>
</table>

Total 62

**Abbreviations:**
- MS = mitral stenosis
- MI = mitral regurgitation
- CHF = congestive heart failure
- mild MS < 15 mmHg of PAW
- severe MS ≥ 15 mmHg of PAW

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METHODOLOGY

Patients (Table I)

Sixty-two patients ranging in age from 11 to 78 years, and averaging 44 years, underwent radionuclide angiography. Eight subjects had no cardiovascular lesion (normal group). Thirty-six patients had pure mitral stenosis or dominant mitral stenosis with minor regurgitation (MS group), six had pure mitral regurgitation (MR group) and 12 had clinically overt congestive heart failure (CHF group) due to underlying heart diseases including acute myocardial infarction, hypertension and valvular heart disease. All
these 54 patients underwent cardiac catheterization within 72 hours of scintigraphic study. For convenience, MS group was divided into two subgroups, 14 milder and 22 severer patients with PA wedge pressure of lower and higher than 15 mmHg.

Pulmonary artery and wedge pressure were measured. Cardiac output was determined by direct Fick’s method or thermodilution technique using 7F Swan-Ganz catheter. Pulmonary vascular resistance was calculated by the following equation: 

\[ \text{PVR (units)} = \frac{PAm - PAwm (mmHg)}{CO (L/min)} \]

Seventeen patients with MS underwent pulmonary ventilation perfusion study using $^{133}$Xe.
Fig. 6. MTT (RV-Lung) values & its U/L ratios in various groups.

<table>
<thead>
<tr>
<th>Table II</th>
<th>MTT (RV-Lung) Values and U/L Ratios (mean ± S.D.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pt. Group</td>
<td>Upper (sec)</td>
</tr>
<tr>
<td>Normal</td>
<td>2.48 ± 0.68</td>
</tr>
<tr>
<td>MS (mild)</td>
<td>3.16 ± 0.86</td>
</tr>
<tr>
<td>MS (severe)</td>
<td>3.85 ± 1.06</td>
</tr>
<tr>
<td>MI</td>
<td>2.99 ± 0.71</td>
</tr>
<tr>
<td>CHF</td>
<td>4.27 ± 1.17</td>
</tr>
</tbody>
</table>

Data acquisition and analysis

A scintillation camera (TOSHIBA type GCA 202) with 30,000 parallel hole high resolution collimator equipped with minicomputer system (TOSHIBA DAP 5000N) was used in this study.

1) RV to lung mean transit time

After rapid injection of 15 mCi of $^{99m}$Tc-pertechnetate or $^{99m}$Tc-HSA as a single bolus, first pass sequential images (0.2 second per frame) were obtained with a patient supine and in the anterior or 30° right anterior oblique position by rotating the detector and stored in computer system in 64 x 64 matrix form. In sum image of right heart pass phase of isotope, regions of interest (ROI) were drawn with a light pen device in the right ventricular outflow tract or main pulmonary artery (RV) and in peripheral part of the right lung (Lung) and time activity curves were generated in both ROIs, respectively. Mean transit time (MTT) from injected site to both ROIs were calculated from the following equation: $\text{MTT} = \Sigma C_i / \Sigma C_t$, where $C$ and $t$ are the count and the second in time $i$ respectively. (Fig. 1)

RV to lung MTT [MTT (RV-Lung)] was calculated as a difference between MTT (Lung) and MTT (RV) and whole process of calculation...
of MTT (RV-Lung) was automated by computer processing except for setting of both ROIs. Using MTT (RV-Lung) as a parameter, functional image of the lung was constructed. Fig. 2 showed the functional image of a normal subject. In this image, the number in encircled lung fields indicates the number of frame (0.4 sec per frame) in ten times; therefore, the number 63, for example, equals 2.52 sec. MTT (RV-Lung) per unit area of upper (U) and lower (L) lung field of the right lung was calculated by averaging 4 unit areas (encircled rectilinearly), respectively. And also, U/L ratio was calculated.

2) Pulmonary ventilation perfusion scintigraphy (Fig. 4)

According to Ball's method, after intravenous administration of 4 mCi of $^{133}$Xe-saline solution, perfusion study was performed (Fig. 5). Perfusion image (Q image) was obtained in breath holding at TLC level. Thereafter, inhalation study was performed by infusion of 8 mCi of $^{133}$Xe-saline solution into the closed spirometer circuit. Ventilation image (V image) was obtained on single breath holding, and after equilibrium of $^{133}$Xe gas concentration in the circuit during rebreathing for a few minutes, V image indicating distribution of lung volume was obtained at TLC level, and after opening the stopcock to exhaust bag, wash out curve of $^{133}$Xe gas was recorded. Dividing by V image corresponding to the same area, Q image and V image were normalized by lung volume. After volume correction, mean counts per unit area in both U and L (Vu, L and Qu, L) and U/L ratio were calculated.

**TABLE III MTT (RV-LUNG) VALUES AND U/L RATIOS IN PATIENTS WITH MS AND CHF TREATED MEDICALLY AND SURGICALLY (mean ± S.D.)**

<table>
<thead>
<tr>
<th>Pt. group</th>
<th>Upper (sec.)</th>
<th>Lower (sec.)</th>
<th>U/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>MS</td>
<td>Pre-op.</td>
<td>4.28 ± 0.61</td>
<td>5.51 ± 0.71</td>
</tr>
<tr>
<td></td>
<td>(n = 4)</td>
<td>3.35 ± 0.29</td>
<td>3.91 ± 0.48</td>
</tr>
<tr>
<td>CHF</td>
<td>Pre-treat.</td>
<td>3.99 ± 1.09</td>
<td>5.06 ± 1.26</td>
</tr>
<tr>
<td></td>
<td>(n = 5)</td>
<td>3.55 ± 0.99</td>
<td>3.98 ± 0.96</td>
</tr>
</tbody>
</table>
RESULTS

1) MTT in all groups are shown in Table II and Fig. 6. In normal group, MTT of U and L averaged 2.48 sec., 2.81 sec., respectively, and U/L ratio averaged 0.87 indicating nearly unity (Table II and Fig. 7). In mild MS group, MTT of U and L were 3.16 and 3.50 indicating mild prolongation in both (Fig. 8). On the other hand, MTTs in severe MS group were 3.85 in U and 5.04 in L, indicating marked prolongation especially in L and U/L ratio (0.78) was lower than that of normal and mild MS group (Fig. 9).

In 4 patients with MS treated surgically, MTT of U and L before operation averaged 4.28 and 5.51, and around 3 months after operation, these values averaged 3.35 and 3.91, respectively (Fig. 10 and Table III) indicating significant shortening of MTT of L (P<0.05). Fig. 11 shows MTT functional images of the right lung of a MS case treated surgically. In MI group, MTT prolongation was minimal and MTT distribution was similar to that of normal group (Fig. 12).

MTT showed maximal prolongation in CHF group (Fig. 13) and in 5 patients of CHF group treated medically, shortening of MTT in both U and L was observed after treatment (Fig. 14 and Table III). Shortening of MTT was especially

Fig. 11. MTT functional image before and after operation of a MS case.

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significant (P < 0.05) in lower lung field, and U/L ratio increased from 0.79 to 0.87, approaching unity. Fig. 15 shows MTT functional images of a CHF case before and after treatment. In the image before treatment, defect of the lung in costophrenic angle appears to be indicating the presence of pleural effusion.

2) Ventilation perfusion study

In normal case, V image showed homogeneous distribution, with straight vertical distribution and Q image showed reduced blood flow in U. U/L ratio was less than 1.0; therefore V/Q ratio indicated higher value in U than L (Fig. 16). In MS case, on the other hand, Q image showed marked reduction of blood flow in L, and also V image showed a tendency of hypoventilation in L as compared to normal (Fig. 17). Fig. 17 shows V, Q and V/Q images before and after operation. This figure shows the slight improvement of ventilation in the lower lung field and the marked improvement of perfusion in the same area. In comparison with hemodynamic parameters, there was the most significant correlation between Qu/L ratio and pulmonary arterial wedge pressure in 18 patients with MS (r = 0.87, P < 0.001). VU/L ratio mostly correlated with pulmonary arterial wedge pressure (r = 0.81, P < 0.01), but never exceeded unity (Fig. 18).

Fig. 12. MTT(RV-Lung) values in MI cases.

Fig. 13. MTT(RV-Lung) values in CHF cases.

Fig. 14. Note that dotted arrows show the direction of change after medical treatment.

DISCUSSION

Since Blumgart et al, have first used a radioactive tracer in the study on velocity of blood
Fig. 15. MTT functional image before and after medical treatment of a CHF case. Note that in before treatment image, defect of lung in costphrenic angle shows the presence of pleural effusion.

Fig. 16. Estimated pulmonary function, functional images and vertical distributions of the values for the indices.

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flow in man, substantial improvements have been made in imaging devices, isotopes and computer system.

Radionuclide angiography has become one of the reliable non-invasive measures of the global as well as regional left ventricular function through its current developments. On the other hand, using the digital autofluorescope, a radionuclide angiography has been applied in determination of chamber to chamber cardiac transit times. In this investigation, we have attempted the estimation of pulmonary mean transit time using Anger type scintillation camera equipped with computer system. Previous investigators have reported the reversed pulmonary blood flow pattern in patients with mitral stenosis by means of radioisotope lung scanning with $^{133}$I-MAA or radioactive gases. The mechanism of this finding has been considered hypothetically as follows, (1) sustained elevation of the pulmonary venous pressure causes perivascular edema in the dependent zones resulting in increase in vascular resistance; (2) vascular engorgement and edema in the lung bases cause loss of compliance or an increase in airway resistance and resultant underventilation and hypoxia could cause vasoconstriction in these regions. However, Glazier and coworkers suggested that regional vasoconstriction was not the predominant mechanism of the reduction in blood flow to the dependent zones.

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but perivascular fibrosis predominated in patients with mitral stenosis. In radionuclide angiography, sufficient mixing of the nuclide injected into the peripheral vein as a bolus occurs in right heart chambers, therefore, estimation of regional MTT (RV-Lung) is considered to represent the characteristics of regional pulmonary circulation. Pulmonary blood flow velocity should be influenced by pressure gradient between pulmonary artery and pulmonary vein and also by either functional or organic changes of pulmonary vascular beds. MTT (RV-Lung) ranged from 2.48 sec to 2.81 sec, as a whole lung in normal group, which well coincided with the results of Jones and coworkers.15 In groups with MS and congestive heart failure, prolongation of MTT (RV-Lung) in the lower lungfield was observed, indicating reduced blood flow in the lower lungfield, which was confirmed by pulmonary perfusion scintigraphy. The reversed distribution of MTT, longer MTT in lower than in upper lungfield remained unchanged when the subjects were placed in supine position, and tended to be normalized after effective medical or surgical treatments. There have been reports of scintigraphic studies on perfusion-ventilation relationship of the lung in cases with MS5,6 however, no study has been reported concerning to the regional analysis on perfusion-ventilation relationship in these clinical conditions. Upper lungfield to lower lung field ratio of ventilation tended to increase in these pathological cases, with parallel increase in upper to lower ratio of perfusion, which seems to be operating as the homeostatic compensation mechanism of ventilation-perfusion mismatch in each region of the lung. Upper limit of compensatory increase in ventilation has been suggested by the fact that U/L ratio of ventilation never exceeded unity.

REFERENCES