Pulmonary Circulatory Disturbances in Pulmonary Hypertension
with Special Reference to Pathophysiological Significances
of Pulmonary Vascular Resistance Index

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Considering the pulmonary circulatory impairments in pulmonary hypertension, the pulmonary arterial wedge pressure (WP) and the pulmonary vascular index (PVRI) are two important factors with which the pulmonary arterial pressure is provided.

Through the experimental and clinical investigations on WP, Mise concluded that WP should be equal to the pressure of the pulmonary small vein. Therefore, the calculated PVRI, considering the cardiac index and the pressure difference between the pulmonary arterial mean pressure (PAm) and the WP, would show the resistance of the resistance vessels lying between the pulmonary small veins and the pulmonary arteries.

There are two problems related to PVRI. The first is that, if the bronchomotor tone concept and the water fall theory were correct, the calculated PVRI would have other meanings than cited above and be less significant. The second is that, the PVRI could be changed by both functional and structural changes of lung vessels.

In this report, our clinical observations on the PVRI in patients of various diseases are reviewed and the clinical significances of the PVRI and two problems mentioned above are discussed.

Subjects and Methods

Key Words:
- Pulmonary hypertension
- Pulmonary vascular resistance index
- Mechanical resistances of the lungs
- Pulmonary arterial compliance

In total of 153 cases, the changes of PVRI were observed under the states of various gas mixtures inhalations, reserpine injection or exercise of slight degree. The patients positions were supine position during all studies.

Simultaneously with the measuring the changes of PVRI, in 7 cases the changes of pulmonary artery compliances during hyperoxia were measured by Reuben's method and 10 cases changes of mean inspiratory and expiratory mechanical resistances of the lungs induced by CO₂ inhalation were measured.

To evaluate the prognostic significances of PVRI, clinical courses of patients whose PVRI had been measured were studied. Subjects of this study were consisted of 62 cases of pulmonary emphysema and 62 cases of mitral stenosis.

Results and Comments

In 24 normal cases, PVRI were under 250 dynes,sec,cm⁻²/M² in breathing room air and at rest.

In Fig. 1, the changes of PVRI in 21 cases in breathing a gas mixture of lower oxygen content (14.5% and/or 10.9%) are shown. In the cases of cardiopulmonary diseases with PVRI over 250 dynes,sec,cm⁻²/M² in breathing room air and at rest, PVRI increased during 14.5% oxygen inhalation and increased furthermore on 10% oxygen inhalation and these changes were most marked in patients with mitral stenosis. In the cases with normal PVRI, PVRI were unchanged on 14.5% oxygen inhalation but increased on 10% oxygen inhalation.

In Fig. 2, the changes of the pulmonary

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haemodynamics in cardiac patients in breathing low oxygen gas mixture are shown. WP was unchanged in all subjects studied. In 4 cases of 5 who had inhaled 14.5% and 10% oxygen successively, increase of PAm on 10% oxygen inhalation was more marked and therefore PVRI increased more. Cardiac index (CI) was unchanged. These results clearly demonstrate that the increase of PVRI induced by low oxygen inhalation produced larger pressure gradient between PAm and WP resulting in elevation of PAm. These mechanisms were also observed in pulmonary patients whose PVRI increased on low oxygen inhalation.

In Fig. 3, the changes of PVRI on inhalation of 40% and/or 100% oxygen in 29 cases are shown. The decrease of PVRI induced by hypoxia was not clear in the cases with normal PVRI, but it was clear in the cases whose PVRI was over 300 dynes,sec,cm⁻²/M².

In Fig. 4, the changes of the pulmonary haemodynamics in cardiac patients in breathing high oxygen gas mixtures are shown. WP was unchanged. CI decreased in 2 cases who had high output at control period. However PVRI clearly decreased in patients with PVRI over 300 dynes, sec,cm⁻²/M² in association with decreased pressure gradient between PAm and WP. In the pulmonary patients whose PVRI decreased on high oxygen inhalation, the pressure gradient between PAm and WP decreased and WP was unchanged same as in cardiac cases.

The changes of PVRI on the high oxygen inhalation were compared with the changes of the pulmonary artery compliances calculated by Reuben's formula (Fig. 5). In 6 cases of 7, the decreases of PVRI were accompanied with the increases of the pulmonary artery compliance.

In 47 cases, the changes of PVRI induced by 4.5% CO₂ inhalation were observed (Fig. 6). In normal and pulmonary diseases, PVRI increased in 16 cases of 34. Inversely, in cardiac cases especially in patients with mitral stenosis, PVRI decreased and in the cases with higher PVRI the decreases of PVRI were more marked.

In 3 emphysema patients with increased PVRI induced by CO₂ inhalation (Fig. 7, cases 1, 2 and 3), WP was unchanged and PAm increased and therefore the pressure gradients between PAm and WP increased. CI decreased in case 1, was unchanged in case 2 and increased in case 3. Increase of PVRI in case 3 was ascribable to more marked relative increase of PAm as compared with the increase of CI.

Acute induced hypoxia

M.S. other card.

PVRI (dyns sec cm⁻²/m²)

0 300 600 900
air 14.5% O₂ 10% O₂

WP (mmHg)

0 30
air 14.5% O₂ 10% O₂

C.I. (L/min/m²)

0 3 5
air 14.5% O₂ 10% O₂

PAm-WP (mmHg)

0 30 60
air 14.5% O₂ 10% O₂

Fig. 2. Effects of acute induced hypoxia on pulmonary haemodynamics in patients with cardiac diseases. (The mid-thoracic level was used for zero reference.)

Abbreviations

WP: pulmonary artery wedge pressure, PAm: pulmonary artery mean pressure, C.I.: cardiac index, on other abbreviations, see Fig. 1.

Oxygen inhalation

normal emphy. other pulm. M.S. other card.

PVRI (dyns sec cm⁻²/m²)

0 300 600
air 40% O₂ 100% O₂

Fig. 3. Effects of oxygen inhalation on pulmonary vascular resistance index (PVRI).

Abbreviations are the same as in Fig. 1.

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Fig. 4. Effects of oxygen inhalation on pulmonary haemodynamics in patients with cardiac diseases. Abbreviations are the same as in Fig. 2.

Fig. 5. Effects of 100% oxygen inhalation on pulmonary arterial compliance and pulmonary vascular resistance index (PVRI).
CO₂ inhalation

Fig. 6. Effects of 4.5% carbon dioxide inhalation on pulmonary vascular resistance index (PVRI).
Abbreviations are the same as in Fig. 1.

CO₂ inhalation

emphy.

WP (mmHg)

PVRI (dyne sec.cm⁻²/m²)

PAm (mmHg)

PAm-WP (mmHg)

Fig. 7. Effects of 4.5% carbon dioxide inhalation on pulmonary haemodynamics in patients with pulmonary emphysema.
Abbreviations are the same as in Fig. 2.

On the other hand, in mitral stenosis patients with decreased PVRI induced by CO₂ inhalation, WP increased in all 7 patients, and PAm was unchanged in 2 cases and increased in 5 cases, and the pressure gradient between PAm and WP decreased in 4 cases and increased in 3 cases. However, CI increased in all cases except one and PVRI increased not only in the cases with decreased pressure gradient but also in the cases with increased pressure gradient because of relatively larger increase of CI (Fig. 8).

If the bronchomotor tone concept would be correct, PRVI should be increased by the increase of the mechanical resistances of the lungs. The changes of PVRI was compared with the changes of the mean inspiratory mechanical resistances and the mean expiratory mechanical resistances. As shown in Fig. 9, in the cases of mitral valvular diseases, the mechanical resistances increased slightly and PVRI decreased inversely. Furthermore in the cases of pulmonary diseases, the changes of PVRI and the mechanical resistances were interesting in cases 3 and 4. In case 3, the mechanical resistances were large at the control period and increased furthermore during CO₂ inhalation, but PVRI decreased inversely. In case 4, PVRI increased during CO₂ inhalation but the inspiratory mechanical resistance decreased and the expiratory mechanical resistance increased only slightly. On this observation, it seems unlikely that the increase of PVRI will be induced by the increase of the intra-alveolar pressure.

In 26 cases, the changes of PVRI were observed at 90 minutes after 1 to 2 mg reserpine intramuscular injection (Fig. 10). In 12 cases of
Fig. 9. Effects of 4.5% carbon dioxide inhalation on pulmonary vascular resistance index (PVRI) and mean mechanical resistance of the lungs.

Fig. 10. Effects of reserpine injection on pulmonary vascular resistance index (PVRI). Abbreviations are the same as in Fig. 1.
Fig. 11. Effects of reserpine injection on pulmonary haemodynamics in normal persons and patients with pulmonary emphysema. Abbreviations are the same as in Fig. 2.

Fig. 12. Effects of reserpine injection on pulmonary haemodynamics in patients with cardiac diseases. Abbreviations are the same as in Fig. 2.
Exercise

Fig. 13. Effects of exercise on pulmonary vascular resistance index (PVRI). Abbreviations are the same as in Fig. 1.

Fig. 14. Effects of exercise on pulmonary haemodynamics in normal persons and patients with pulmonary emphysema. Abbreviations are the same as in Fig. 2.

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Exercise

M. S.

Fig. 15. Effects of exercise on pulmonary haemodynamics in patients with mitral stenosis. Abbreviations are the same as in Fig. 2.

Fig. 16. Relationships among pulmonary vascular resistance index (PVRI) pulmonary artery mean pressure (PAm) and duration until last checking-up or until death in patients with pulmonary emphysema.
13 whose PVRI were over 300 dynes, sec,cm$^{-5}/M^2$, PVRI decreased after the injection.

In emphysema patients, PAm decreased and WP were unchanged except one and therefore the pressure gradient decreased uniformly and in cases 1 and 2 whose CI increased, PVRI decreased clearly (Fig. 11).

In cardiac patients especially in cases 1 and 2 with PVRI markedly decreased, WP decreased and PAm decreased more than the fall in WP and CI increased (Fig. 12).

In 44 cases, the changes of pulmonary haemodynamics during mild leg exercise test performed in a supine position were investigated. In this test, a steady state was obtained at the 6th minute of exercise and at that time one minute oxygen uptake was 258 cc/min/M$^2$ on an average. In normals, CI increased and PVRI decreased. In 7 cases of 10 pulmonary patients whose PVRI were under 250 dynes, sec,cm$^{-5}/M^2$ in control periods, PVRI decreased similarly as in normal group. However, in 10 cases of 20 cardiopulmonary patients whose PVRI were over 300 dynes,sec,cm$^{-5}/M^2$ in control periods, PVRI increased during exercise test (Fig. 13).

In emphysema patients whose PVRI increased on exercise, as shown in cases 1 and 2, the increase of CI was very small and the increase of PVRI was chiefly due to the increase of the pressure gradient between PAm and WP caused by the increase of PAm (Fig. 14).

In patients of mitral stenosis whose PVRI increased on exercise, as shown in case 1 of Fig. 15, WP increased and PAm increased more than the rise of WP and CI increased slightly in majority of the cases. These findings are specific to this group and suggest that in these cases the pulmonary congestion will be enhanced by leg exercise and accompanied by the increase of PVRI.

The differences of the changes of PVRI induced by these various tests are thought to be based on the differences of the basal pathophysiological states between the cardiac patients, especially with mitral stenosis, and the pulmonary patients, especially with pulmonary emphysema, and also based on the differences of the severity of pulmonary circulatory disturbances in each of the patients. In every test, in
patients of cardiac disease with large PVRI, PVRI changed markedly. In patients of pulmonary disease, the majority of the cases with larger PVRI tended to produce more marked change in PVRI, but the change was less marked in such cases as advanced structural changes of the lung vessels were considered even in the cases with large PVRI.

During these tests, the patterns of WP curve continued to be the venous wave pattern. Therefore it is concluded that so-called water fall phenomenon was not observed in these tests.

The relationships between PVRI and the prognosis of the patients were studied to evaluate the prognostic significances of PVRI.

In Fig. 16, the relationships among the pulmonary circulatory disturbances and the prognosis or the present walking tolerances of 62 patients of pulmonary emphysema are shown. In this figure, closed circle indicates patient died of cor pulmonale. Patient indicated by semiclosed circle can not walk over 400 meters at his pace and patient indicated by open circle can walk over 1200 meters at his pace. It is clearly noticed that both patients with PVRI over 300 dynes/sec, cm⁻⁵/M² and patients with PAm over 22 mmHg have poor prognosis. Picked up the cases died of cor pulmonale, a reverse correlation between PVRI and the life-span is seen.

In 62 cases of mitral stenosis (who are divided into two groups; 20 cases treated only conservatively—group A, and 42 cases treated surgically—group B), the relationships among PVRI, WP and the prognosis or present walking tolerances are shown in Fig. 17. In both groups, the prognosis of the cases with PVRI over 300 dynes/sec, cm⁻⁵/M² is worse than that of the cases with PVRI under 300 dynes/sec, cm⁻⁵/M². In group B, there were 6 decreased cases, whose WP was under 25 mmHg and only 2 decreased cases, whose PVRI under 300 dynes/sec, cm⁻⁵/M². It seems likely that PVRI has a high clinical significances to evaluate the prognosis of the patients.

**Summary and Conclusions**

The differences of the changes of PVRI induced by various gas inhalations or reserpine injection or exercise are thought to be based on the differences of the basal pathophysiological states between the cardiac patients, especially with mitral stenosis, and the pulmonary patients, especially with pulmonary emphysema, and also based on the differences of the severity of pulmonary circulatory disturbances in each of the patients.

During these tests, the patterns of WP curve continued to be the venous wave pattern. Therefore, so-called water fall phenomenon was not observed in these test.

On CO₂ inhalation, the changes of PVRI were compared with the changes of mechanical resistances of the lungs. On this observation, it seems unlikely that the increase of PVRI will be induced by the increase of the intra-alveolar pressure.

On oxygen inhalation, the decreases of PVRI were accompanied with the increases of pulmonary artery compliance. This result is very interesting to be considered that PVRI is an important pathophysiological factor in pulmonary circulatory disturbance or pulmonary hypertension.

The relationships between PVRI and the prognosis of patients were studied and the prognostic significances of PVRI were noticed.

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**REFERENCES**