# ROLE OF PULMONARY HYPERTENSION, HYPOXAEMIA AND RIGHT VENTRICULAR HYPERTROPHY ON THE RIGHT HEART FAILURE IN PULMONARY HEART DISEASES

By Tatsuo Satake, Kazuo Ryuge and Takeo Iida

Pulmonary arterial pressure measured by many previous workers seemed to be a function of arterial oxygen tension in the normal residents living at various high altitudes. When alveolar and arterial oxygen tension was reduced by increasing altitude, the mean pulmonary arterial pressure was inversely increased. This was not only observed in the normal residents living at altitudes, but also observed in the sea level patients whose arterial oxygen tension was remarkably decreased by chronic obstructive lung diseases as indicated in Fig. 1.

According to Hultgren,[1] the ratio of the weight of the right ventricle to that of the total heart was 30% in the subjects living at about 12,000 feet of altitude. This value was considerably higher than 21% obtained in the sea level residents, and indicates a marked right ventricular hypertrophy due only to chronic alveolar hypoxia, of course, without primary anatomical changes of lungs. Authers have been particularly interested in these physiological and anatomical changes occurred in the pulmonary circulatory system of both subjects, one of them subjected to high altitudes and the other is the patient with chronic obstructive lung disease living at sea level.

In this brief paper, authers would like to represent some of the interesting results on the effects of pulmonary hypertension and others upon the mean tissue oxygen tension of right ventricular muscles. Many attempts were undertaken to measure the myocardial tissue oxygen tension directly, however, not yet sufficiently succeeded on account of many methodological limitations. Consequently, authers attempted to calculate it mathematically in the tissue model[2] under different physiological and anatomical conditions by means of digital computer.

## METHOD

The gases exchanged in the tissues might not be much dependent on the size of the cells, but greatly dependent on the half-intercapillary distance of the tissues. Authers assumed as same as Myers and Honig[3] that its distance is approximately 14 micron in the right ventricle, and 18 micron in the left ventricle. These values were estimated considering that the mean transverse diameter of right ventricular muscle fibres was 101 $\pm$ 2.0 micron and those of the left was 13.1 $\pm$ 2.7 micron in 49 autopsy hearts of our cases,[4] but tissue length and diameter in vivo was different from in vitro, and that tissues shrinkage in the course of preparing the specimens. Now, if the cells between the two capillaries were swollen, the intercapillary distance must be increased proportionally with the increase of the cell volume, without any reserved vascular beds opened.

A simplified tissue model of the ventricular tissue as shown in Fig. 2 was invented, in order to make clear understanding of the relationship between the tissue oxygen tension and the cardiac muscle fibre hypertrophy of the right ventricle. A cylinder is shown with only one capillary through its longitudinal axis. Mean tension of this tissue cylinder could be obtained by integrating the oxygen tension between the limit of small and capital R at the L section which must be the half way between the arterial and venous end of the capillary. The final equation by which the mean myocardial tissue oxygen tension, shown as $\bar{p}$, is represented like Kety.[2] However, with all necessary parameters, namely, equation showing the characteristics of the oxyhemoglobin dissociation curve and physiological properties of the right ventricle to a digital computor, could assume a very characteristic changes.

## RESULTS

Fig. 3 represents the changes of the mean myocardial tissue oxygen tension of the right ventricle in the various parameters. The mean myocardial oxygen tension of the right ventricle in the normal condition in which all parameters are absolutely within normal physiological limits was 33mmHg. As indicated by the curve R, when only the half-intercapillary distance increases by 50%, without any change in other parameters, the mean myocardial oxygen tension was decreased only by 5mmHg. On the contrary to this lesser change in the oxygen tension, with the increase of the mean pulmonary arterial pressure by 21mmHg, in other words, with the increase of the total work of the right ventricle by about 50%, the mean myocardial oxygen tension was decreased by 11mmHg as shown in the curve A. With the increase of the mean pulmonary arterial pressure by 28mmHg, in other words, with the increase of the total work of the right ventricle by about 100%, the mean myocardial oxygen tension was greatly decreased by 20mmHg. On the other hand, the mean myocardial oxygen tension was increased by 10mmHg with the increase in coronary blood flow by 50% as indicated by the curve F.

After knowing this type of beautiful work done by a computer, authers would like to show as follows: Though the arterial oxygen tension was decreased to 55mmHg, for instance due to pulmonary cripp'es, hypoxaemia itself lowered both the mean intercapillary oxygen tension and the mean myocardial oxygen tension by only 5mmHg owing to the special characteristics of oxyhaemoglobin curve. On the other hand, as shown in the middle of Fig. 4, if the pulmonary arterial pressure elevated by 100% accompanied with increase in the half-intercapillary distance by 50%, the mean myocardial oxygen tension of the right ventricle would go down from 33mmHg to 13mmHg supposing that the arterial oxygen tension remained within the normal range. Of course, no increase in coronary blood flow was observed in these cases. However, these events had the serious influence upon such patients. Because, the rapid decrease in their alveolar oxygen tension under the ventilatory impairments resulted in a marked increase in pulmonary arterial pressure and work of the right ventricle as shown in the right of Fig. 4. If these conditions are prolonged and coronary blood flow could not increase less than 50%, the mean myocardial oxygen tension should be greatly decreased as far below the critical level at which fibers of the cardiac muscle must be destroyed markedly due to metabolic disturbances as presented in Figs. 5 and Fig. 6.

These two figures show electron-microscopic findings of the right cardiac muscle fibres of experimental dogs with chronic precapillary pulmonary hypertension. Destroyed cardiac muscle fibres with marked hypertrophy, extended diameter and no increase in capillary beds are shown.

## DISCUSSION

According to our preliminary report,[5] the appearance of congestive cardiac failure in the patients with

IInd Department of Internal Medicine, Nagoya University School of Medicine, Nagoya, Japan.

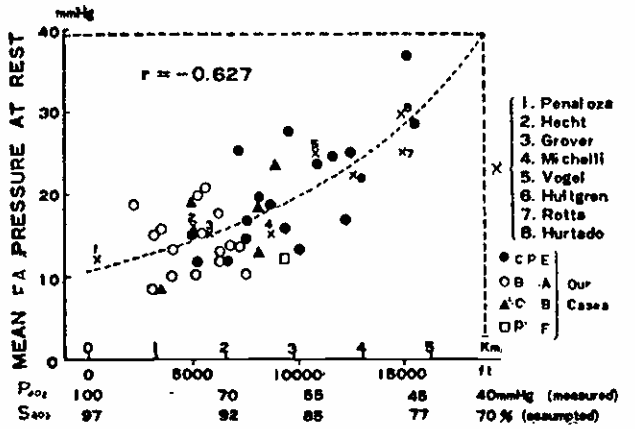


Fig. 1. Pulmonary arterial mean pressure in residents correlated with altitudes (×1 i ×8) and in chronic obstructive lung diseases.
( O; Chronic Pulmonary emphysema; BA: bronchial asthma; ▲: Chronic bronchitis; □: Pulmonary fibrosis).

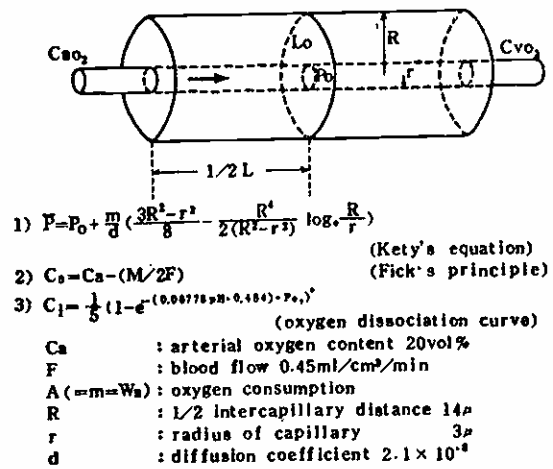


Fig. 2. A simplified tissue model and all necessary parameters in order to calculate the mean tissue oxygen tension of right ventricle.

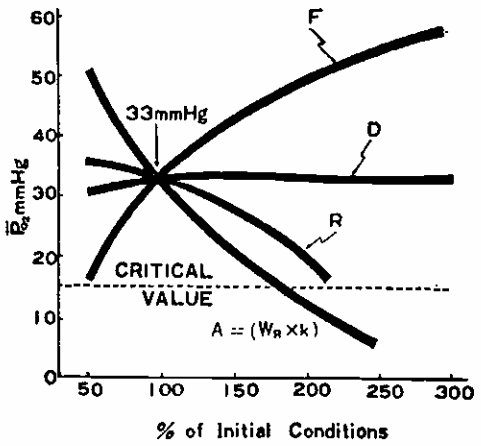


Fig. 3. Myocardial tissue oxygen tension of right ventricle as determined by regional conditions.
A: oxygen consumption ⟷ work
D: diffusion coefficient
F: blood flow
R: ½ intercapillary distance ⟷ hypertrophic ratio of ventricular muscles.

TABLE I

THE INCIDENCE OF CONGESTIVE CARDIAC FAILURE AT THE RESPECTIVE DEGREE OF PULMONARY FUNCTIONS IN 127 PATIENTS WITH CHRONIC OBSTRUCTIVE LUNG DISEASES

| Respiratory Function | Degree | Number of Cases | Incidence of Congestive Heart Failure |
|---|---|---|---|
| % VC | over 76% | 87 | 4·6% |
| | below 75% | 40 | 20·0% |
| | below 55% | 15 | 40·0% |
| $FEV_1$ % | over 56% | 57 | 0·0% |
| | below 55% | 70 | 17·1% |
| | below 40% | 36 | 22·2% |
| % MVV | over 41% | 71 | 4·2% |
| | below 40% | 56 | 14·7% |
| | below 30% | 39 | 21·5% |
| $Pao_2$ | over 71 mm. Hg. | 40 | 0·0% |
| | below 70 mm. Hg. | 45 | 21·1% |
| | below 55 mm. Hg. | 13 | 69·2% |
| $Paco_2$ | below 49 mm. Hg. | 61 | 3·3% |
| | over 50 mm. Hg. | 24 | 41·7% |
| | over 60 mm. Hg. | 3 | 100·0% |

TABLE II

ABNORMAL FINDINGS IN E.C.G. OF 38 CASES, CONTAINING 12 CASES WITH EPISODES OF CONGESTIVE CARDIAC FAILURE IN 127 PATIENTS WITH CHRONIC OBSTRUCTIVE LUNG DISEASES

| ECG Findings | |
|---|---|
| Axis deviation | |
| RAD | 18·4% |
| LAD | 7·9 |
| ST-T abnormality | |
| at rest | 47·4 |
| on exercise | 26·3 |
| P-Pulmonale only | 21·1 |
| Right bundle branch block | |
| incomplete | 10·5 |
| complete | 2·6 |
| RVH | |
| suggestive | 7·9 |
| definite | 18·4 |
| LVH | |
| suggestive | 13·2 |
| definite | 5·3 |
| abnormal cardiac rhythm | |
| sinus tachycardia | 5·3 |
| auricular fibrillation | 2·6 |
| premature beat | 21·1 |
| other abnormality | 5·3 |

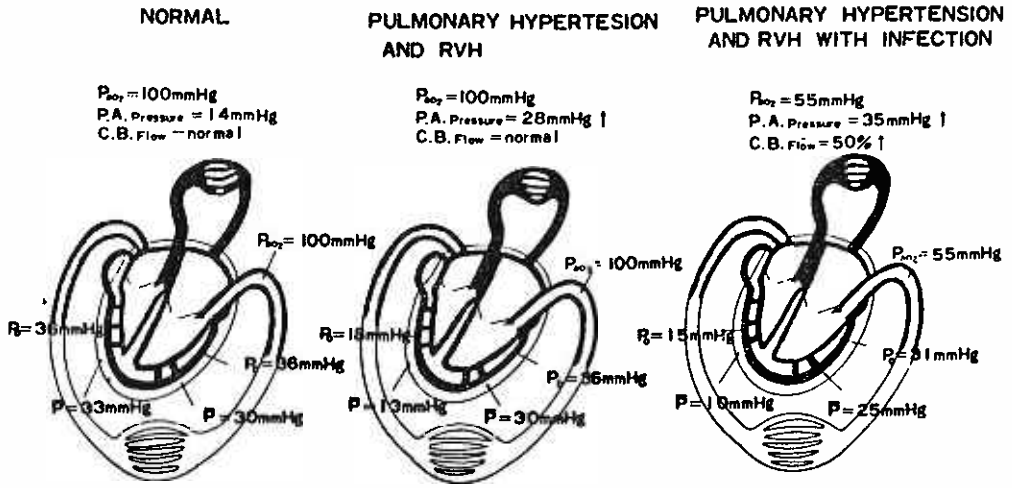


Fig. 4. Myocardial tissue oxygen tension in normal and pulmonary heart disease (chronic cor pulmonale).

Fig. 5. Electron-microscopic figure of the right cardiac muscle fibres of experimental chronic cor pulmonale (mean pulmonary arterial pressure 21 mg)

Fig. 6. Electron-microscopic figure of the right cardiae muscle fibres of experimental chronic cor pulmonale (mean pulmonary arterial pressure 28 mg).

Figs. 5. and 6. not reproduced here due to poor quality prints.

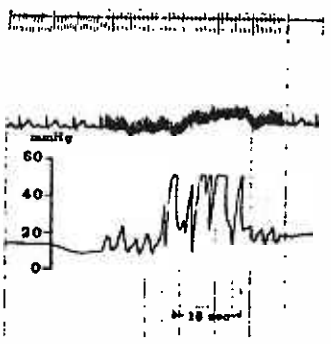


Fig. 7. Changes of pulmonary arterial mean pressure due to an attack of coughing in bronchial asthma.

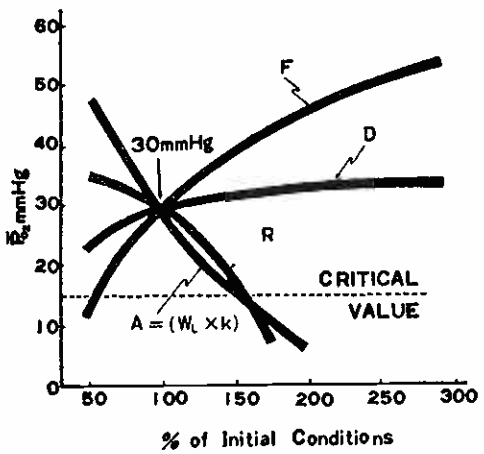


Fig. 8. Myocardial tissue oxygen tension of left ventricle as determined by regional conditions
A: Oxygen consumption ⟷ work
D: diffusion coefficient
F: blood flow
R: ½ intercapillary distance ⟷ hypertrophic ratio of ventricular muscles.

TABLE III

REVERSIBILITY OF ARTERIAL BLOOD GASES AND ABNORMAL E.C.G. FINDINGS AFTER PROLONGED AIRWAY CLEARINGS IN THE PATIENTS WITH CHRONIC OBSTRUCTIVE LUNG DISEASES

| | Name | Age | Sex | Before Treatment | | | | After Treatment | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | $Pao_2$ mmHg | $Paco_2$ mmHg | ECG | | $Pao_2$ mmHg | $Paco_2$ mmHg | ECG | |
| | | | | | | Axis | ST-T | | | Axis | ST-T |
| 1 | J.N. | 64 | M | 40 | 78 | +121° | R (+) RVH | 75 | 58 | +60° | M (−) |
| 2 | S.T. | 28 | M | 41 | 66 | +115° | R (+) RVH | 102 | 38 | +90° | M (−) |
| 3 | T.O. | 62 | M | 41 | 62 | + 80° | R (+) LVH | 68 | 67 | +70° | R (+) LVH |
| 4 | T.S. | 62 | M | 46 | 52 | + 73° | R (+) LVH | 45 | 61 | +53° | R (+) LVH |
| 5 | H.Y. | 31 | M | 50 | 58 | + 96° | R (+) RVH | 73 | 47 | +99° | M (−) RVH |
| 6 | S.M. | 68 | M | 59 | 62 | + 70° | M (+) | 79 | 43 | +70° | R (+) |
| 7 | N.K. | 32 | M | 59 | 48 | + 90° | M (±) | 85 | 45 | +83° | M (−) |
| 8 | S.N. | 68 | M | 64 | 53 | + 75° | M (−) | 84 | 41 | +77° | M (−) |
| 9 | S.A. | 68 | M | 65 | 52 | + 81° | M (−) | 92 | 42 | +77° | M (−) |
| 10 | H.Y. | 42 | M | 65 | 45 | + 82° | R (+) | 80 | 40 | +82° | M (±) |
| 11 | M.N. | 43 | M | 64 | 46 | + 82° | M (−) | 64 | 52 | +78° | M (−) |
| 12 | S.N. | 62 | M | 82 | 40 | + 87° | M (±) | 83 | 40 | +86° | M (±) |
| 13 | Y.T. | 58 | M | 71 | 49 | + 76° | M (−) | 86 | 34 | +80° | M (−) |
| 14 | K.K. | 50 | M | 82 | 48 | + 69° | M (±) | 67 | 49 | +74° | M (±) |
| 15 | A.T. | 39 | M | 71 | 42 | + 80° | M (−) | 84 | 36 | +80° | M (−) |
| 16 | S.S. | 46 | F | 71 | 46 | + 79° | M (±) LVH | 78 | 59 | +77° | M (−) LVH |
| 17 | S.M. | 70 | M | 75 | 48 | + 70° | M (+) | 79 | 48 | +70° | R (+) |
| 18 | U.U. | 53 | F | 50 | 57 | − 63° | R (+) RVH | 75 | 43 | −35° | M (−) |
| 19 | A.Y. | 65 | M | 59 | 47 | + 79° | R (+) RVH | 70 | 47 | +81° | R (+) RVH |
| 20 | U.O. | 58 | M | 76 | 44 | + 73° | M (±) LVH | 81 | 32 | +74° | M (−) |
| 21 | B.T. | 62 | M | 78 | 38 | + 82° | M (−) | 65 | 46 | +60° | M (−) |

R : at rest (ST-T abnormality)
M: on exercise (ST abnormality)

TABLE IV

PRINCIPAL CAUSES OF DEATH AND ANATOMICAL CHANGES OF HEART IN 9 CASES WITH CHRONIC COR PULMONALE

| | | Basic Disease | Immediate Cause of Death | Total Heart Weight (T) g | Weight of Right Ventricle (R) g | $\frac{R}{T}$ % | Wall Thickness of Right Ventricle mm | Increase Ratio of D % |
|---|---|---|---|---|---|---|---|---|
| (1) | 37 ♂ | chronic pulmonary emphysema pleural adheision | Pneumonia | 440 | 110 | 25 | 10 | 107 |
| (2) | 40 ♂ | tuberculosis | Bronchitis | 222 | 77 | 35 | 4 | 81 |
| (3) | 42 ♂ | tuberculosis | Bronchitis | 172 | 52 | 30 | 4 | 6 |
| (4) | 49 ♀ | cancer of the hilum pleuritis | Respiratory Failure | 270 | 42 | 15 | 5 | 20 |
| (5) | 62 ♂ | tuberculosis | Respiratory Failure | 300 | 72 | 24 | 6 | 31 |
| (6) | 64 ♂ | chronic pulmonary emphysema | Pneumonitis Infarction | 270 | 65 | 24 | 5 | 56 |
| (7) | 65 ♂ | tuberculosis | Pneumonia | 350 | 88 | 25 | 5 | 9 |
| (8) | 70 ♂ | chronic pulmonary emphysema | Infarction | 370 | 65 | 18 | 6 | 53 |
| (9) | 77 ♂ | chronic pulmonary emphysema | Pneumonia | 285 | 54 | 19 | 6 | −3 |
| | | | | 298 ± 79 | 69 ± 22 | 24 ± 6 | 5·7 ± 1·7 | 40 ± 37 |

D: means transverse diameter of right ventricular muscle fibres

chronic obstructive lung diseases seemed to be related to respiratory functions, especially to changes in arterial blood gases which were affected by the disturbances of the pulmonary gas exchange. Of course, the congestive cardiac failure disappeared as arterial blood gases tended to return to normal values. Table I shows the incidence of congestive cardiac failure at the respective degree of respiratory functions in 127 patients with chronic obstructive lung disease. Generally, it seems that arterial oxygen tensions below 55mmHg and carbon dioxide tension above 50mmHg tend to predispose to congestive cardiac failure. Furthermore, some abnormal electrocardiograms were observed in 38 patients and 47% of them had ST-T changes as shown in Table II. These findings were considered as the relative coronary insufficiency caused by the discrepancy of oxygen demand and supply in the heart.[5] [6] These abnormal electrocardiographic findings including right axis deviation and right ventricular hypertrophy were often observed in the patients with lower arterial oxygen tension below 55 mmHg. However, most cases showed improvement of electrocardiographic findings as hypoxia was improved as shown in Table III. Needless to say, there was inverse correlation between the arterial oxygen tension and the pulmonary arterial pressure. These hypoxaemia and right ventricular hypertrophy were frequently observed not only in the residents at high altitudes but also in the residents at sea level with chronic obstructive lung disease, but both factors might participate relatively little in causing a reduction of myocardial tissue oxygen tension. The increase in the work of the right ventricle caused by the pulmonary alterial hypertension due to chronic alveolar hypoxia and acute alveolar under the restrictive ventilatory impairment might participate mainly in causing reduction of myocardial tissue oxygen tension. But, authors[7] could not find typical hypertrophy of the right ventricle in patients died by cardiac failure, except only one case which had the increase in the radius of muscle fibre by 107% as shown in Table IV. In such cases, the real cause of the death might be interpreted by the congestive cardiac failure caused by the marked decrease of the myocardial tissue oxygen tension induced by a transient marked increase in pulmonary arterial pressure due to pulmonary cripples, especially in the cases with both prolonged chronic pulmonary hypertension and right ventricular hypertrophy.

Of course, these results would indicate that any factor which causes a rise in the pulmonary arterial pressure predisposes to failure of the heart. There are many factors to be taken into consideration at this point, however among all them authors think it is worth pointing out the unfavourable effect of cough. Needless to say, cough is one of the most general symptoms of respiratory diseases, and it is often very frequent beyond our expectation in some patients. Our recording of cough in a few patients, by using the tape-recorder with voice controlled microphone, revealed that they coughed as many as one hundred times during one night. Fig. 7 shows the mean pulmonary arterial pressure changes of one subject with bronchial asthma, who coughed continuously during right heart catheterization. It can be seen that a couple of coughs cause a marked rise in the pulmonary arterial pressure from 17mmHg to above 50mmHg. Although authors[8] happened to know the extent of the effect of cough on pulmonary arterial pressure, this is due to the continuous elevation of intraalveolar pressure which is caused by check valve mechanism of lung airways.

On the other hand, it should be considered that hypercapnia would not only increase pulmonary arterial pressure but also decrease cardiac output and predispose to congestive cardiac failure similar to serious hypoxia, as authors[9] had presented another papers which was studied in experimental dogs under isoventilation using body respirator.

Finally, authors would like to present that in the case of the left ventricle, in order to compare the difference between the right ventricle and the left ventricle, the very decline to the proportion of the increase in R and A were shown as Fig. 8. This result shows that in the same condition the left ventricle is more easily apt to fall into congestive cardiac failure than the right ventricle.

## COMMENT

Causative factors of congestive cardiac failure during the course of pulmonary heart disease could often be considered as follows, one of them would be pulmonary hypertension related to alveolar hypoxia or asphyxia caused by disturbances of pulmonary gas exchange and the other would be relative coronary insufficiency due to increase in work of the right ventricle caused by pulmonary hypertension.

Therefore, in most cases without serious complications such as mechanical disturbances of coronary vessels, ateriosclerosis, diabetes and so forth, could pulmonary infections be protected, clearing of airways be maintained and arterial gas compositions would remain near normal in the outside views, signs of congestive cardiac failure would not appear even if there existed much impairments of tissues in the lungs.

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