原　　著

Studies on the Peripheral Pulmonary Circulation Time in COPD

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SUMMARY

The pulmonary circulation time was assessed by measuring the parameter "τ_P", which had been developed and reported elsewhere,[1] for detecting the disturbances of pulmonary blood flow in patients with respiratory diseases. The materials were thirteen normal subjects, seven cases of slight COPD (group I), nine cases of severe COPD (group II), and three cases of old tuberculosis with restrictive ventilatory impairement (group III). The mean τ_P value were 1.78 ± 0.48 in normal subjects, 1.55 ± 0.39 in group I, 2.0 ± 1.13 in group II, and 1.60 ± 0.46 in group III.

The mean τ_P value was increased in severe COPD patients compared with that in normal subjects or in slight COPD patients, but the difference between them was not significant. This is because the τ_P values of some severe COPD cases were increased but others were not. Meanwhile the computer simulation showed that τ_P values were the sensitive parameter to assess the circulatory disturbances in the lung, by detecting the uneven distribution of $Q/\dot{Q}$ in adition to delay and stagnation of the blood flow. These findings showed that the circulatory impairement would not increase in parallel with the ventilatory impairement and would be brought about at the critical advanced emphysematous stage in this type of COPD patients.

INTRODUCTION

Disturbances of pulmonary blood flow in patients with respiratory diseases, such as COPD, has been assessed mainly from the pulmonary arterial side, using right heart cathetherization, and increases of pulmonary arterial mean pressure, pulmonary arterial wedge pressure and pulmonary vascular resistance, decrease of cardiac output and so forth have been reported. Comparing these findings with histological studies of the operatively resected lungs, Wright et al[2] showed thickened pulmonary small muscular arterial walls in patients with minimal emphysema and to a greater degree in patients with more severe emphysema. Also a significant reduction in the diameter of 2, 3, 4 orders of branching of the pulmonary artery (diameters

2–7 mm) were shown by Horsfield et al.[3] using PA angiography. Brachii et al.[4] reviewed the microangiographic studies and described a reduction in the number and size of intralobular arterial branches, loss of capillary back ground displacement and distortion of vessels and the presence of A-V anastomosis. From these studies, as the cause of disturbances of pulmonary blood flow, destruction of lung capillary bed, narrowing of the muscular small pulmonary arteries, hypoxic vasoconstriction, polycythemia due to hypoxia and constriction of vessels by increased alveolar pressure due to airway obstruction have been suggested and generally accepted.[5] On the other hand pulmonary scintigrams, using radioisotopes, showed the existence of the uneven distribution of pulmonary blood flow in COPD patients, these perfusion-unevenness has been discussed comparing it with ventilation-unevenness.[6]

Although numerous studies on hemodymanics of pulmonary blood flow have been reported and compared with anatomical changes as mentioned above, to our knowledge, there are limited data available about the time factor of pulmonary blood flow in the lung, because there had been no proper method for measureing merely the pulmonary circulation time independently. Recently a method for measuring the time constant of wash out curve in the lung, which could be the parameter indicating the circulation time in the lung was reported by Kuno, one of our co-workers,[1] and it was designated as "τ_P".

In this paper, with the use of this method, τ_P of COPD patients were measured and reported. And the factors which might increase the τ_P value in this disease was studied using computer simulation and compareing it with that of normal subjects, tuberculosis and congestive heart failure.

MATERIALS AND METHODS

MATERIALS

The materials were thirteen normal candidates and nineteen patients of respiratory diseases in the Respiratory Department of Tsukaguchi Hospital. The patients were divided into four groups on the basis of diseases: Group I; slightly affected COPD patients (mainly bronchial asthma) whose FEV 1.0% was 50 or more during the non-attack period, six cases. Group II; severe COPD whose FEV 1.0% was less than 50, nine cases. Group III; old pulmonary tuberculosis with severe respiratory impairment, three cases.

METHODS

The method used in this study for assessing the circulation time in the peripheral lung field was the same as the one reported by Kuno.[1] Briefly followings: As shown in Fig. 1, precardial radio-activity of isotopes which were injected via the cubital vein as the bolus was detected by a Seale Radiographic PHO/Gamma LEOV camera and recorded on videotapes. Playing back these data, the time activity curves of each ROIs (1. whole heart, 2. right heart, 3. right lung field, 4. superial vena cava) were acquired for thirty seconds, and transferred to the magnetic tape in 0.1 second intervals up to a total of 300 data, and were analysed by an off-line HP 1000 computer system. These measurements were performed in supine position.

As shown in Fig. 2, theoretical formulations were made using the serial two-compartment

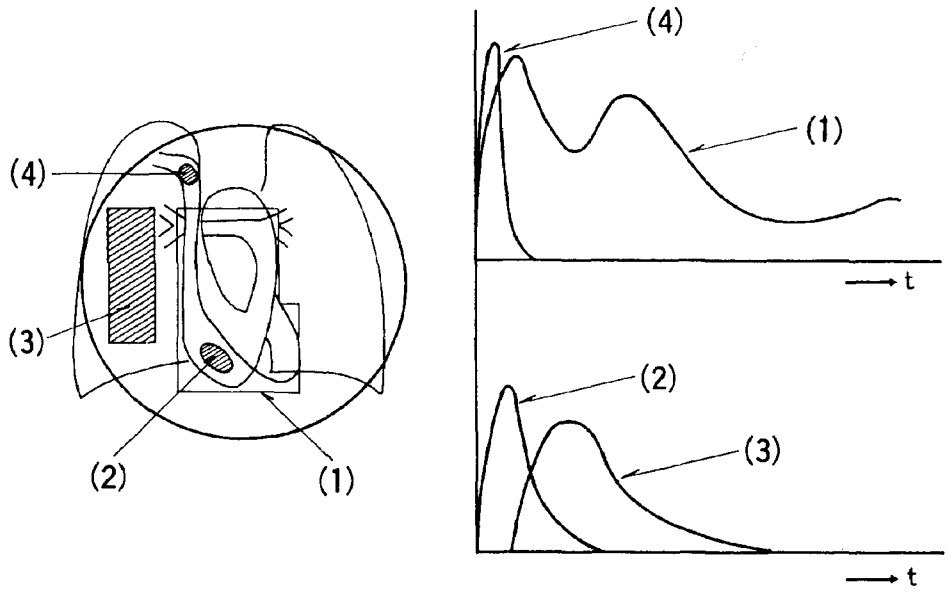


Fig. 1. Setting of ROI (Region of Interest) and the time activity curve of each ROI. (1): whole heart, (2): right heart, (3): right lung field, (4): superial vena cava.

open dilution model whose first compartment was the right heart and the second compartment the lung. Radioactivity curves of ROI of the right heart ($C_R(t)$) and right lung field ($C_P(t)$) were expressed as follows:

$$C_R(t)=\frac{\alpha}{\dot{Q}_R}e^{-t/\tau_R} \tag{1}$$

$$C_P(t)=K(e^{-t/\tau_R}-e^{-t/\tau_P}) \tag{2}$$

Where $C_R(t)$ and $C_P(t)$ were concentrations of radioisotopes, Q_R and Q_P were blood volumes and τ_R and τ_P are time constants, R and P meant right heart and lung respectively. $\dot{Q}$ is the blood flow of the right heart and lung, K was the proportion constant.

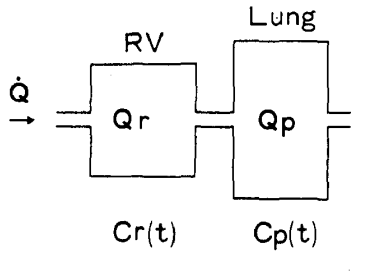
τ_R could be calculated from the slope of the regression line of $C_R(t)$-time curve which was plotted on a semilogarithmic scale. The value of τ_P was selected to minimize the sum of squares of difference between measured PVDC and simulated PVDC. Simulations of PVDC were performed using equation (2) in which τ_R was calculated as described above, K and T(0) were calculated from the height and time of maximum point of the measured PVDC. The sum of square was calculated at each τ_P; 1.0, 1.1, 1.2, 1.3, ... 10.0, and compared to find the minimum value. The Flow-Chart of the computer processing is shown in Fig. 3.

The effect of intrapulmonary uneven perfusion upon the τ_P value was studied using computer simulation, assuming that the pulmonary circulation system was composed of n (=120) parallel compartments, and each had a different $Q/\dot{Q}$, the following differential equations could be formulated.

$$\frac{d}{dt}C_R(t)Q_R=-\dot{Q}_RC_R(t) \qquad \text{(right heart)}$$

$$\frac{d}{dt}C_i(t)Q_i=\dot{Q}_iC_R(t)-\dot{Q}_iC_i(t) \qquad \text{(lung)}$$

where Q_R, Q_i and $\dot{Q}_R$, $\dot{Q}_i$ and $C_R(t)$, $C_i(t)$ were blood volume, blood flow and concentration of radioisotopes respectively, symbol R meant right ventricle and i meant compartment i of



$t = 0$: bolus Injection of RI into RV

(1) at RV

$$\frac{dCr(t)}{dt}\cdot Qr = -\dot{Q}Cr(t) \rightarrow Cr(t) = C\cdot e^{-\frac{\dot{Q}}{Qr}t}$$

$$Cr(0) = \frac{\alpha}{Qr} \rightarrow C = \frac{\alpha}{Qr}$$

$$\therefore\ Cr(t) = \frac{\alpha}{Qr}\cdot e^{-\frac{\dot{Q}}{Qr}t} \quad \cdots\cdots ①$$

(2) at Lung

$$\frac{dCp(t)}{dt}\cdot Qp = \dot{Q}\cdot Cr(t) - \dot{Q}\cdot Cp(t)$$

from ①

$$\frac{dCp(t)}{dt}\cdot Qp = \frac{\dot{Q}\alpha}{Qr}e^{-\frac{\dot{Q}}{Qr}t} - \dot{Q}\cdot Cp(t)$$

$$Cp(t) = e^{-\frac{\dot{Q}}{Qr}t}\left\{ C + \frac{\alpha}{Qr-Qp}e^{\frac{Qr-Qp}{QrQp}\dot{Q}t} \right\}$$

$$Cp(o) = 0 \rightarrow C = -\frac{\alpha}{Qr-Qp}$$

$$\therefore\ Cp(t) = \frac{\alpha}{Qr-Qp}\left(e^{-\frac{\dot{Q}}{Qr}t} - e^{-\frac{\dot{Q}}{Qp}t}\right)$$

$\tau r = \frac{Qr}{\dot{Q}}$: Time Constant of RV

$\tau p = \frac{Qp}{\dot{Q}}$: Time Constant of Lung

$$\boxed{Cp(t) = \frac{\alpha}{Qr-Qp}\left(e^{-\frac{t}{\tau r}} - e^{-\frac{t}{\tau p}}\right)}$$

Fig. 2. Theoretical formulation of the hemodynamic behavior in the right ventricle and in the pulmonary vascular system assuming that they are serial two compartment open dilution system.

the pulmonary circulation system.

Solving these differential equations, by assuming that the initial condition was $C_i(0)=0$ and the total injected radioisotope was α.

$$C_R(t) = \frac{\alpha}{Q_R}e^{-(\dot{Q}_R/Q_R)t}$$

$$C_i(t) = \frac{\dot{Q}\cdot\alpha}{Q_R\dot{Q}_i - \dot{Q}_RQ_i}\left(e^{-(\dot{Q}_R/Q_R)t} - e^{-(\dot{Q}_i/Q_i)t}\right)$$

Radioactivity of compartment "i" was expressed as follows

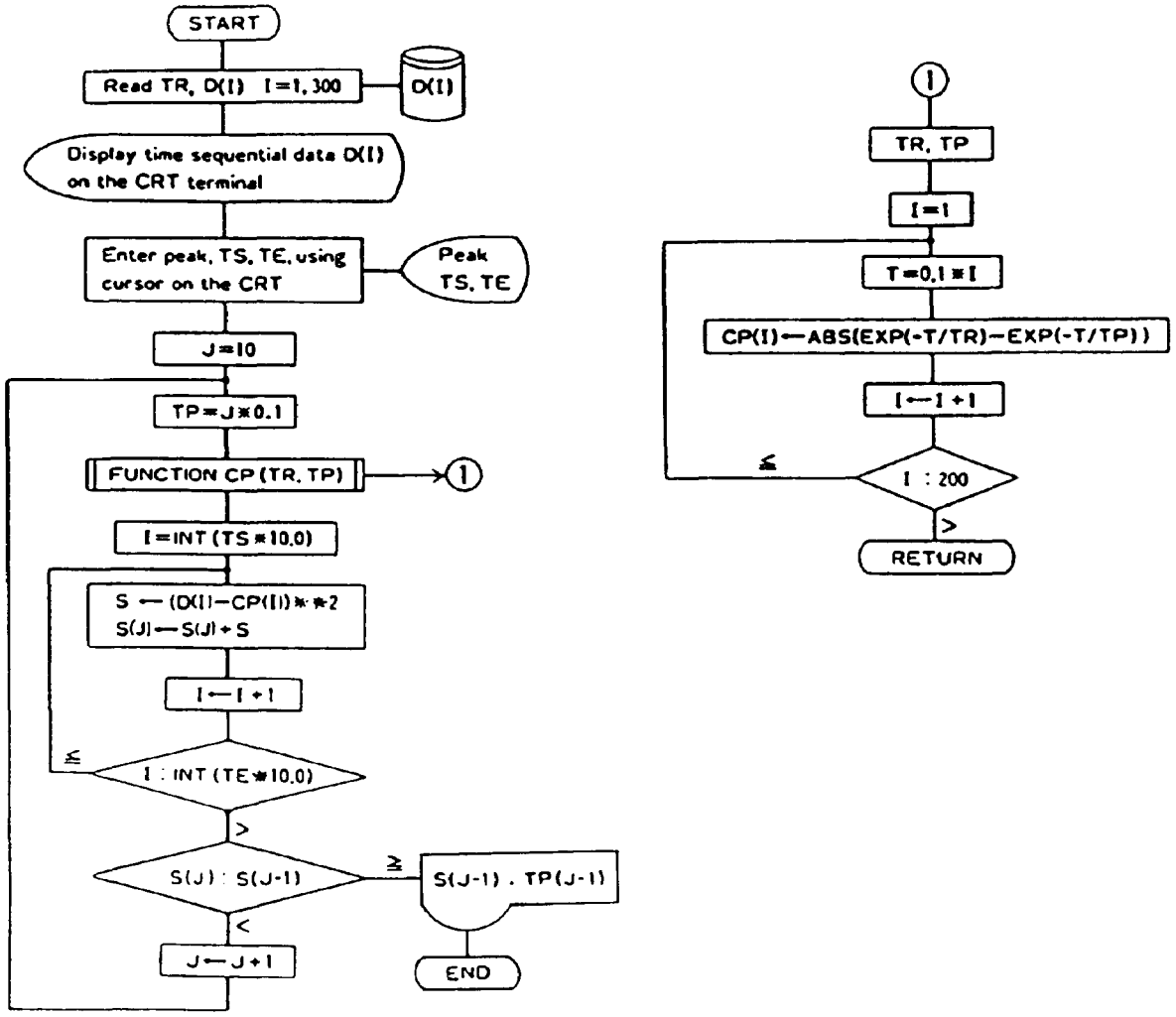


Fig. 3. The flow chart of computer programing for assessment of τ_P.

$$G_i(t)=KQ_iC_i(t)$$

$$=\frac{K\alpha Q_i\dot{Q}_i}{Q_R\dot{Q}_i-\dot{Q}_RQ_i}(e^{-(\dot{Q}_R/Q_R)t}-e^{-(\dot{Q}_i/Q_i)t}) \quad (1)$$

Assuming that $\dot{Q}_P(=\dot{Q}_R)$ was distributed to the compartment of $\dot{Q}_i/Q_i(=X_i)$ according to the distribution function $f(X_i)$.

$$\dot{Q}_i=f(X_i)\dot{Q}_R \quad (2)$$

from

$$Q_i=(Q_i/\dot{Q}_i)\dot{Q}_i=X_i\dot{Q}_i$$
$$Q_i=X_if(X_i)\dot{Q}_R \quad (3)$$

from equation (1) (2) and (3)

$$G_i(t)=K\alpha\frac{X_i*f(X_i)}{R-X_i}(e^{-t/R}-e^{-t/X_i}) \quad (4)$$

where $R=Q_R/\dot{Q}_R$

Therefore the total radioactivity was expressed as follows

$$G(t)=K\alpha\sum_{i=1}^{n}\frac{X_i*f(X_i)}{R-X_i}(e^{-t/R}-e^{-t/X_i})$$

Using this equation, radioactivity-time curves of various distribution function ($f(X_i)$) were formulated and compared.

Simulation models were set as follows:

1. Distrubution function $f(X_i)$ was log normal distribution (normal distribution against log variables ($\log X_i$)).

$$f(X_i)=\frac{\log e}{\sqrt{2\pi}(\log \sigma_0)X}e^{(-\log X-\log \mu_0)^2/2(\log \sigma_0)^2}$$

2. (Total blood volume)/(Total blood flow) ($=\sum Q_i/\sum \dot{Q}_i$) was constant ($=3.0$)
3. $\tau_R(=Q_R/\dot{Q}_R)$ was constant ($=2.0$)

RESULT

CONVENTIONAL PULMONARY FUNCTION

The mean value of %VC in group I was 100.9±14.0, %VC value of all cases was over 80, there was no restrictive ventilatory imparement in this group. The mean value of FEV1.0% of this group was 59.4±5.32, three cases out of six were under 60, the values of FEV1.0% in five cases ranged from 55.0 to 62.2, therefore the ventilatory impairement of this group was classified as moderate obstructive, MMF was decreased to 0.89±0.36 L/sec, Rr was increased to 5.48± 1.39 cmH_2O/L/sec. The arterial gas tensions were not measured in most cases in this group, because they had no symptom of respiratory insufficiency. PaO_2, $PaCO_2$ of measured case was in normal limit.

The mean value of %VC in group II was slightly decreased, 68.9±19.8, two cases out of nine was within normal limit (over 80) and two cases under 50, this group had wide variety of %VC, either normal or severe restrictive ventilatory imparement. The mean value of FEV1.0% was 39.6±5.34 in this group, six out of nine was under 40, relatively sever obstructive ventilatory imparement was seen. MMF was also decreased to 0.38±0.15 L/sec. Rr was increased to 6.81±3.82 cmH_2O/L/sec. The mean value of PaO_2 was 71.6±13.0 mmHg, among them established hypoxic respiratory insufficiency was only one case (T. N. paO_2 54.3 mmHg), subclinical hypoxia (60–79 mmHg) was seen in two cases (62.1 mmHg Ta. O., 62.6 mmHg K K.) two cases of hypercapnea were seen (57.6 mmHg T. N., 48.0 mmHg K. K.), other four measured cases were within normal limit.

Marked decreases of %VC were seen in group III, mean value was 41.5±15.2, all cases of this group had severe to moderate restrictive ventilatory impairement Marked obstructive ventilatory imparements were also seen except one case, mean FEV1.0% was 58.4±31.1 (36.8, 44.4 and 94.0). All cases of this group were under the condition of respiratory insufficiency, mean value of PaO_2 was 51.6±4.3 mmHg, all of them showed increased $PaCO_2$, its mean value was 57.7±1.2 mmHg.

THE VALUES OF τ_R AND τ_P

The mean value of τ_P of 12 normal candidates was 1.89 and the standard deviation was 0.70, as shown in table 1. However τ_P of one case (M. Mu) was 3.50, it was larger than the mean

Table 1. τ_P of 12 normal candidates

Name	Age	Sex	τ_R	τ_P
M. Mu.	24	male	1.88	(3.50)
K. Ka.	24	male	3.49	1.10
A. O.	24	male	2.20	2.30
M. Hi.	25	male	3.88	1.20
K. U.	27	male	2.61	2.50
J. Mu.	29	male	3.94	2.30
M. Na.	30	male	2.70	2.10
S. O.	30	male	2.57	1.80
M. Mi.	32	male	2.38	1.60
M. I.	37	male	1.54	1.10
K. I.	44	male	2.62	1.50
S. Ka.	57	male	2.41	1.70
		mean	2.69	1.75
		SD	0.74	0.50
		n	12	11

τ_P of M. Mu. was excluded because its value was greater than mean+2SD.
(total mean=1.89, SD=0.70)

+2SD (3 29), and we decided to exclude this case. Therefore as the normal value of τ_P, 1.25–2.25 was taken (mean; 1.75, SD; 0.50). The mean value of τ_R of these normal subjects was 2.69±0.74.

In patients of group I, the τ_P values were within normal limit and the average value was 1.55±0.39 (mean SD). The mean value of τ_R was 2.17±1.03, also was in normal limit.

The average τ_P value of group II was 2.00±1.13 which was larger than the value of group I or normal candidates. Although the difference between them was not statistically significant, a marked increase in τ_P was seen in three cases out of nine, they were 2.90, 4.30, 2.50. The average τ_R value was 2.46±1.05, slightly larger than the value of group I but within normal limit.

As for the group III, the old tuberculosis with severe ventilatory impairement, the τ_P value was within normal limits even in the cases with obstructive ventilatory impairment (cases Mi. Y. and K O.), the mean value was 1.60±0.46. The τ_R value was slig increased in this group, and the mean value was 3.20±0.99.

COMPUTER SIMULATION

The theorettcal radioactvity-time curves of the ROI in the lung in which the blood flow distributed to the multiparaller compartment each has different $Q/\dot{Q}$ were presented by the computer simulation as shown in Fig. 7-a.

The simulated distribution of blood flow against $Q/\dot{Q}$ were shown in Fig. 7-b (frequency-$Q/\dot{Q}$) and Fig. 7-c (frequency-log $Q/\dot{Q}$). The blood flow was suposed to distribute as the normal distribution against log $Q/\dot{Q}$, therefore the curves shown in Fig. 7-c would be the normal distribution curve, and when the scale of x-axis changed to linear, the shape of curve changed as shown in Fig. 7-b. The height of the curve in this figure were standarized to show the deformation of the curve more instinctively.

The even distribution means all compartment has one $Q/\dot{Q}$, therefore the unevenness would be expressed as the increase of the standard deviation of the curve of Fig. 7-c. When the value of log SD increase from 0.1 to 1.0, 2.0, 3.0, the shape of the distribution curve becoming flatter and the maximum point (Mode) is shifting to the left as shown in Fig. 7-c. The radioactivity curve at each distribution was shown in Fig. 7a, the peak value was dwindling and the slope of the curve was becoming gentler as the standard deviation was increasing from 0.1 to 1.0, 2.0, 3.0. In this figure the height of the curve was standarized to show the change of the shape of the curve precisely.

DISCUSSION

Reported normal values of mean pulmonary transit time are as followings; 5.8 seconds and 6.6 seconds by Shipley et al.,[7] the former was measured by peak to peak time and the latter by mean transit time of the radiocardiogram, 5.8 seconds by Giuntini,[8] 4.0 seconds by Segre et al.,[9] 6.6 seconds by Jones.[10] All of them are much larger than our $\tau_P = 1.75 \pm 0.50$. This is because all these reported values were measured by radiocardiogram and include the dilution time of the right heart and left heart, also include the transit time of right atrium, main pulmonary artery and main pulmonary vein. On the other hand our τ_P includes only the circulation time of the peripheral lung field.

There are not many data available about the mean pulmonary transit time in COPD patients, Giuntini et al.[8] reported the data, which suggest that the pulmonary transit time of COPD patients is increased compared with normal subjects; the average value of mean pulmonary transit time of seven cases of chronic bronchitis and chronic obstructive emphysema was 7.4 ± 1.2, meanwhile that of 17 cases of normal candidates was 5.8 ± 0.9, although Giuntini makes no remarks about it. However, in our studies, the τ_P values in slight COPD, whose FEV1.0% was 55–70, were within normal limits. In severe COPD, whose FEV1.0% was under 55, three cases which had increased τ_P were recognized out of nine cases. These findings show that τ_P does not increase in slight COPD and may increase in some probably emphysematous cases of advanced severe COPD.

The relationship between τ_P and ventilatory functions such as FEV1.0%, %VC, MMF, was very poor as shown in Figure 4. It suggests that ventilatory impairement and circulatory disturbances are not parallel. The relationship between τ_P and arterial gas pressure, such as PaO_2, $PaCO_2$, $A\text{-}aDO_2$ was also very small as shown in Figure 5. But as shown in Figure 6, the correlation between τ_P and C. I. was significant ($R = 0.457$) which might be reasonable because theoretically τ_P was defined as $Q_P/\dot{Q}$. This was also supported by the fact that τ_P was increased to 3.40 in the patient who was 67 year old male with ischemic heart disease, his ventilatory function was as followings; %VC 98.2, FEV1.0% 65.7, MMF 1.16 L/sec, arterial gas tension were PaO_2 80.2 mmHg, $PaCO_2$ 36.3 mmHg, and $A\text{-}aDO_2$ 34.5 mmHg. His cardiac index was decreased to 1.56. Therefore the increase of τ_P in this case might be explained by decreased $\dot{Q}$. As for Q_P, it might be possible that the decrease of %VC decreased the pulmonary blood volume (Q_P) and consequently decreased the τ_P value which offset the increase of τ_P due to obstructive ventilatory impairement in group III patients. This might explain the fact that the τ_P value of

Table 2. τ_P of 19 patients of lung diseases

Group	Name	Age	Sex	Disease	τ_R	τ_P	C.I.	%VC	FEV1.0%	MMF	Rr	Pao_2	$Paco_2$	$AaDo_2$
I	F. K.	66	♂	br. asthma	1.17	1.40	—	87.4	54.0	0.7	6.0	—	—	—
	E. F.	71	♂	br. asthma	3.43	1.50	—	108.5	61.8	—	3.6	—	—	—
	K. Sh.	58	♂	br. asthma	1.61	1.80	3.42	123.5	55.0	1.5	—	—	—	—
	I. U.	59	♀	br. asthma	1.28	1.10	—	95.2	67.6	0.88	7.0	—	—	—
	N. A.	72	♀	br. asthma	2.06	1.30	4.14	87.0	55.9	0.55	6.3	—	—	—
	M. O.	70	♂	br. asthma	3.44	2.20	2.18	103.6	62.2	0.81	4.5	93.0	38.0	9.2
	mean				2.17	1.55	3.25	100.9	59.4	0.89	5.48	93.0	38.0	9.2
	SD				1.03	0.39	0.99	14.0	5.32	0.36	1.39	—	—	—
II	Y. M.	52	♂	br. asthma	1.22	2.10	4.36	76.8	36.9	0.38	16.0	92.4	29.7	20.5
	K. Sa.	65	♂	br. asthma	2.04	1.90	2.30	73.0	42.9	0.49	7.0	74.8	41.3	23.6
	T. Ao.	50	♂	br. asthma with chr. emphysema	1.86	2.90	—	104.1	48.5	0.71	3.7	62.1	36.1	42.5
	T. N.	57	♂	br. asthma with chr. emphysema	2.00	4.30	2.05	47.2	40.0	0.23	6.5	54.6	57.6	23.4
	H. T.	63	♂	br. asthma with chr. emphysema	3.53	1.40	1.78	69.2	30.8	0.32	3.8	73.0	36.2	36.7
	K. K.	50	♂	br. asthma with chr. emphysema	1.83	2.50	3.38	51.6	36.0	0.26	6.5	62.6	48.0	27.4
	K. Su.	58	♂	chr. bronchitis	2.56	0.90	3.72	67.2	45.5	0.38	4.0	—	—	—
	T. Am.	68	♂	chr. branchitis	4.69	0.70	2.43	42.9	37.8	0.26	8.5	82.2	41.7	15.8
	O. Y.	67	♂	chr. emphysema	2.44	1.30	4.66	88.0	38.0	0.39	5.3	—	—	—
	mean				2.46	2.00	3.09	68.9	39.6	0.38	6.81	71.6	42.5	23.7
	SD				1.05	1.13	1.10	19.8	5.34	0.15	3.82	13.0	9.11	13.0
III	K. Y.	48	♂	old Tbc	2.21	1.20	3.53	30.8	94.0	2.43	6.0	46.8	58.8	29.7
	Mi. Y.	57	♂	old Tbc	4.18	1.50	3.39	58.9	36.8	0.24	—	55.1	56.4	24.4
	K. O.	52	♂	old Tbc	3.20	2.10	2.18	34.7	44.4	0.23	—	52.8	57.6	25.2
	mean				3.20	1.60	3.03	41.5	58.4	0.97	6.0	51.6	57.6	26.4
	SD				0.99	0.46	0.74	15.2	31.1	1.26	—	4.28	1.2	2.85

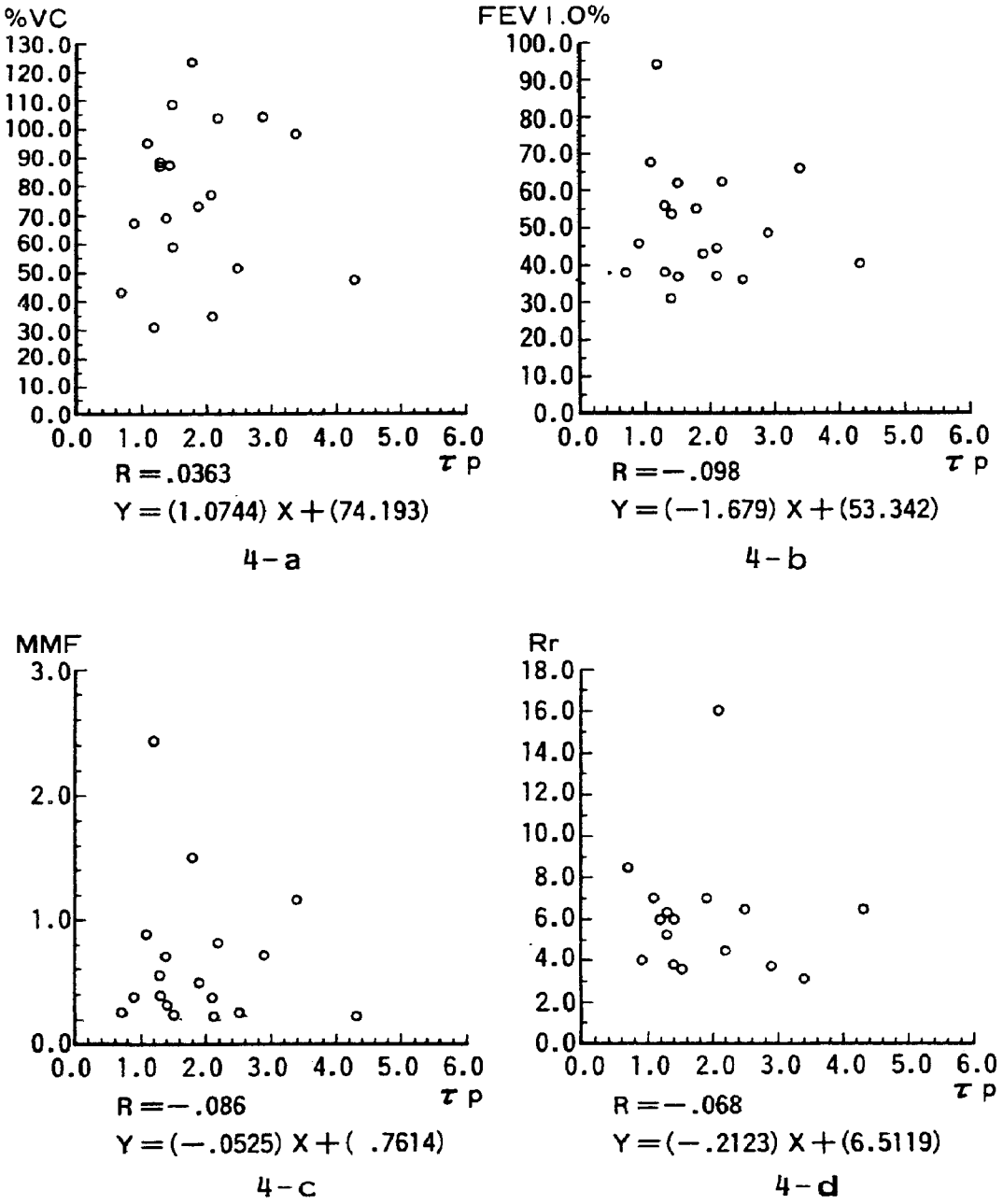


Fig. 4. Correlation between τ_P and ventiratory functions (%VC, FEV1.0%, MMF, and Rr).

this group was not increased. Although in the patients of group I and II, there were three cases whose τ_P increased, two of them had normal C. I. (K. K. 3.88 and T. M. 2.91). The increased τ_P in these two cases could hardly be explained by $Q/\dot{Q}$ because our patients, including these two cases, were not in the terminal stage or in a congested stage, and it is generally accepted that the pulmonary blood volume is not increased in COPD patients unless there is congestion.[8,11] Therefore, there should be some important factor for increasing the τ_P, other than Q and $\dot{Q}$. This is why we studied theoretically the effect of an uneven blood volume blood flow ratio in the lungs on the PVDC by computer simulation.

The result of the computer simulation showed that the slope of the simulated PVDC would become gentler as the standard deviation increases, as shown in Figure 7-a. Therefore if the τ_P value which is measured and calculated as a single compartment from this gently sloped curve,

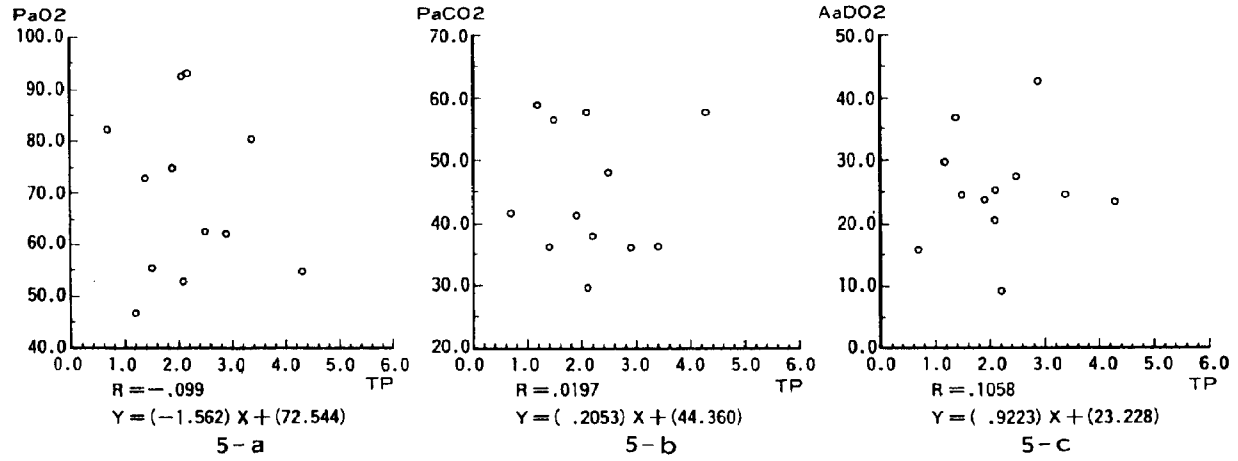


Fig. 5. Correlation between τ_P and arterial gas pressures.

would be larger than $\sum Q_i/\sum \dot{Q}_i$ (=3.0 in this simulation). Then it may be safely said that the increased unevenness causes the apparently increased τ_P.

It is possible, theoretically, to calculate the standard deviation of the distribution of τ_P against log $(Q/\dot{Q})$ in addition to the τ_P itself from measured PVDC by least square method using a computer but we failed to calculate them because of the too gentle upslope curve of PVDC, probably due to imcomplete bolus inflow to the right heart or the dilution effect in the main pulmonary artey.

Histologically, Horsfield et al.[3] pointed out the stricture of pulmonary small arteries as the main lesion of the pulmonary vascular system in COPD. If that stricture in the pulmonary arterial system occures unevenly, the vascular resistnace should increase in this constricted region and the blood flow decreases in this part, consequently τ_P $(=Q_P/\dot{Q})$ may increase if the blood volume of the pulmonary vascular bed does not change. Adding the redistributed blood flow, $\dot{Q}$ may increase in the remaining part of the lung and therefore the τ_P of this remaining part will

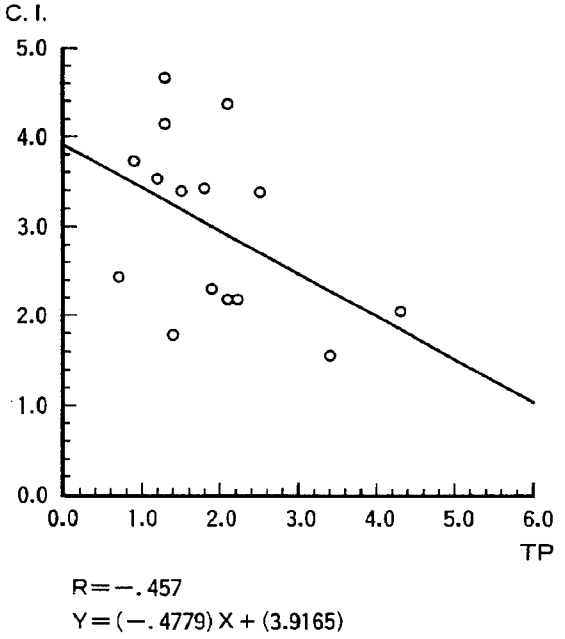
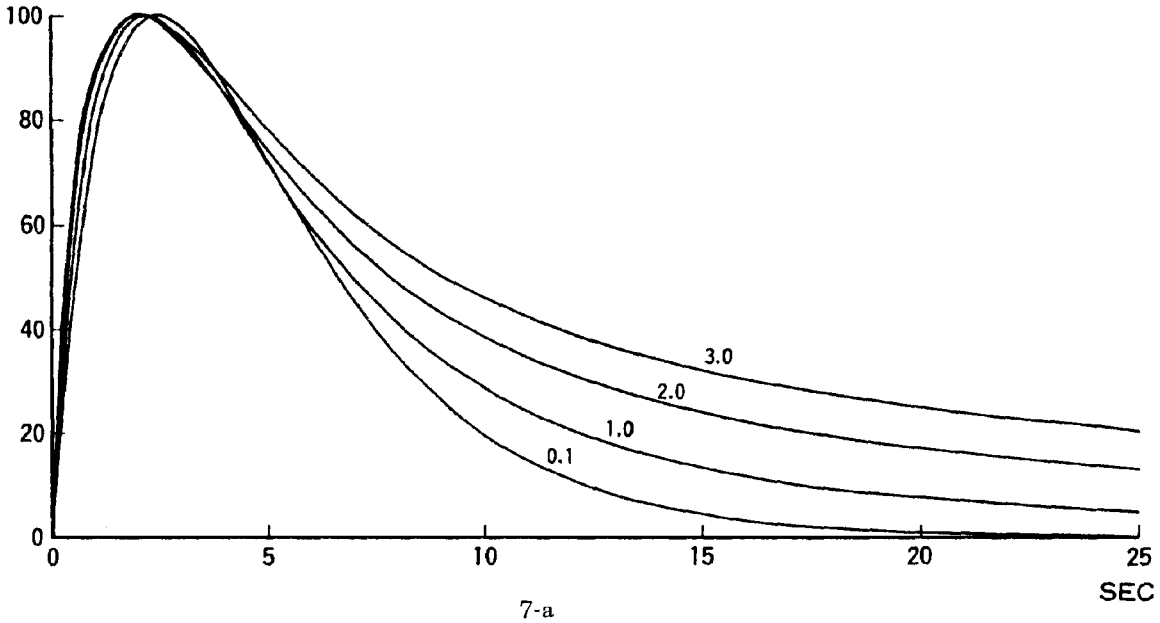
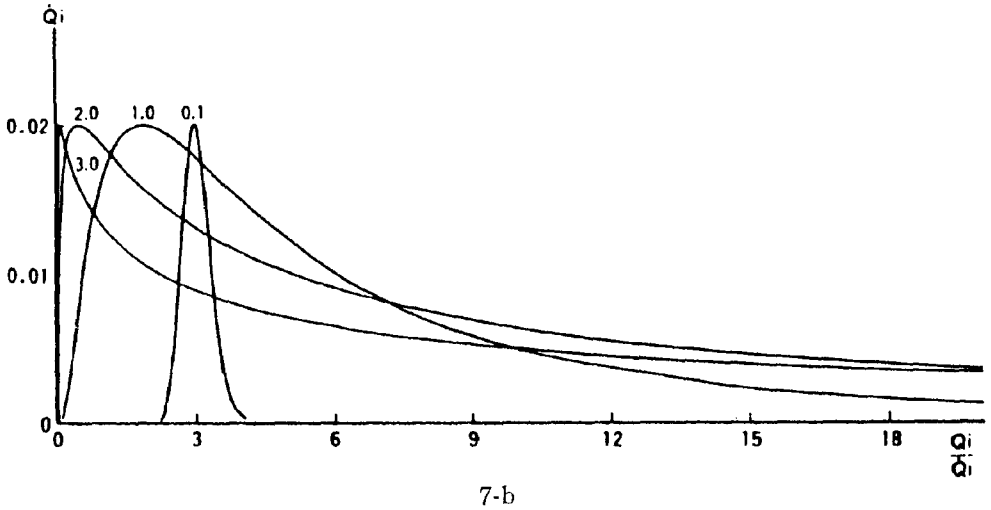


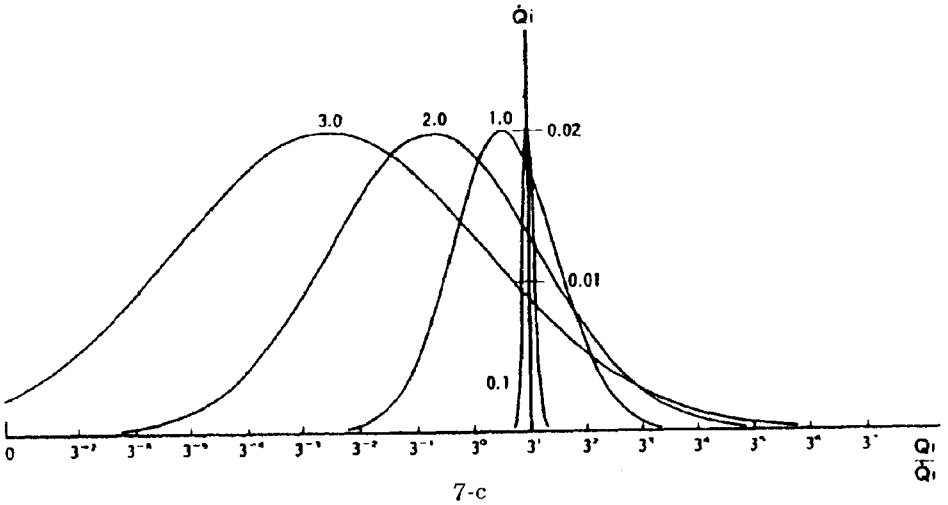
Fig. 6. Correlation between τ_P and cardiac index. R: correlation efficient.



7-a



7-b



7-c

Fig. 7. The effect of uneven blood volume blood flow ratio in the lung upon the PVDC. (by the computer simulation) Assumption: (total Q)/(total $\dot{Q}$)=3.0, τ_R=2.0, $\dot{Q}$ is normally distributed against log ($Q/\dot{Q}$) at SD of 0.1, 1.0, 2.0, 3.0 respectively.
7-a: Simulated PVDC. 7-b: Distribution function of $\dot{Q}$ against $Q/\dot{Q}$. 7-c: Distribution function of $\dot{Q}$ against log ($Q/\dot{Q}$).

Table 3. τ_P, τ_R and ECG findings

Name	τ_R	τ_P	right axis deviation >90°	R>S in V_1	R>S in aVR	R>S in V_5	P>2.5 mm	inverted T in $V_{1\sim3}$	ST depression in II, III, aVF
Y. M.	1.22	2.10	−	−	−	−	−	−	−
K. Sa.	2.04	1.90	−	−	−	−	−	−	−
T. Ao.	1.86	2.90	−	−	−	−	−	−	−
T. N.	2.00	4.30	+	−	−	−	+	−	−
H. T.	3.53	1.40	−	−	−	+	−	−	+
K. K.	1.83	2.50	−	−	−	−	−	−	−
K. Su.	2.56	0.90	−	−	−	−	−	−	−
T. Am.	4.69	0.70	−	−	−	−	−	−	−
O. Y.	2.44	1.30	−	−	−	−	−	−	−

decrease. Thus the unevenness of distribution of τ_P would be made up in COPD patients. Other factors may also have an influence on the τ_P, for eaxmple, A-V shunt such as described by Brachii[3] may decrease the τ_P, and pooling of the blood in the lung or constriction of the pulmonary venous system may increase the τ_P. There is also the posibility that the reserve of the pulmonary blood volume may be called in, this will increase the effective Q value and subsequently increase the τ_P value.

Since the τ_P is a parameter directly indicating the state of the pulmonary vascular system, as mentioned above, then it is more direct and may be more sensitive parameter for detecting the pulmonary vascular lesion in COPD than that of ECG. It is shown in Table 3 that two cases of increased τ_R and three cases of increased τ_P were detected with this method, in the meantime there were two cases of abnormal ECG.

However in some cases it was imposible to get the bolus inflow into the right heart which was needed to measure the τ_P, probably due to anatomical factors of the vein, in this study the measurement of τ_P was unable in 6 cases out 37 (16.2%).

Meanwhile, since the value of τ_R was defined theoretically as $Q_R/\dot{Q}$ (right heart volume/cardiac output), increase of τ_R suggest the increased right heart ventricular volume or decreased cardiac output. Therefore τ_R indicate the performance status of right ventricle. In our cases the τ_R value of group III was increased to 3.20 ± 0.99, this might be relevant to the increased Q_R due to right heart strain, for the $\dot{Q}$ (C. I.) of these cases was within normal limit. The τ_R value of group II (2.46 ± 1.05) was larger than that of group I (2.17 ± 1.03) but they were within normal limit. This is explained by the fact that there were only a little cases of right heart strain in this group as shown in the data of ECG (Fig. 8).

In conclusion, the pulmonary circulation time in peripheral lung field (τ_P) which was assumed, to be the sensitive parameter for assessing the circulation disturbances by the computer simulation, was increased in some cases of severe emphysematous COPD but not increased in moderate COPD or respiratory insufficiency due to old tuberculosis. These increase of τ_P was not correlated with conventional ventilatory functions or arterial gas tensions. These findings showed that the circulatory disturbances would not increase side by side with the ventilatory function, but it would be brought about at the critical advanced emphysematous stage

in COPD.

The increase of τ_R was suggested to be brought about by the increased right heart ventricular volume or dicreased cardiac output. Meanwhile the decrease of pulmonary blood volume (accompanied by decrease of lung volume) and the increase of blood flow or A-V shunt were suggested as the cause of decreased τ_P. As the causes of increase of τ_P, uneven distribution of $Q/\dot{Q}$ was suggested in addition to the decreased blood flow, increased blood volume and the localized stagnation of blood flow in the lung.

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