FREQUENCY-DEPENDENCY OF PULMONARY COMPLIANCE AND ITS RELATION TO AIRWAY CONDUCTANCE

Yoshimi MIYAMOTO,* Takehito NAKABAYASHI,** Hiroshi SAJI,*
and Tomohisa MIKAMI*

*Bio-Medical Control, Research Institute of Applied Electricity,
Hokkaido University, Sapporo 060, Japan

**Department of Internal Medicine, National Hospital Sapporo, Sapporo 062, Japan

Abstract Dynamic compliance was determined in patients with 6 chronic obstructive lung diseases, 2 sarcoidosis and in 4 control healthy subjects at several breathing frequencies ranging between 0.2 and 1.3 Hz. The compliance exhibited an apparent fall with the increase in frequency of the patients, while it remained unaltered in the controls. A significant correlation was found between the frequency-dependency of compliance and the airway conductance determined plethysmographically. A similar relationship was also found in previous data appearing in the literature. Mathematical simulation based on the time constant theory revealed that the above correlation might be expected when airway obstruction occurred inhomogeneously in the peripheral region of the lungs leaving the central airways intact.

It is generally believed that the peripheral airways are mainly affected in chronic obstructive lung diseases (HOGG *et al.*, 1968). Since the obstructions take place in an uneven fashion both at their loci and in their grade of advancement, an inhomogeneity arises in the mechanical time constant of the lung regions, producing spatial and temporal unevenness in ventilation distribution of the lungs. The frequency-dependent nature of pulmonary compliance, the sequence of appearance which was ingeniously explained by the time constant theory developed by OTIS *et al.* (1956) is widely known as one of the characteristics of the mechanical property of unevenly ventilated lungs. WOOLCOCK *et al.* (1969) reported that the frequency-dependency of compliance was found in patients with airway obstruction who exhibited no abnormality in routine pulmonary function tests, and suggested that the compliance measurement related with breathing frequency might be utilized as a test to detect peripheral airway obstruction. Thus it is expected that if the abnormalities in compliance appearing in these patients can be

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宮本嘉巳, 中林武仁, 佐治 裕, 三上智久

explained by the time constant theory, a significant correlation should be observed between the frequency-dependency of compliance and the airway conductance. The present study was thus undertaken for the purpose of finding relationships if any between both the parameters from experiments in patients and simulation using several mathematical models. Insofar as the authors are aware, no such attempts have been made to date.

EXPERIMENTAL PROCEDURES

The patient group studied consisted of 5 chronic pulmonary emphysematous cases, 2 sarcoidosis and a mild case of bronchial asthma. Sarcoidosis was included in the group with expectation that the disease might produce some abnormalities in the peripheral region of the lungs although routine pulmonary function tests indicated no serious defect. The biometrical data and lung volumes obtained in these patients are given in Table 1. The FRC was determined using the technique of body plethysmography (DuBois *et al.*, 1956 a). The control group consisted of 4 healthy young men ranging in age from 20 to 22 years. None had any past history of pulmonary diseases, and moreover there were no smokers in the group.

Table 1. Pulmonary function tests of patients.

Case (No)	Age (Yrs)	Sex	VC (% of predicted normal values)	FRC	RV	TLC	FEV ₁ (% of VC)	Clinical diagnosis
1	70	m	91	230	320	162	33	Emphysema
2	64	m	40	231	388	147	13(26)	Emphysema
3	81	m	119	223	295	173	56	Emphysema
4	70	m	79	216	373	138	46	Emphysema
5	34	m	118	120	108	116	75	Asthma
6	25	f	131	122	138	132	80	Sarcoidosis
7	80	m	75	172	255	130	41	Emphysema
8	45	m	124	132	123	124	81	Sarcoidosis
Mean	59		97	181	250	140	53	
SD	20		29	47	106	18	23	

VC: vital capacity; FRC: functional residual capacity; RV: residual volume; TLC: total lung capacity; FEV₁: forced expiratory volume at 1 sec. FEV₁ in parentheses (case 2) is the result of re-measurement on another day.

Dynamic compliance was determined from simultaneous measurements of tidal volume and transpulmonary pressure by dividing the volume change by the pressure change between both ends of inspiration and expiration. Tidal volume was obtained by electrical integration of the flow signal measured by a pneumotachograph fitted to the mouth. Transpulmonary pressure was estimated from the difference between the mouth pressure and the esophageal pressure, which was introduced using the intraesophageal balloon technique of MILIC-EMILI *et al.* (1964). The frequency characteristics of the pneumotachograph-integrator system and the balloon-manometer system were tested using a pump generating a sinusoidal

volume change. The amplitude response of each system was found to be uniform up to a frequency of 4 Hz. No appreciable phase shift between the input and output signals was detected up to this frequency. The compliance was determined in each subject at three to five different breathing frequencies from 0.2 to 1.3 Hz.

Static compliance was also determined from the lung volume and the transpulmonary pressure changes measured during a period when the airflow was intermittent. The subject was allowed to breathe at a spontaneous rate at rest. The airway opening was repeatedly interrupted at each end of an inspiration and subsequent expiration by closing a shutter inserted between the mouth and the pneumotachograph for about 1 sec. The compliance was then found as the ratio of the net volume change to the corresponding pressure change observed during the period between both interruptions.

Airway conductance was determined by taking a reciprocal of the airway resistance measured by the standard technique of body plethysmography (DuBois *et al.*, 1956 b).

EXPERIMENTAL RESULTS

Airway conductance and static compliance determined in the patients are shown in Table 2 together with other parameters which will be mentioned later. Mean values and standard deviation thereof were 0.33 ± 0.17 l/sec/cmH₂O and 0.26 ± 0.12 l/cmH₂O, respectively. Corresponding values determined in the control group were 0.95 ± 0.34 l/sec/cmH₂O and 0.19 ± 0.06 l/cmH₂O, respectively. Dynamic compliances measured in the control and patient groups are plotted in Figs. 1 and 2, respectively, as a function of the breathing frequency. Since the compliance value was dependent on the lung volume, it was normalized by taking its ratio to the static compliance of each subject for convenience of comparison. The dynamic compliances measured in the patient group exhibited an apparent tendency to fall with an increase in the breathing frequency although the slope of each curve was widely scattered from patient to patient. On the other hand, the compliance measured in the control group did not apparently deviate from the static compliance up to a frequency of 1.3 Hz.

THEORETICAL CONSIDERATION

Let us consider a model having two parallel compartments, each of which consists of a single resistive and elastic component (Fig. 3). Symbols, C , R , and T with subscripts 1 and 2 represent static compliance, resistance and time constant of the peripheral regions of the lungs, respectively. For convenience sake, let us define compartments 1 and 2 as representing the intact and obstructed regions of the diseased lungs, respectively. Resistance in the central airway is represented by R_c in this model. Similarly, transpulmonary pressure is represented by voltage applied to the terminals, airflow by current and gas volume by electric quantity.

Fig. 1. Relationships between the breathing frequency (F) and the ratio of the dynamic compliance to the static compliance (C_e/C_s) measured in 4 control subjects. Numerals at each curve indicate airway conductance (l/sec/cmH₂O).

When the voltage is sinusoidal and of a constant frequency, the relationship between the voltage and current observed in such a circuit can be duplicated with an equivalent circuit consisting of a single resistance and compliance connected in series. When an AC voltage $P=P_0 \sin \omega t$, where P_0 =peak amplitude of P , $\omega=2\pi f$ and F =breathing frequency, is applied, effective resistance and compliance of an equivalent series circuit of the two-compartment part of the model, R_e and C_e , may be given as follows by referring to OTIS *et al.* (1956).

$$R_e = \frac{\omega^2 T_1 T_2 (T_1 C_2 + T_2 C_1) + (T_1 C_1 + T_2 C_2)}{\omega^2 (T_1 C_2 + T_2 C_1)^2 + (C_1 + C_2)^2} \quad (1)$$

$$C_e = \frac{\omega^2 (T_1 C_2 + T_2 C_1)^2 + (C_1 + C_2)^2}{\omega^2 (T_1^2 C_2 + T_2^2 C_1) + (C_1 + C_2)} \quad (2)$$

C_e may be regarded as a synonym of the dynamic compliance and $C_1 + C_2$ corresponds to static compliance. According to MACKLEM and MEAD (1967) the resistance of peripheral airways is assumed to be about 10 percent of the total airway resistance in healthy normal men. Provided that total airway resistance and compliance of the normal lungs are 1 cmH₂O/l/sec and 0.2 l/cmH₂O, respectively, the time constant of the peripheral region of the lung is about 0.02 sec. If we are allowed

Fig. 2. Relationships between the breathing frequency (F) and the ratio of the dynamic compliance (C_e/C_s) measured in 8 patients. The case numbers correspond to those given in Table 1 and numerals at each curve indicate airway conductance (l/sec/cmH₂O).

to assume that the airway obstruction occurred sequentially from one branch to another of parallel pathways without alteration of the mechanical property of the intact region, T_1 should always retain the 0.02 sec value until all pathways are closed. This may be said because when total compliance decreased by a reduction in the number of pathways involved in the compartment, total resistance of the compartment must be increased. Recently, MIYAMOTO *et al.* (1975) made a mathematical analysis based on the time constant theory on the relationship between the breathing frequency and simultaneously measured pulmonary resistance and compliance; he estimated that the time constant of the intact lung region did not exceed 0.08 sec in patients with chronic obstructive lung diseases. In the following, let us consider how the C_e varies with frequency using the parameter values estimated by MIYAMOTO *et al.* (1975). Since Eq. (2) involves too many

parameters, let us rewrite it as follows where $C_s = C_1 + C_2$ and $S = C_2/(C_1 + C_2)$.

$$C_e/C_s = \frac{\omega^2 \{T_1 S + T_2 (1-S)\}^2 + 1}{\omega^2 \{T_1^2 S + T_2^2 (1-S)\} + 1}$$

In Fig. 3 (A)–(C) are shown the frequency vs. C_e/C_s relationships calculated by the above equation provided that $T_1 = 0.02$ sec, $T_2 = 0.5$ – 2.0 sec and $S = 0.2$ – 0.8 . The parameter, S , may imply the volume ratio of the diseased region to the total lung volume in a particular case in which the elastic property of the regional lung units are uniform. This may be said since gas volume contained in a lung unit is primarily determined by its static compliance. On the other hand, T_2 implies in this case the size of resistance of the obstructed pathway. Figure 3 suggests

Fig. 3. Relationships between the breathing frequency (F) and the ratio of the effective compliance to the static compliance (C_e/C_s) simulated by the two-compartment model is as shown in the figure.

that the slope of fall of the compliance with frequency, dC/dF , is predominantly determined by T_2 . When T_2 increases, the dC/dF becomes so steep that the curve seems to reach an asymptote within the frequency range adopted (Fig. 3, C). On the other hand, height of the asymptote seems to be predominantly dependent on S .

Returning to Eq. (2), C_e would reach an asymptote when ω is increased infinitely as follows.

$$C_{ei} = \frac{(T_1 C_2 + T_2 C_1)^2}{T_1^2 C_2 + T_2^2 C_1} \quad (3)$$

where, C_{ei} is the C_e at infinite ω . Since T_1 is a very small quantity compared with the other parameters, Eq. (3) may roughly be represented by C_1 letting T_1 be zero. Then,

Fig. 4. Theoretical and experimental relationships between the ratio of the effective compliance at the infinite frequency to the static compliance (C_{ei}/C_s) and the airway conductance (G). Dashed lines represent the theoretical curves and the open circles with a solid regression line represent the experimental.

$$C_{ei}/C_s \approx C_1/C_s \quad (4)$$

Since airway conductance depends upon the number of intact pathways arranged in parallel or volume of healthy region relative to the total lung volume, a significant correlation between the C_{ei}/C_s and the airway conductance may be expected if regional compliance of the lungs does not differ in excess from each other and if R_o remains unaltered. Dashed lines in Fig. 4 show such relationships calculated under the same parameter values given in Fig. 3. Airway conductance, G , was calculated by the following equation with the frequency of spontaneous breathing rate at rest, *i.e.*, 0.3 Hz.

$$G = 1/(R_o + R_e) \quad (5)$$

where, R_o is assumed to be 1.0 cmH₂O/l/sec. Figure 4 suggests that a significant correlation lies between C_{ei}/C_s and G . Although a decrease in T_2 seems to make the linearity of the relationship lower, it is still favorable within the area of higher conductance.

It is of interest to examine whether the theoretical relationship between C_{ei}/C_s and G agrees with the experimental results. The C_{ei} of the dynamic compliance was estimated by a mathematical extrapolation of the frequency *vs.* compliance relationship observed experimentally. Let us rewrite Eq. (2) as,

$$C_e = \frac{A\omega^2 + C_s^2}{B\omega^2 + C_s}$$

Since C_s is already known, A and B can be obtained if a dual number of C_e s are measured at different ω s by solving the simultaneous equation. Thus,

$$A = \frac{C_s\{\omega'^2 C_e''(C_e' - C_s) - \omega'^2 C_e'(C_e'' - C_s)\}}{\omega'^2 \omega''^2 (C_e'' - C_e')}$$

Table 2. Parameters indicating airway obstruction and frequency-dependency of compliance determined in patients.

Case	G (l/sec/cmH ₂ O)	C_s (l/cmH ₂ O)	A	B	C_{ei} (l/cmH ₂ O)
1	0.24	0.267	0.00250	0.0294	0.085
2	0.12	0.177	0.00018	0.0092	0.019
3	0.31	0.543	0.00187	0.0348	0.054
4	0.22	0.151	0.00015	0.0057	0.026
5	0.36	0.225	0.00185	0.0205	0.090
6	0.50	0.291	0.00203	0.0188	0.108
7	0.22	0.187	0.00144	0.0299	0.048
8	0.67	0.254	0.00288	0.0206	0.139
Mean	0.33	0.262	0.00161	0.0211	0.071
S.D.	0.17	0.115	0.00093	0.0094	0.039

G : airway conductance; C_s : static compliance; A, B : coefficients of the equation, $C_e = (A\omega^2 + C_s^2) / (B\omega^2 + C_s)$; C_{ei} : predicted value of C_e at infinite ω . Explanations are in the text.

and

$$B = \frac{C_s \{ \omega'^2 (C_e' - C_s) - \omega''^2 (C_e'' - C_s) \}}{\omega'^2 \omega''^2 (C_e'' - C_e')}$$

where, C_e' and C_e'' are dynamic compliance measured at different angular velocities ω' and ω'' . It is evident from Eqs. (2) and (3) that C_{ei} is given by the ratio of A to B . The C_{ei}/C_s of the present eight patients was determined adopting this procedure and presented in Table 2. These values are also plotted in Fig. 4 in relation to the airway conductance of each individual. The correlation between both the parameters is significant ($\gamma=0.827$, $p<0.01$), and the experimental relationship fits well to the theoretical ones.

DISCUSSION

A favorable correlation between the frequency-dependency of compliance and the airway conductance stands on the basis of (1) obstruction occurs only in the peripheral region of the lungs without any change in resistance of the central airway, and (2) the obstruction does not occur uniformly throughout the entire lungs but rather unevenly leaving a considerable amount of the lungs intact. According to the measurement in the isolated lungs made by HOGG *et al.* (1968), resistance of the central airway of the emphysematous lungs did not differ from the control although that of the peripheral airways increased from four to forty. Another investigation by these authors on the lungs of elderly persons likewise showed similar results (HOGG *et al.*, 1970). Thus, the first assumption may hold true. Little is known, however, about the actual process of advancement of the airway obstruction in the disease. According to NAKAMURA *et al.* (1966), who estimated the distribution of time constant in the lungs using a distribution function of complex-compliance, the time constant variations of the healthy lungs were concentrated in a narrow range, while those of the diseased lungs were scattered widely. This suggests that the two-compartment model may be oversimplified to simulate the mechanical property of diseased lungs. Thus, we tried to examine whether the correlation between the compliance and airway conductance holds true in a more elaborate model consisting of multi-compartment. Let us consider an eight-compartment model such as shown in Fig. 5. The time constant of each compartment was then arranged according to a geometric progression as seven combinations shown in Fig. 5 (A). Variation in the time constant was assumed to be dependent solely in the resistive component. In order to obtain C_e and R_e of the model, the following procedures were taken. First, effective compliance and resistance, C_e'' and R_e'' , of a given pair from the eight compartments were calculated using Eqs. (1) and (2). Similar procedures were repeated for remaining three pairs. Secondly, C_e' and R_e' were calculated using a given pair of C_e'' and R_e'' . Since we had four pairs of C_e'' and R_e'' , two pairs of C_e' and R_e' were thus obtained. C_e and R_e were finally calculated using these C_e' and R_e' .

Fig. 5. (A): Possible seven combinations, a-g, of uneven distribution in time constants of the eight-compartment model shown in the left, which simulates the lungs with chronic obstructive disease; (B): relationships between the breathing frequency (F) and the ratio of the effective compliance to the static compliance (C_e/C_s) simulated by the model for the above seven cases; (C): relationships between the ratio of the effective compliance at infinite frequency to the static compliance (C_{ei}/C_s) and the airway conductance (G).

In Fig. 5 (B), the frequency vs. C_e/C_s relationship calculated for the above seven cases were shown. Frequency-dependency of C_e does not seem to differ from that demonstrated in the two-compartment model. The C_{ei}/C_s vs. G relationship of the eight-compartment model calculated for the case that $R_o = 1.0$ cmH₂O/l/sec, $C_s = 0.2$ l/cmH₂O and $F = 0.3$ Hz was also shown by open circles in Fig. 5 (C). Each point corresponds to each case shown in Fig. 5 (A). It is evident that a significant correlation between both the parameters still holds in the multi-compartment model as well as in the two-compartment model.

There, however, still remains a question as to whether the relationship dis-

Fig. 6. Relationships between the ratio of the dynamic compliance at 1 Hz to the static compliance (C_e/C_s) and the airway conductance (G) measured in 4 patients with asthma. These were rearranged from the data appearing in an article of MCFADDEN and LYONS (1969).

cussed above is generally applicable in various obstructive lung diseases. Figure 6 gives another example exhibiting a similar relationship between the compliance and conductance, which was obtained from data presented by MCFADDEN and LYONS (1969) who made 17 serial measurements on 4 asthmatic patients. A significant correlation between the ratio of dynamic compliance ($F=1$ Hz) to static compliance and the airway conductance ($\gamma=0.833$, $p<0.01$) was shown. A favorable but slightly lesser correlation ($\gamma=0.658$, $p<0.01$) was obtained from 15 measurements on 5 asthmatic patients made by the same authors (MCFADDEN and LYONS, 1968). Almost the same correlation was observed in the measurement on 4 asthmatic patients reported by WOOLCOCK *et al.* (1969), but this was not the case for bronchitic patients appearing in their report.

It may be said that the present theoretical concept is valid in many cases of asthma, and at least partially in emphysema as shown in the present paper. In general, pathological characteristics of asthma appear predominantly in the resistive

property of the lung mechanics, while those of emphysema appear in the elastic property. Although the present model designated neither resistance nor compliance as the cause of the time constant increment, the correlation between C_{ei}/C_s and G would be less favorable if the regional elasticities of the lungs were to a large extent different from each other. In this sense, it seems conceivable that application of the present theory should be limited to obstructive airway diseases at a relatively early stage.

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