



# Quantitative Relationship Between Expiratory Airflow Limitation and Dynamic Hyperinflation: A Thermo-statistical Model

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**Abstract:** Clinical assessment of expiratory flow limitation (EFL) is important for diagnosing chronic pulmonary disease (COPD). Either EFL or dynamic hyperinflation (DH) in COPD has been understood based on wave speed theory, which is widely accepted as the standard concept. However, a theoretical perspective on the relationship between EFL and DH may require another approach. This article proposed another explanation for EFL with the introduction of pulmonary entropy with thermo-statistical considerations on choke state of the pulmonary system. According to Gibbs' thermodynamic equilibrium theory, the choke state of the pulmonary system was characterized by a critical pressure ( $P_c$ ) emergence in the pulmonary parenchyma, which was proportional to the elastic recoil pressure ( $P_{el}$ ) and the slope of maximal flow-volume curve ( $\sigma$ ). Thermodynamic balance between energies (supplied from the body as heat, stored as the entropy of lungs, and dissipated in the respiratory system) explained the work of breathing (WOB), by which it was explained that an intrinsic PEEP ( $PEEP_i$ ) was emerging as a difference between sufficient and insufficient WOB for energy demands of the body. It was concluded that EFL would limit the WOB into less than demanded during exercise, and that the difference between demand and performance would induce a product of  $PEEP_i$  and DH in volume.

**Keywords:** Thermo-statistical Model, Entropy Elasticity, Expiratory Airflow Limitation (FEL), Dynamic Hyperinflation (DH), Intrinsic Positive End-expiratory Pressure (PEEP<sub>i</sub>), Work of Breathing (WOB)

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## 1. Introduction

Clinical assessment of lung function is commonly explained by a phenomenon known as expiratory flow limitation (EFL), which means that a flow approaches a maximal value ( $\dot{V}_{max}$ ) as the choke state that cannot be exceeded regardless of the extra effort exerted. [1] The maximal expiratory flow ( $\dot{V}_{max}$ ) decreases proportionally with lung volume ( $V_L$ ). [2] EFL is also expressed by the volume excreted in the first one second during a forced expiration as FEV<sub>1</sub>. When FEV<sub>1</sub> is coupled with a measure of the total gas volume expired during an entire forced expiration, known as forced vital capacity (FVC), we can differentiate between obstructive disease (both FEV<sub>1</sub> and the ratio FEV<sub>1</sub>/FVC are lower than normal) and restrictive disease (FVC is lower than normal but FEV<sub>1</sub>/FVC is normal).[3]

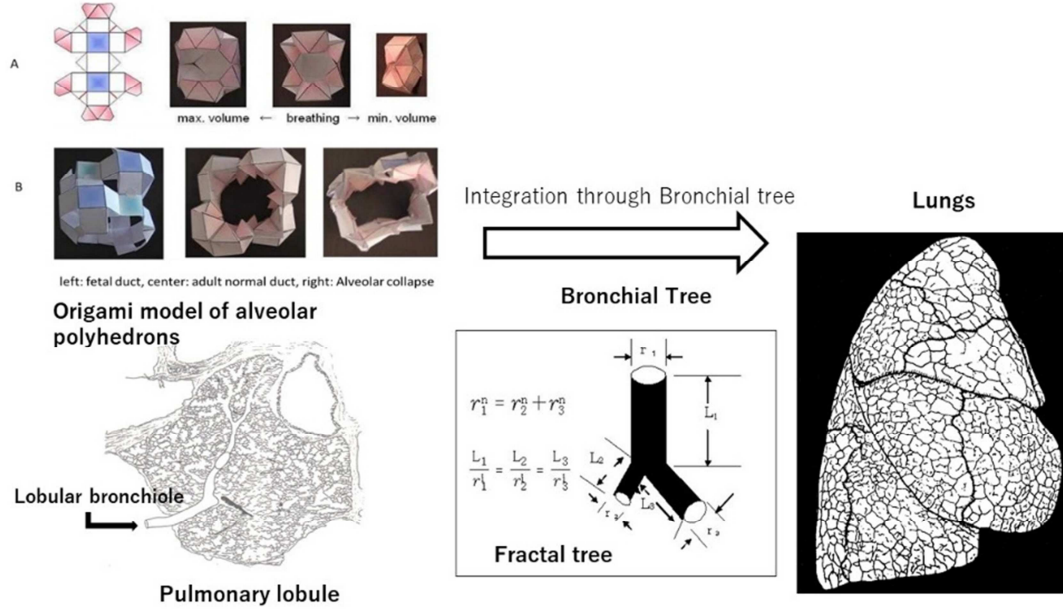
EFL has been described by wave speed theory in the

conducting airway introduced based on fluid mechanics by Dawson and Elliot [4]: the pressure gradient along the airway branch is necessary to drive the air along the airway conduit. When an aliquot of air is incompressible, it is accommodated by lateral expansion of the conduit's upstream walls. This expansion propagates toward the other end of the conduit at a rate determined by the speed of movement of the elastic deformation of the wall, meaning that each point in the wall must radially oscillate either side of its relaxed position. To accommodate a steady stream of air in this way, the conduit walls must move in a continuous wave. Because the air is moved along the wave motion of the conduit walls, the velocity of propagation of air equals the speed of these elastic waves. The actual flow transmitted is given the product of this velocity and the amplitude of oscillations. Once these oscillations reach an amplitude equal to the conduit radius, the opposing walls bump into each other at the peak of their

inward excursions, thereby limiting the flow that can be carried this way. The lung conducting airway is not a single conduit but an irregular and fractal branching tree, and the pulmonary parenchyma are segmented into a large number of secondary pulmonary lobules, each of which also contains numerous alveoli [5, 6].

Leibniz advocated a mechanical alternative from Newton's with introducing the concept of state of system, from which energy functions produce dynamic action of forces.[7] Thermo-statistical dynamics is a branch of Leibniz's mechanics that includes thermodynamic functions and

investigates new parameters of heat ( $Q$ ) and temperature ( $T$ ). [8] In this study, after introducing a parameter of temperature ( $T$ ) as fluctuations of alveolar dynamics a thermo-statistical state function of entropy ( $S_L$ ) was introduced [9], and based on laws of thermodynamic equilibrium in the respiratory system the elastic recoil pressure ( $P_{el}$ ), the expiratory flow limitation (EFL), and the dynamic hyperinflation (DH) were theoretically defined from the thermodynamic viewpoint. Then, we concluded that there is a close relationship between EFL and DH through the elastic recoil pressure  $P_{el}$ .



**Figure 1.** Fractal bronchial tree and aggregated secondary pulmonary lobules. A secondary lobule has a lobular bronchiole and numerous alveoli, each of which is modeled as an origami (paper craft) polyhedron: the panel A describes changes in volume of the alveolar polyhedron, and the panel B indicates collapsed alveolar polyhedrons and corresponding dilatation of alveolar duct. The panel C shows the secondary pulmonary lobule of packed alveolar polyhedrons. The bronchial tree branches (D) in asymmetric fractals from trachea to lobular bronchioles to form the whole lungs (E) as unity (See text in detail).

## 2. Assumptions

### 2.1. Pulmonary Lobules and a Fractal Bronchial Tree

The lungs consist of Miller's secondary pulmonary lobules, each of which is the basic unit of pulmonary parenchyma from the viewpoint of structural functional relationship [5-7] as follows:

- 1) The secondary pulmonary lobule has one corresponding bronchiole, through which air flow goes inward and outward. The secondary pulmonary lobule has numerous alveoli with bronchioles anatomically interrelated, and functions as a unit.
- 2) According to the origami (paper craft) model of alveolar structure, alveolar polyhedrons are packed in the secondary pulmonary lobule, and the angle between the alveolar walls changes depending on the degree of inflation in the volume of the pulmonary lobule. (Figure 1A, B and C)
- 3) The bronchial tree branches in asymmetric fractals to form approximately three thousand secondary pulmonary lobules. (Figure 1 D)

### 2.2. Physiological States of Expiratory Flow Limitation

Expiratory flow limitation (EFL) is characterized by physiological observations as follows [1, 9]:

- 1) The magnitude of the flow leaving the lungs approaches a maximal value ( $\dot{V}_{max}$ ) that cannot be exceeded regardless of how much extra effort is exerted, and  $\dot{V}_{max}$  decreases with lung volume.
- 2) The critical alveolar pressure ( $P_c$ ) emerged in the pulmonary parenchyma at the choke state is described with  $\dot{V}_{max}$  and resistive coefficient  $\gamma_c$  as follows,

$$P_c = \gamma_c \dot{V}_{max} \quad (1)$$

The dissipation energy  $D_c$  through airways is defined as follows,

$$D_c = \frac{1}{2} \gamma_c \dot{V}_{max}^2 \quad (2)$$

When  $\sigma$  is the slope of maximal flow-volume curve in the flow-volume plane, a derivative of  $D_c$  is obtained as follows,

$$dD_c = \gamma_c \dot{V}_{max} \cdot \left( \frac{d\dot{V}_{max}}{dV_L} \right) \cdot dV_L = P_c \cdot \sigma \cdot dV_L \quad (3)$$

### 3. Laws of Thermodynamic Equilibrium

Zeroth law: If two systems are in thermal equilibrium with a third system, then all three systems are in thermal equilibrium with each other. That is to allow the existence of an empirical parameter, the temperature, as a property of a system such that systems in thermal equilibrium with each other have the same temperature.

First law: The first is the law of conservation of energy adapted for thermodynamic systems. For a thermodynamic process without transfer of matter, the first law is often formulated as follows,

$$\Delta U_{system} - \Delta D_{system} = Q - W \quad (4)$$

where  $\Delta U_{system}$  and  $\Delta D_{system}$  denote the change in the internal energy and dissipating energy of a closed system, respectively.  $Q$  denotes the quantity of energy supplied to the system as heat, and  $W$  denotes the amount of thermodynamic work (expressed here with a negative sign) done by the system on its surroundings.

Second law: The second law of thermodynamics states the irreversibility of natural processes, and, in many cases, the tendency of natural processes to lead towards spatial homogeneity of matter and energy, and especially temperature. The notion of entropy is needed to provide the second law as that the entropy of an isolated system never decreases over time towards thermodynamic equilibrium, the state with maximum entropy. Entropy of  $S$  is related to the number of microstates in  $\theta$  and its corresponding probability  $\rho(\theta)$  as follows [10, 11],

$$S \propto - \int \rho(\theta) \ln \rho(\theta) d\theta \quad (5)$$

The probability  $\rho(\theta)$  relates to temperature  $T$  and energy  $\varepsilon(\theta)$  as follows,

$$\rho(\theta) \propto e^{-\varepsilon(\theta)/T} \quad (6)$$

In thermodynamics, the internal energy  $U_{system}$  of a system is the energy contained within the system. It is the energy necessary to create or prepare the system in any given state. The internal energy does not include the kinetic energy of motion of the system as a whole, or the potential energy of the system as a whole due to external force fields, which includes the energy of displacement of the system's surroundings.

Classical thermodynamics deals with states of dynamic equilibrium.[10] The state of a system at thermodynamic equilibrium is that at which some thermodynamic potential is minimized, or in which the entropy ( $S$ ) is maximized, for specified conditions. One such potential is the Helmholtz free energy ( $F$ ), for a system with surroundings at controlled constant temperature and volume:

$$F = dQ - TS \quad (7)$$

Another potential, the Gibbs free energy ( $G$ ), is minimized at thermodynamic equilibrium in a system with surroundings at controlled constant temperature and pressure:

$$G = dQ - TS + PV \quad (8)$$

where  $T$  denotes the absolute thermodynamic temperature,  $P$  the pressure,  $S$  the entropy, and  $V$  the volume. The above-mentioned potentials are mathematically constructed to be the thermodynamic quantities that are minimized under particular conditions in the specified surroundings as follows,

$$dF = dQ - TdS = 0 \quad (9)$$

$$dG = dQ - TdS + PdV = 0 \quad (10)$$

### 4. Thermodynamic Model

#### 4.1. Temperature ( $T$ )

Each pulmonary lobule has numerous alveolar walls and changes its volume as a change in the angles ( $\theta: 0 \leq \theta \leq \pi$ ) between adjacent alveolar walls. The probability density of  $\rho_j(\theta)$  is obtained as the distribution of angles ( $\theta$ ) in number of  $n_j$  in the pulmonary lobule of  $j$  ( $j = 1, 2, 3, \dots, N$ ). When the surface energy of  $\varepsilon(\theta)$  is necessary for holding the angle in  $\theta$  between alveolar walls, the probability density is defined according to the statistical theory as follows,

$$\rho_j(\theta) \propto e^{-\varepsilon(\theta)/T} \quad (11)$$

where  $T$  is a thermo-statistical parameter describing fluctuations of angles in the pulmonary parenchyma based on the zero law of thermodynamic equilibrium. [11]

#### 4.2. First law of Thermodynamics at the Choked State

Suppose that the chest wall transfers energy of  $q_j$  as heat to the pulmonary lobule  $j$ , where we can measure an alveolar pressure  $P_{Aj}$  and its volume of  $v_j$ . When the energy  $Q$  is divided at each pulmonary lobule as  $q_j$  for the lobule  $j$ , the first law of thermodynamics is described as follows,

$$dq_j = -P_{Aj} dv_j + T ds_j \quad (12)$$

The maximal expiratory flow  $\dot{V}_{max}$  is formed from summation of lobular flows through a fractal bronchial tree, when each alveolar pressure  $P_{Aj}$  is choked to a critical pressure  $P_c$ . The energy in choked state is dissipated as  $D_c$  in the bronchial tree. Then, according to the first law of thermodynamics for the whole respiratory system, the following equation is obtained as follows,

$$\begin{aligned} dQ + dD_c &= \sum_{j=1}^N dq_j = -P_c \sum_{j=1}^N dv_j + T \sum_{j=1}^N ds_j \\ &= -P_c dV_L + TdS_L \end{aligned} \quad (13)$$

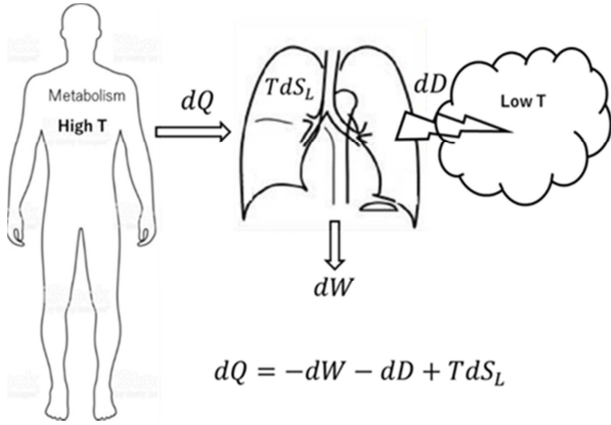


Figure 2. Thermodynamic balance among energies in the body.

Q is the total energy supplied to the respiratory system from the body as heat, which is produced by metabolism of the body. D is the dissipating energy from the respiratory system to the environment. W is the WOB. Dynamic balance of energy is described as follows,  $dQ = -dW - dD + TdS$ .

## 5. Results

### 5.1. Elastic Recoil Pressure ( $P_{el}$ )

Static refers to the determination of lung volume components from the static pressure-volume relaxation curve of the respiratory system. Dynamic refers to the influence of dynamic events, such as expiratory timing, during maximal forced or spontaneous tidal breathing, on lung volume measurements. The static pressure-volume relaxation curve is obtained as a quasi-static relaxation curve, which is described by constant temperature and volume without energy dissipation according to thermodynamic equilibrium. Thus, the static elastic recoil pressure  $P_{el}$  was obtained as follows,

$$dF = dQ - TdS_L = dU_L - TdS_L = 0 \quad (14)$$

$$dU_L = -P_{el}dV_L \quad (15)$$

$$P_{el} = -T \left( \frac{dS_L}{dV_L} \right) \quad (16)$$

Functional residual capacity (FRC) is usually described as a static lung volume at which the elastic recoil pressures of lung and relaxed chest wall are equal and opposite in sign. In other words, the elastic recoil pressure  $P_{el}$  at FRC is also described as balancing in pressures between components of ribcage by zero transdiaphragmatic pressure ( $P_{di} = 0$ ). FRC is also the dynamic lung volume as repeated at the end of spontaneous stable breathing [i.e., end-expiratory lung volume (EELV)], thus from the second law of thermodynamics, the entropy  $S_L$  of pulmonary parenchyma would be a maximum or  $dS_L = 0$  at FRC. [11] When the pleural pressure is measured at FRC as value of  $c$ , the elastic recoil pressure is measured as  $P_{el} + c$ .

### 5.2. Maximal Flow-static Recoil Pressure (MFSR) Relationship

During the state of choke, a thermodynamic equilibrium was defined as follows,

$$dG = dQ - TdS_L + P_c \cdot (-dV_L) = 0 \quad (17)$$

Thus,

$$dQ + (P_{el} + c) \cdot dV_L - P_c \cdot dV_L = 0 \quad (18)$$

The critical alveolar pressure  $P_c$  was independent from extra efforts. Thus, extra energy from efforts should be dissipating. Then  $dQ$  would be equal to  $dD_c$  as follows,

$$dQ = dD_c = \sigma \cdot \gamma_c \dot{V}_{max} \cdot dV_L = \sigma P_c \cdot dV_L \quad (19)$$

Thus,

$$\sigma P_c \cdot dV_L + (P_{el} + c) \cdot dV_L - P_c \cdot dV_L = 0 \quad (20)$$

$$P_c = \frac{P_{el} + c}{1 - \sigma} \quad (21)$$

By combining the equations (1) and (21), the maximal flow-static recoil pressure (MFSR) relationship was obtained as follows,

$$\dot{V}_{max} = \frac{P_{el} + c}{\gamma_c(1 - \sigma)} \quad (22)$$

### 5.3. Dynamic Hyperinflation (DH) in Campbell's Diagram and Flow-volume Plane

When expiratory time is not sufficiently long to allow the inspired gas to be expired to the original equilibrium lung volume, inspiratory efforts are necessary to overcome the elastic recoil of the respiratory system before inspiratory flow can start. This condition is termed dynamic hyperinflation (DH), and positive alveolar pressure during end-expiratory airway occlusion, reflecting elastic recoil pressure of the respiratory system due to incomplete lung emptying, is termed intrinsic positive end-expiratory pressure (PEEP<sub>i</sub>). DH and PEEP<sub>i</sub> have been reported in patients with COPD.

According to the thermodynamics of breathing in Campbell's diagram [7], breathing is expressed as follows,

$$\oint dQ = -\oint P_A dV_L + T \oint dS \quad (23)$$

Exercise energy Q is supplied as heat to the respiratory system, and induced work of breathing (WOB) and elastic change in entropy. When the pressure volume loop of breathing is seen closed at FRC in Campbell's diagram, the entropy change is zero at FRC, and supplied energy becomes the WOB done. When the pressure volume loop of breathing is seen closed at end-expiratory lung volume [EELV] different from FRC, the difference between EELV and FRC is DH in volume ( $\Delta V_{DH}$ ) and PEEP<sub>i</sub> is an elastic recoil pressure due to incomplete lung emptying. (Figure 3) According to the equation (11), breathing at rest and at exercise with  $\Delta V_{DH}$  were described as follows,

$$Q_{res} = -W_{res} \quad (24)$$

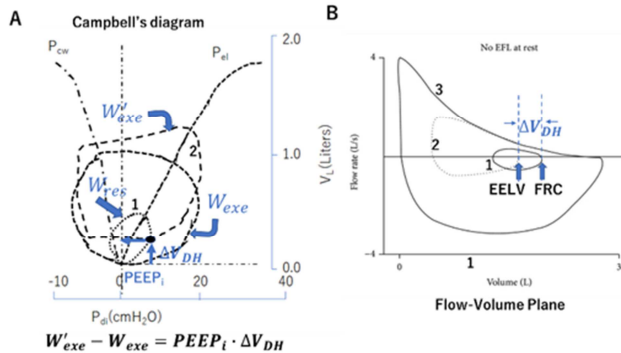
$$Q_{exc} = -W_{exc} + T\Delta S = -W_{exc} - PEEP_i \cdot \Delta V_{DH} \quad (25)$$

$$Q_{exc}/Q_{res} = \xi \quad (26)$$

where  $\xi$  is a relative ratio of energy demand for breathing

during exercise to that during resting.  
Then,

$$PEEP_t \cdot \Delta V_{DH} = \xi W_{res} - W_{exc} \quad (27)$$



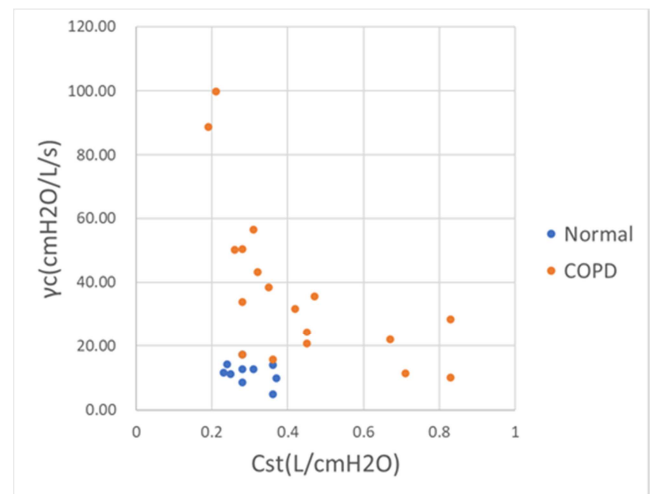
**Figure 3.** Work of breathing in Campbell's diagram and flow-volume loops during exercise. The panel A represents the Campbell' diagram of normal subject describing the pressure-volume loop for work ( $W_{res}$ ) during resting and for work ( $W_{exc}$ ) during exercise.  $W'_{exc}$  describes the pressure-volume loop for work for COPD during exercise, where  $PEEP_t$  and  $\Delta V_{DH}$  represent the airway pressure remained and the difference in lung volume from FRC at the end of expiration, respectively. The panel B represents typical flow-volume loops for COPD during resting (1) and exercise (2) under the maximal flow-volume loop (3), where the difference in volume between the end-expiratory lung volume (EELV) and the functional residual capacity (FRC) is described as  $\Delta V_{DH}$ .

## 6. Discussion

Classical physiology has explained that alveolar pressure,  $P_A$ , is the driving pressure that causes gas to flow through the airways. [1, 2] The alveolar pressure exceeds pleural pressure,  $P_{pl}$ , by an amount equal to the recoil pressure of the lungs,  $P_{st}(L)$ , all of which are expressed relative to the atmosphere since the observer is assumed in atmospheric position. This study for during exercise positioned the observer in the pulmonary parenchyma. Thus, the standard lung position was defined as a relaxed position or at the maximal entropic position in the pleural pressure  $c$  as expressed by the equation (16). That is, the standard lung position was defined as the position of zero transdiaphragmatic pressure  $P_{di}$ , or may be recognizable the pleural pressure of  $c$  as the functional residual capacity (FRC).

Based on the classical model of the equal pressure point (EPP), Mead et al. introduced maximal flow-static recoil curves (MFSR) for analyzing the upstream segment from alveoli to EPP using two components [12]: one due to frictional losses from drag imparted by the airway walls and the other to convective acceleration of the flowing gas. Their approach aims to identify the position of EPP but does not explain how flow is limited. Dawson and Elliott's [4] wave-speed theory has explained the mechanism of expiratory flow limitation (EFL) using the concept of choke state as the standard theory today. However, the wave speed formula should be viewed more as providing physical insight into the determinant of expiratory flow limitation rather than accurately predicting actual  $\dot{V}_{max}$ . The current study describes the choke state of the lung from a thermodynamic formula of the lung system using Gibbs' equilibrium as the equation (18), which explains neither the position of EPP nor the mechanism

of EFL. Thermodynamic explanation aims to characterize the state of the whole respiratory system as an equilibrium. As a result the relationship for the choke state was expressed by the equation (22) among physiological parameters including maximal expiratory flow ( $\dot{V}_{max}$ ), frictional airway loss ( $\gamma_c$ ), elastic recoil pressure ( $P_{el}$ ) measured from the atmospheric pressure, and the slope of EFL in the flow-volume plane ( $\sigma$ ). Here,  $\sigma$  appeared as representing the degree of EFL. The equation (22) explains a method to evaluate the airway resistance (the dissipating coefficient) of  $\gamma_c$  at the choke state by use of measurements  $\dot{V}_{max}$ ,  $c$  and  $\sigma$  at EELV or FRC all of which are obtainable in the clinical situation such as mechanical ventilation. After the study of Mead et al., with MFSR analysis of 17 COPD patients compared with 10 normal subjects Leaver and Pride investigated the contribution of intrinsic disease of the airways, loss of lung recoil and enhanced airway collapsibility to the airflow obstruction. [13] The author calculated the individual  $\gamma_c$  by use of estimates reported by Leaver and Pride, and plotted individual static compliance ( $C_{st}$ ) and its corresponding  $\gamma_c$  as the static compliance-airway resistance at choke diagram for 27 subjects as shown in Figure 4, which represents significant difference between normal and COPD in contribution of intrinsic disease of airways and that of loss of lung recoil, and close co-relationship between them in COPD as well.



**Figure 4.** Relationship between Static compliance at FRC and Dissipative coefficient (Airway resistance) at choke. Leaver and Pride [13] reported the forced expiratory volume in one second (FEV1), the vital capacity (VC), the static lung recoil pressure ( $P_{st}$ ) at FRC, and the maximal expiratory flow at 50% VC ( $\dot{V}_{max}$ ) for 27 subjects. Based on the equation (22), individual  $\gamma_c$  was calculated by  $P_{st}/\dot{V}_{max}/(1 - FEV1/VC)$  for 10 normals (dots in blue) and 17 COPD patients (dots in orange).

The Campbell's diagram plots chest wall and lung recoil pressure versus lung volume as shown in Figure 3, where the area of the pressure-volume loops represents the WOB [14] of steady breathing during exercise. From a thermodynamic point of view, a steady metabolic condition of the whole body demands an appropriate action of ventilation through supplying energy  $dQ$  to the respiratory system as heat, and the lung system responds to act as the WOB as ventilation  $dW$  with dissipation  $dD$  and the internal energy  $TdS$

(Figure 2). As described in the equation (27), the difference of the WOB between resting and exercise states induced the end-expiratory lung volume (EELV) greater in volume than FRC. The result in the difference in volume  $\Delta V_{DH}$  produced an intrinsic PEEP ( $PEEP_i$ ) from a change in entropy of lungs  $T\Delta S_L$ . Stepwise loading in cardiopulmonary exercise testing was expressed by the parameter  $\xi$ . Then a diagram plotting WOB in a set of successive steps would show a linear correlation indicating an intercept of line at  $PEEP_i \cdot \Delta V_{DH}$ .

Measurement of the pleural pressure for WOB is difficult and invasive. An alternative method to easily evaluate the WOB is necessary. DH is also seen in the flow-volume plane, where EELV is described as a position of flow-volume loop crossing the volume axis (Figure 3). EFL is described as trajectories of the flow-volume loop limited under the maximal forced expiratory flow-volume curve, as well. Early study of quantum mechanics has shown that area  $J$  enclosed by a flow-volume loop is related to the WOB ( $W$ ) [Joule/min] with corresponding time  $\tau$ [min] of a cycle as follows (see Appendix and Figure 5) [15],

$$\frac{dJ}{dW} = \tau \quad (28)$$

Therefore, WOB at rest and at exercise ( $W_{res}$  and  $W_{exc}$ ) were described related to corresponding areas in the flow-volume loop ( $J_{res}$  and  $J_{exc}$ ) as follows,

$$W_{res} = J_{res} \cdot \omega_{res} \quad (29)$$

$$W_{exc} = J_{exc} \cdot \omega_{exc} \quad (30)$$

where  $\omega_{rest}$  and  $\omega_{exc}$  denote frequency of breathing per minute at rest and at exercise, respectively. Therefore, from the equations (27), (29) and (30), a theoretical relationship was obtained as follows,

$$J_{exc}\omega_{exc} = \xi J_{res}\omega_{res} - PEEP_i \cdot \Delta V_{DH} \quad (31)$$

The flow-volume loop during exercise is always limited the maximal flow-volume loop. Thus, narrowed area under the expiratory flow-volume curve would limit the flow-volume loop during exercise. Through limitation of the flow-volume loop during exercise, the variables of  $J$  are limited. Thus, the equation (31) helps to understand quantitatively the relationship between the expiratory flow limitation (EFL) and the dynamic hyperinflation (DH).

## 7. Conclusion

From the classical viewpoint of physiology, it has been explained that the development of EFL is associated or promotes dynamic pulmonary hyperinflation (DH) by fixing the time required for the respiratory system to reach its relaxation volume (EELV or FRC). [16] If the expiratory time is long enough, DH can be avoided. EELV is more often dynamically raised and invariably increases with increasing ventilatory request. [17] DH promotes neuromechanical dissociation and implies a positive alveolar end-expiratory pressure ( $PEEP_i$ ) with a concomitant increase in inspiratory work, due to  $PEEP_i$  acting as an elastic threshold load and impairment of the respiratory muscles function. [9] However,

this classical explanation cannot describe quantitatively the relationship among EFL, DH, and  $PEEP_i$ .

The thermodynamic explanation of EFL in this study may provide a novel theoretical insight to understand quantitatively the relationship among elastic recoil pressure ( $P_{el}$ ), maximal expiratory flow ( $\dot{V}_{max}$ ), degree of obstructive airflow limitation ( $\sigma$ ), and dynamic hyperinflation ( $\Delta V_{DH}$ ) with internal positive end-expiratory pressure ( $PEEP_i$ ). By use of the flow-volume loop during steady breathing, the relationship among EFL, DH and  $PEEP_i$  may be understood quantitatively.

## Appendix (from Tomonaga, 1962): Proof of the Relation $dJ/dW = \tau$

A flow-volume loop is a closed loop in the flow-volume plane or phase plane of the respiratory system. The loop is a trajectory of change in state of the system defined by an energy of  $W$ . The Hamiltonian motion equations for the trajectory of loop is described as follows,

$$\frac{dV}{dt} = \frac{\partial H}{\partial F} \quad (32)$$

$$\frac{dF}{dt} = -\frac{\partial H}{\partial V} \quad (33)$$

where  $H$  is a Hamiltonian function for the system. A representing point ( $V, F$ ) has a velocity  $v$  as follows,

$$v = \sqrt{\left(\frac{dV}{dt}\right)^2 + \left(\frac{dF}{dt}\right)^2} = \sqrt{\left(\frac{\partial H}{\partial F}\right)^2 + \left(\frac{\partial H}{\partial V}\right)^2} \quad (34)$$

The point ( $V, F$ ) moves around the loop by the time  $\tau$  as follows,

$$\tau = \oint \frac{ds}{v} = \oint \frac{ds}{\sqrt{\left(\frac{\partial H}{\partial F}\right)^2 + \left(\frac{\partial H}{\partial V}\right)^2}} \quad (35)$$

where  $ds$  is a linear element of the loop.

Here, we consider another loop characterized by an energy of  $W + \delta W$ , where  $\delta W$  is very small. The distance  $\delta n$  between the trajectory of  $W$  and another of  $W + \delta W$  in the flow-volume plane is described as follows,

$$\delta W = \sqrt{\left(\frac{\partial H}{\partial F}\right)^2 + \left(\frac{\partial H}{\partial V}\right)^2} \delta n \quad (36)$$

Therefore, the relationship between  $\delta W$  and  $\delta n$  is obtained as follows,

$$\frac{\delta n}{\delta W} = \frac{1}{\sqrt{\left(\frac{\partial H}{\partial F}\right)^2 + \left(\frac{\partial H}{\partial V}\right)^2}} \quad (37)$$

Thus, the time  $\tau$  is obtained as follows,

$$\tau = \frac{1}{\delta W} \oint \delta n ds \quad (38)$$

The product of  $\delta n ds$  denotes the area shadowed in Figure 5. Thus, when  $J$  is the area of flow-volume loop,  $J(W + \delta W) - J(W)$  is expressed as follows,

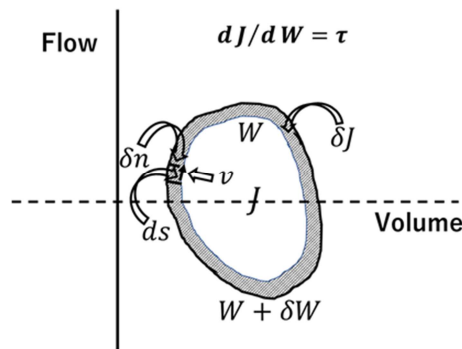
$$\oint \delta n ds = J(W + \delta W) - J(W) \quad (39)$$

Therefore,  $\tau$  is expressed by the equation as follows,

$$\tau = \frac{1}{\delta W} \{J(W + \delta W) - J(W)\} \quad (40)$$

When  $\delta W$  becomes zero, the following relationship is obtained,

$$\tau = \frac{dJ}{dW} \quad (41)$$



**Figure 5.** Relationship between flow-volume loop, work of breathing and breathing time.  $J$  is the area enclosed by the flow-volume loop.  $W$  is the energy of the system describing the state on the flow-volume loop. The cyclic time  $\tau$  of the flow-volume loop is defined by the differential of  $J$  with regard to  $W$ .

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