The physical origin of sigmoidal respiratory pressure–volume curves: Alveolar recruitment and nonlinear elasticity

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ARTICLE INFO

ABSTRACT

An important unsolved problem in medical science concerns the physical origin of the sigmoidal shape of pressure–volume curves of healthy (and some unhealthy) lungs. Conventional wisdom holds that linear response, i.e., Hooke's law, together with alveolar overdistention play a dominant role in respiration, but such assumptions cannot explain the crucial empirical sigmoidal shape of the curves. Here, we propose a theory of alveolar recruitment together with nonlinear elasticity of the alveoli. The proposed model surprisingly and correctly predicts the observed sigmoidal pressure–volume curves. We discuss the importance of this result and its implications for medical practice.

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1. Introduction

The long-studied static pressure–volume (P–V) curves of the respiratory system are largely unexplained [1]. Static P–V curves of systems such as a balloon made of an elastic material, or a soap bubble, can be easily derived from static equilibrium equations. In these equations, a recoil term compensates exactly for the expansion force caused by a pressure difference across the boundaries of the retractable structures. This derivation is not so easy in the case of the static respiratory curves mainly because the effective elastic behaviour of the respiratory system is not well known. Consequently, the approximately sigmoidal shape of the P–V curves is not well understood. These facts lead to paradoxes in established physiological interpretations [2–4].

Such difficulties are expected because the lung, which is the most important structure in the respiratory system, is extremely complex. Its rheological properties are unknown and seem to depend on phenomena occurring from the alveolar scale up to the thoracic scale. Its role in gas exchange at capillaries is related to its macroscopic behaviour as a gas pump. The system organizes itself in such a way that perfusion of the parenchyma is finely adjusted to ventilation through a fractal structure having a time-dependent connectivity and presenting scale-dependent hydrodynamical properties, just to mention aspects taken into consideration recently [5–9]. In spite of this inherent complexity, the simplicity of the sigmoidal function given in Eq. (1),

$$V - V_{\min} = \frac{V_{\max} - V_{\min}}{1 + e^{-(P - P_{i,d})/\kappa_{i,d}}},$$ (1)

whose graphic is shown in Fig. 1, suggests that a comprehensive explanation may exist for this "comprehensive equation" [3,4].

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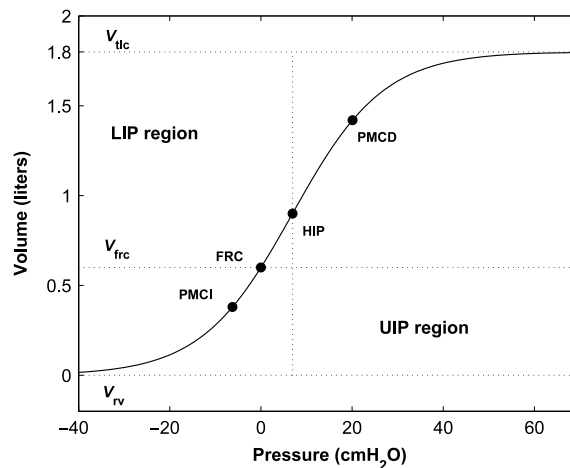E-mail address: jbn@ppgcsa.com.br (J. Brandão-Neto).

Fig. 1. A maximal respiratory P–V curve represented as a sigmoidal given in Eq. (1). The parameters in this example are $V_{\max} = V_{\text{tlc}} = 1.8$ l, $V_{\min} = V_{\text{rv}} = 0.0$ l, $\kappa_{\text{i,d}} = 10$ cmH$_2$O, and $P_{\text{i,d}} = 6.93$ cmH$_2$O. In this sigmoidal $V_{\text{frc}} = 0.6$ l.

In Eq. (1), the lung volume V is presented as a function of the pressure P at airway opening, and of four free parameters $V_{\max}$, $V_{\min}$, $P_{\text{i,d}}$, and $\kappa_{\text{i,d}}$ (see Ref. [3] for the original notation). Here, the indices "i" and "d" mean "inflation" and "deflation", respectively. Variable V denotes a volume coordinate measured in relation to some arbitrary origin. This origin is ultimately defined by the experimental technique and criteria used for volume measurement. However, if these are used consistently in a study, certain volume coordinates will have a distinctive mechanical meaning. Coordinate V_{rv} indicates the point when no further deflation is possible and the residual volume (RV) has been reached. Similarly, the impossibility of further inflation is denoted by coordinate V_{tlc}, indicating the total lung capacity (TLC). Finally, when the respiratory system is relaxed, the corresponding volume coordinate is denoted by V_{frc}, marking functional residual capacity (FRC). The volume difference $\Delta V_{\text{vc}} \equiv V_{\text{tlc}} - V_{\text{rv}}$ is called vital capacity (VC). Maximal P–V curves involve the entire ΔV_{vc}, while non-maximal involve only a partial tidal mobilization $\Delta V < \Delta V_{\text{vc}}$.

A common phenomenological approach to static respiratory P–V curves is based on the best-fits of function in Eq. (1) to experimental data from patients with acute respiratory distress syndrome (ARDS), and acute lung injury (ALI) [3,10–13], or to data from animal models [14–17]. The main features of a general respiratory P–V curve determined from such fits are its asymptotic volumes $V_{\max}$ and $V_{\min}$, as well as the parameters $P_{\text{i,d}}$, and $\kappa_{\text{i,d}}$, which have dimensions of force per unit area. A thorough investigation of the physiological meaning of these parameters will be provided in the next sections.

Certain points in respiratory P–V curves are named in connection with variations of lung compliance $C \equiv \partial V / \partial P$: these are the lower inflection point (LIP), and the upper inflection point (UIP). It has been suggested that application of a positive end expiratory pressure (PEEP) could have a protective effect on ARDS/ALI patients during artificial ventilation [18–20]. In this context, there were various attempts at using LIP as an estimate of the ideal PEEP, while UIP is used for estimating acceptable plateau pressures. The regions of LIP and UIP are situated, respectively, below and above the half-inflation point (HIP). A numerical (and more objective) determination of these regions is preferable to a visual identification.

The sigmoidal shape in Eq. (1) can reproduce with high accuracy the respiratory P–V curves, with appropriate parameters. Using Eq. (1), the point of maximum compliance increase (PMCI), and the point of maximum compliance decrease (PMCD) can be precisely defined from the condition $\partial^2 C / \partial P^2 = 0$, giving $P_{\text{mci}} = P_{\text{i,d}} - \alpha \kappa_{\text{i,d}}$, $P_{\text{mcd}} = P_{\text{i,d}} + \alpha \kappa_{\text{i,d}}$, where P_{mci} is the pressure at the PMCI, and P_{mcd} is the pressure at PMCD, with $\alpha = \ln\left[\left(\sqrt{3}+1\right)/\left(\sqrt{3}-1\right)\right] \approx 1.317$. The use of this criterion helps in making the analysis of P–V curves for protective purposes more objective [10].

The previous exposition gives evidence that the sigmoidal function is appropriate as a descriptive parameterization of static respiratory P–V curves, but what does this fact mean? An issue of great interest is the development of a theory in which this role of the sigmoidal can be naturally understood, and connected to physiology.

The purpose of our paper is to address this problem. Contrary to other approaches to the modeling of static respiratory P–V curves [3,21–25], here we formulate a coherent and simple framework in which sigmoidal law is considered exact. If the theory is correct, recruitment may be an important mechanism that contributes towards the shape of static pressure–volume curves. Other effects, like the sudden increase in compliance when opening lungs affected by ARDS, should be explained as corrections to Eq. (2), to Eq. (3), or to Eq. (10). We stress that the methods that we use, based explicitly on these equations, open a novel perspective for theoretical approaches to the subject. In fact, we may consider the entire class of theories based on a static equilibrium equation, a recruitment mechanism, and a relation between volume variation and recruitment as a generalization of our theory. Since this paper serves also to introduce this novel perspective we prefer to expose our ideas in the particular case of the sigmoidal function, which will have a concrete meaning to most physiologists and medical doctors working in the important area of critical care of ARDS/ALI patients and artificial ventilation in general. Our paper is organized