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NON-DIMENSIONAL PHYSIOLOGICAL INDICES IN MEDICAL DIAGNOSTICS ANDINTERVENTIONAL GUIDELINES: LUNG VENTILATORY INDEX FOR WEANING MECHANICALLY VENTILATED COPD PATIENTS

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ABSTRACT

Objectives: A Non-Dimensional Physiological Index (NDPI) is a dimensionless parameter that can help characterize an abnormal state associated with a particular physiological system. NDPIs can be used to effectively compare data across different studies The distribution of the values of such NDPIs in an extensive patient population can enable us to designate normal and disordered ranges of NDPI, with a critical value of NDPI separating these two ranges.This paper proposesaLung Ventilatory Index (LVI) and a non-dimensional index (LVI_2) to provide the guidelines for successfully weaning mechanically ventilated Chronic Obstructive Pulmonary Disease (COPD) patients. ***Methodology:*** First, we have developed the Lung Ventilation Model (LVM) of the differential equation of lung volume response to driving pressureapplied by the ventilator to a COPD patient, involving the parameters of lung compliance (C_a) and airway resistance-to-airflow (R_a). The LVM is employed to determine the lung volume response to the applied ventilator pressure for intubated COPD patients to obtain the values of $C_a$and R_a. ***Clinical Studies and Results:*** We used patient datafrom a clinical study to determine the values for LVI. We have shown thatLVI can distinguish between an intubated COPD patient and a weaned patient. We then developed a non-dimensional ventilatory index LVI_2 that presents distinctly different values for an intubated COPD patient and a successfully weaned patient. ***Conclusions:*** In this paper, we have proposed anovel NDPI to differentiate intubated COPD patients from weaned patients. This non-dimensional ventilatory index LVI_2can enable precision diagnosis of a successfully weaned COPD patient. In future work, we can test the efficacy of this LVI_2index in assessing the need of COPD therapy in an intensive care unit for a larger patient population.

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I. INTRODUCTION

A Nondimensional Physiological Number or Index (NDPI) is a mathematical parameter used in various fields of physiology and engineering to characterize and analyze physiological processes, often in a non-dimensional or normalized form. The concept of NDPI is relatively new and has been pioneered by us (Ghista, 2004; Ghista *et al.,* 2005; Ghista, 2009; Ghista, 2011a; Ghista, 2011b). This idea has been adopted from engineering, wherein nondimensional numbers formulated using several parameters are employed to characterize disturbance regimes. In physiology, these indices are designed to provide insights into how certain physiological factors or variables relate to one another without being influenced by the units of measurement.

In physiological investigations, nondimensional indices or numbers can provide a generalized approach for integrating several parameters (representing isolated but related events) into one NDPI. NDPIs can help to characterize an abnormal state associated with a particular physiological system. By making these parameters dimensionless, comparing data across different studies or populations becomes easier. The evaluation of the distribution of the values of such NDPIs in an extensive patient population can enable us to designate normal and disordered ranges of NDPI, with a critical value of NDPI separating these two ranges. In this way, NDPIs can help us formulate physiologicalhealth indices to facilitate the assessment of and alteration in the states of physiological systems. We have been developing NDPIs for various physiological subsystems, ranging from lung ventilation to cardiaccontraction (Ghista, 2004; Ghista, *et al.,* 2005; Ghista, 2009; Ghista, 2011a; Ghista, 2011b).

Our novel contributions in this research direction are (i) precise designation of normal and disordered states of various physiological systems and (ii) evaluation of the performance characteristics of hospital units anddetermination of budget and resource allocations among hospital systems for their cost-effective operation (Ghista, 2004). This paper presents an NDPI called the Lung Ventilatory Index for successfully weaning mechanically ventilated COPD patients. Chronic Obstructive Pulmonary Disease (COPD) is a debilitating and progressive respiratory condition affecting millions worldwide.

This complex lung disorder encompasses a range of conditions characterized by persistent airflow limitation, making breathing difficult. COPD is typically caused by long-term exposure to harmful substances, such as tobacco smoke, air pollution, or occupational dust and chemicals. It leads to symptoms like chronic cough, excessive mucus production, shortness of breath, and reduced exercise tolerance, significantly impacting a person's quality of life. Early diagnosis and management are crucial in managing COPD and improving patients' respiratory health.

II. Ventilatory Functional Assessment of mechanically ventilated COPD patients modelling (in an intensive care unit) using a lung ventilatory index

Purpose and Scope: We have developed a Lung Ventilatory Index (LVI) based on a lung ventilation model to assess lung function in COPD patients who require mechanical ventilation because of acute respiratory failure. We have evaluated the efficacy of LVI in identifying improving or deteriorating lung conditions in mechanically ventilated COPD patients to see if it could be used as a potential indicator for ventilator discontinuation.

Lung Ventilation Model (LVM) that shows lung volume response to pressure applied by the ventilator: The lung ventilation model is illustrated and described in Figure 1. Lung mechanics involves inhalation and exhalation pressure and volume changes. Three pressures are involved in the ventilatory function, namely atmospheric pressure or pressure at the mouth (*Pm*), alveolar pressure (*Pa*), and pleural pressure (*Pp*). The pressure gradient between the atmospheric and alveolar pressures causes respiration to occur. During inspiration, *Pa* < *Pm*, and air enters the lungs. During expiration, *Pa* >*Pm*, and air is expelled from the lungs passively. The pressure differential between *Pm* and *Pp* provides the driving pressures (*PL*) for gas flow into the lung. Thus, assessing respiratory mechanics involves measuring flows, volumes, pressure gradients, and their dynamic interrelationships. The Lung VentilationModel (LVM) enables the computation of lung compliance (*C*) and airway resistance-to-airflow (*R*), which are the parameters of the governing differential equation. Lung ventilatory dysfunction due to various diseases is characterized by the altered values of *R* and *C* or by using an index involving a combination of *R* and *C*. Hence, the LVM can be employed to detect and characterize lung disease states. Based on the LVM shown in Figure 1, we can formulate the following differential equation, expressing lung volume response to pressure across the lung.

$$Ra\dot{V} + \frac{V}{C_a} = P_L(t) - P_e = P_N(t) = B\sin\omega t \qquad \text{..................(1)}$$

wherein: (i) P_L (pressure across the lung) $=P_m-P_p$; (ii) the parameters of the lung model governing equation are lung compliance (C_a) and airflow-resistance (R_a); (iii) V (lung volume) = $V(t) - V_e$ (where Ve is the end-expiratory lung volume); (iv) P_e is the end-expiratory pressure; (iv) B is the amplitude of the net pressure waveform applied by the ventilator to the intubated COPD patient; (v) the driving pressure $P_N = P_L - P_e = B\sin(\omega t)$.

The volume response to P_N (the solution to Eq.(1)) is given by:

$$V(t) = \frac{BC_a\{\sin(\omega t) - \omega k_a\cos(\omega t)\}}{1+\omega^2 {k_a}^2} + \frac{BC_a\omega k_a e^{-t/k_a}}{1+\omega^2 {k_a}^2} \qquad \text{..............(2)}$$

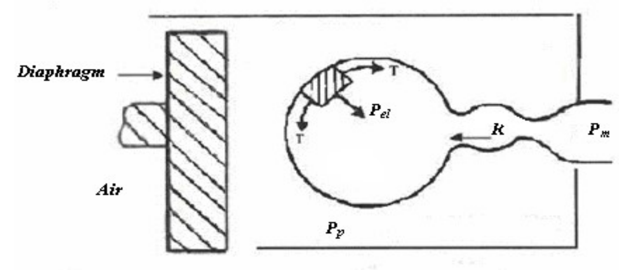

Figure1. Lung Ventilatory model. In the figure, $P_m$is the mouth pressure, and P_p is thepleural pressure; P_{el} (lung elastic recoil pressure) = P_a- P_p= 2 T/r (radius of alveolar chamber) = V/C+ P_e (at end of expiration); R (resistance to air flow rate) = (P_m- P_a)/(dV/dt); P_L (total pressure across the lung) = P_m–P_p; P_L = (P_m - P_a) + (P_a- P_p) = R(dV/dt) + V/C + P_e; P_N (driving pressure) = P_L–P_e= B sin(ωt). Hence, we get: $R(dV/dt) + V/C = P_L - P_e = P_N = B\sin(\omega t)$. Adopted from Ghista *et al.* (2006)

where in: (i) k_a ($=R_aC_a$) is the time constant, (ii) the model parameters are C_a and k_a (i.e.,C_a and R_a), (iii) ω is the frequency of the oscillating pressure profile applied by the ventilator.

In Eq. (2), the exponential term is much smaller than the trigonometric term beyond t = π /2ω. Hence, by neglecting the exponential term, we obtain:

$$V(t) = \frac{BC_a\{\sin(\omega t) - \omega k_a\cos(\omega t)\}}{1+\omega^2 {k_a}^2} \qquad \text{..................(3)}$$

Figure 2 illustrates a typical lung ventilator model data of lung volume V, air flow rate $\overset{o}{V}$,and the driving pressure P_N. For evaluating the parameter k_a, we determine the time t_m at which $V(t)$ is maximum and equal to the tidal volume (TV). Hence, by putting dV/dt = 0 in Eq. (3), we obtain:

$$k_a = \frac{-1}{\omega\,\mathrm{ta}\ (\omega t_m)}, \quad or, \quad tan^{-1}(1/\omega k_a) = \theta = \pi - \omega t_m \ ;\ \tan\theta = 1/\omega k_a\ ,\ k_a = \frac{1}{\omega\, tan\theta} \qquad \text{.................(4)}$$

so that:

$$\sin(\theta) = \frac{1}{\sqrt{1+\omega^2/{k_a}^2}}\ ,\ \cos(\theta) = \frac{\omega k_a}{\sqrt{1+\omega^2/{k_a}^2}},\ \tan\theta = 1/\omega k_a \ \text{........(5)}$$

Hence, from Eqs.(3), (4), and (5), we get:

$$V(t = t_m) = TV = \frac{BC_a}{\sqrt{1+\omega^2/{k_a}^2}} \qquad \text{..................(6)}$$

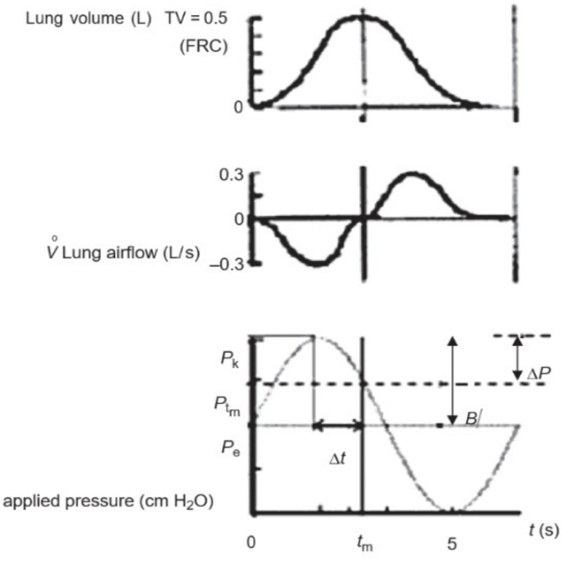

Figure 2. Typical lung ventilatory model data showing airflow ($\overset{o}{V}$), lung volume (V), and net pressure (P_N). In the P_N waveform, the Peak pressure is P_k (which can also be P_m), the Pause pressure (P_{tm}) occurs at t_m, at which the volume is maximum (TV = tidal volume). The figure shows that Δt is the phase difference between the time of maximum volume and peak pressure (P_k). It also the time lag between the peak and pause pressures. B is the amplitude of the net pressure waveform P_N applied by the ventilator. This P_N oscillates about P_e with amplitude of B. The difference between peak pressure P_k and pause pressure P_{tm} is Δp. For a typical COPD patient, P_k is of the order of 10 cm H_2O. Adopted from Ghista et al., (2006).

Developing the Formulae for Model parameters Lung-Compliance (Ca) and Airflow Resistance (Ra)

From Eq. (6), we get: $C_a = \frac{TV\sqrt{1+\omega^2 k_a^2}}{B} = \frac{TV}{B\sin(\theta)}$ ……………(7)

Based on Figure 2, we can note that:

$P_k - P_{tm} = \Delta p = B - B\ sin\ \theta = B\,(1 - sin\,\theta)$; hence $B = \Delta p\ /\ (1 - sin\,\theta)$ …………………(8)

Hence, from Eqs. (7) and (8), we get the expression for the parameter C_a:

$$C_a = \frac{TV\sqrt{1+\omega^2 k_a^2}}{B} = \frac{TV}{B\sin(\theta)} = \frac{TV(1-\sin\ \ )}{\Delta P\sin(\theta)} \quad \text{………………..(9)}$$

Then, based on Figure 2 and from Eqs.(4) and (9), we obtain the expression for the parameter R_a:

$$R_a = K_a/C_a = \frac{\Delta P\sin\theta(1/\omega\tan\theta)}{TV(1-\sin\ \ )} = \frac{\Delta P\ co}{TV\omega(1-\sin\ \ )} \quad \text{………………(10)}$$

Formulating the Lung Ventilatory Index (LVI) incorporating Ra and Ca

Now that we have determined the expressions for parameters *Ra* and *Ca*, the next step is to develop an integrated Lung Ventilatory Index (LVI) incorporating these parameters to distinguish between the intubated COPD patient and the patient successfully discontinued of mechanical ventilation. For a COPD patient, R_a will be high, C_a will be low, respiratory frequency (*RF*) will be high, peak pressure (P_k) will be high, and tidal volume (*TV*) will be low. Let us assume that we want the LVI to have a high value for a COPD patient and further increasing LVI for deteriorating lung status and decreasing LVI for improving lung status in a mechanically ventilated COPD patient in acute respiratory failure, then the LVI can be formulated as

$$LVI = \frac{R_a(RF)P_k}{C_a(TV)} \quad \text{…………………(11)}$$

III. Clinical Studies - Evaluating the Lung-Ventilatory model parameters and Index (LVI)

In our clinical studies, we recruited 13 mechanically ventilated patients with COPD (aged between 54 and 83 years) in acute respiratory failure (Ghista et al., 2006). All patients met the diagnostic criterion of COPD. The intubated patients were from one of two categories: (i) patients who were successfully discontinued (6 patients) and (ii) patients who failed discontinuation (7 patients). The first attempt at weaning these patients off the ventilator happened within a short duration not exceeding 88 hrs. All the patients were on Synchronized Intermittent Mandatory Ventilation (SIMV) mode with mandatory ventilation at initial intubation. Based on the physician's judgment, the modes were changed for the eventual discontinuation of mechanical ventilation. The period for recording observations was 1 hr. For all purposes in this study, a successful ventilator discontinuation is defined as the toleration to extubation for 24 hrs or longer. A failed ventilator discontinuation is defined as either a distress when ventilator support is withdrawn or the need for reintubation. Using Eqs. (9) and (10), we determined that the computed ranges of values of the parameters for our recruited patients, as:

R_a= 9 to 43(cmH_2O)sL^{-1}, C_a= 0.02 to 0.08 (L/cmH_2O)$^{-1}$ (12)

Let us now obtain the order-of-magnitude values of *LVI* for two typical mechanically ventilated COPD patients in acute respiratory failure (by using representative computed values of the parameters R_a, C_a, RF, TV, and P_k), to verify that the formula for *LVI* (Eq. 11) can enable distinct separation in mechanically ventilated COPD patientsinacute respiratory.

(a) For a representative incubated COPD patient, we have:

R_a =15 (cmH_2O) s/L , C_a =0.035 L/cmH_2O, *RF* = 0.33s^{-1}, TV = 0.5 L, and P_k = 20 cm H_2O. Hence,

$$LVI\ (intubated\ COPD) = \frac{[15\ (cmH_2O)s/L][0.33\ s^{-1}][20\ cmH_2O]}{[0.035\ L/cmH_2O][0.5\ L]} = 5654\ (cm\ H_20/L)^3 \quad \text{…………………..(13)}$$

(b) For a representative COPD patient with improving lung status at successful discontinuation of mechanical ventilation (or outpatient COPD), we have:

R_a =10 (cmH_2O) s/L, C_a = 0.050 L/cmH_2O, *RF* = 0.33s^{-1}, TV=0.35L, and P_k= 12 cmH_2O. Hence,

$$LVI\ (at\ sucessful\ discontinuation) = \frac{[10\ (cmH_2O)s/L][0.33\ s^{-1}][12\ cmH_2O]}{[0.05\ L/cmH_2O][0.35\ L]} = 2263\ (cm\ H_20/L)^3 \quad \text{…….(14)}$$

It is noted that at successful discontinuation, the resistance R_a decreases while compliance C_a increases. We can now employ this LVI index to distinctly indicate the successful discontinuation of mechanical ventilation.

For LVI to reflect lung status improvement in a mechanically ventilated COPD patient in acute respiratory failure, the LVI for successful discontinuation must decrease from its value at the time of admission to a range of value of LVI for an outpatient COPD at the time of discontinuation. Hence, the Lung Ventilatory Index Variation (LVIV) can be represented as

$$LVIV = LVI\ (t) = LVI_0\, e^{-mt} \quad \text{………………(15)}$$

where LVI_0 represents the value of LVI at the time of admission of the patient to the respiratory care unit; the Coefficient *m* represents the rate of improvement (or deterioration) of the patient's lung status; m = 0 implies no change in lung condition. The Coefficient *m* (the rate of decrease of LVI or improvement in lung status) will be positive for deteriorating lung condition and negative for improving lung condition.

We can also formulate a Lung Improvement Index (LIMI or DLVI%), as a measure for overall lung status improvement at the time of discontinuation, as

$$LIMI = \Delta LVI = \frac{\text{LVI (at entry or intubation)-LVI (at discharge or extubation)}}{\text{LVI (at entry)}} \times 100 \quad (16)$$

IV. Development of a Nondimensional Lung Ventilatory Index LVI_2

In this section, we are presenting a nondimensional lung ventilatory index, called the LVI_2, given by Eq. 17. This index also has high value for a COPD patient, and it increases for deteriorating lung status and decreases for improving lung status in a mechanically ventilated COPD patient in acute respiratory failure. The nondimensional lung ventilatory index is given by:

$$LVI_2 = \left[\frac{R_a(TV)^2(RF)}{C_a(P_m)^2}\right] \times (60)^2 \quad (17)$$

where *RF* is the respiratory-rate frequency and P_m is the mouth pressure.

Let us obtain the order-of-magnitude values of this LVI_2 index for a mechanically ventilated COPD patient in acute respiratory failure (by using representative computed values of the parameters R_a, C_a, RF, TV, and P_m), in order to verify that the formula for LVI_2 (given by Eq.17) can enable distinct separation of COPD patients in acute respiratory failure from patients ready to be weaned off the respirator. For an intubated COPD patient, we have (based on the values of the model parameters mentioned above):

Table 1. Range of *LVI* values at Intubation and Outcome, for Successful and Failed Discontinuation (Ghista et al., 2006).

Outcome	Number of patients	Age Range (Years)	Sex(M/F)	Time of intubation (Hrs)	*LVI* at intubation $(cmH_2O/L)^3$	*LVI* atoutcome $(cmH_2O)/L^3$
Successful Discontinuation	6	54-74	6/0	11 -55	3959to 13568	1194 to4589
Failed Discontinuation	7	64-83	5/2	29 -88	3350to 21152	7144to 15658

$$LVI_2\ (\text{Intubated COPD}) = \frac{[15(\text{cmH}_2\text{O})\text{sL}^{-1}][0.5\ \text{L}]^2[0.33\ \text{s}^{-1}]}{[0.035\ \text{L}(\text{cmH}_2\text{O})^{-1}][20\ \text{cmH}_2\text{O}]^2} \times (60)^2 = 318 \quad (18)$$

where in R_a = 15 $(cmH_2O)sL^{-1}$, C_a = 0.035 $L(cmH_2O)^{-1}$, RF = 0.33 s^{-1}, TV = 0.5 L, and P_m (= P_k) = 20 cmH_2O.

Now, let us obtain the order-of-magnitude of LVI_2 (by using representative computed values of R_a, C_a, RF, TV, and P_m) for a COPD patient with improving lung status just before successful discontinuation. For a successfully weaned COPD patient (examined in an outpatient clinic), we have (based on the above-mentioned values of the model parameters for equation 14):

This LIMI can be employed to justify the discontinuation of mechanical ventilation.

Clinical Evaluation of the Lung Ventilatory Index (LVI), for successful and failed extubation:

For this purpose, we have categorized the intubated patients into two categories, (i) patients who were successfully discontinued and (ii) patients who failed discontinuation. Table 1 provides the range of LVI values for these two categories of patients. For all successful discontinuations, the LVI value at outcome is considerably less than for the unsuccessful-weaning category, and close to the value for an outpatient COPD patient. Based on this Table, LVI indicates a clear separation between successful and failed weaning. Based on these findings, we now intend to obtain distinctly separate distributions and ranges of LVI at outcomes for successful and failed discontinuation of mechanicallyventilated COPD patients in acute respiratory failure.

$$LVI_2(Outpatient\ COPD) = \frac{[10(cm\ \ _2O)sL^{-1}][0.35L]^2[0.33\ \ ^{-1}]}{[0.05\ L(cmH_2O)^{-1}][12c\ \ \ _2O]^2} \times (60)^2 = 202 \quad (19)$$

wherein R_a = 10 $(cmH_2O)sL^{-1}$, C_a = 0.05 $L(cmH_2O)^{-1}$,
RF = 0.33 s^{-1}, TV = 0.35 L and P_m (= P_k) = 12 cmH_2O.

For LVI_2 to reflect lung status improvement in a mechanically ventilated COPD patient in acute respiratory failure, there is a pronounced decrease in the value of LVI_2. This shows that the non-dimensional index LVI_2 given by Eq. (17) can enable effective decision-making to wean off a COPD patient from the mechanical ventilator.

V. DISCUSSION

In this paper, we have developed a Lung Ventilatory Index (LVI) based on the lung ventilation model to assess lung function in COPD patients requiring mechanical ventilation because of acute respiratory failure. We then evaluated LVI's efficacy in identifying improving or deteriorating lung conditions in mechanically ventilated COPD patients to see if it could be used as a potential indicator for ventilator discontinuation. We first developed the Lung Ventilation Model (LVM) of Differential Equation Eq. (1)of lung volume response to driving pressure $P_N = B\ sin(\omega t)$ applied by the ventilator to COPD patients. The LVM enables the computation of lung compliance (C) and airway resistance-to-airflow (R), which are the parameters of the model's governing differential equation. Lung ventilatory dysfunction due to various diseases is characterized by the altered values of R and C, or in terms of an index involving a combination of R and C. We then derived the solution to the LVM, given by Eq. (3) in terms of(i) applied pressure amplitude B, (ii) model parameters C_a and R_a,(iii) time constant k_a (=R_aC_a), and (iv) ω, the frequency of the oscillating pressure profile applied by the ventilator.

Figure 2 illustrates a typical LVM data of lung volume *V, dV/dt,* and P_N. For evaluating the parameter k_a, we determine the time t_m at which *V(t)* is maximum and equal to the tidal volume (TV). Hence, by putting dV/dt=0 in Eq. (3), we obtained V ($t = t_m$) terms of *B, C*, k_a, and ω. We thereby derived the expressions for R_a and C_a. For our patients, the computed ranges of values of the parameters are: R_a= 9 to 43 (cmH_2O) s/L, C_a= 0.020 to 0.080 (L/cmH_2O).

Our intent is to distinguish between the intubated COPD patient and the patient who successfully discontinued mechanical ventilation. For that purpose, in Section II we have developed a Lung Ventilatory Index (LVI), given by Eq. (11). For a COPD patient, R_a will be high, C_a will be low, respiratory frequency (RF) will be high, the peak pressure (P_k) will be high, and tidal volume (TV) will be low. So, this is reflected by the formulation of LVI given by Eq. (11). We then obtained the values of LVI for two typical mechanically ventilated COPD patients in acute respiratory failure (by using representative computed values of the parameters R_a, C_a, RF, TV, and P_k). For a representative incubated COPD patient, we got $\text{LVI (Intubated Patent)} = 5654\ (\text{cm H}_2 0/\text{L})^3$, as given by Eq. (13). Then, for a successfully discharged patient, we got the value of $\text{LVI (at successful discontinuation)} = 2263\ (\text{cm H}_2 0/\text{L})^3$,
as given by Eq (14) This shows that we can apply LVI to distinctly indicate the successful discontinuation of mechanical ventilation of a COPD patient.

We then developed a novel nondimensional ventilatory index LVI_2 given by Eq. (17). For an intubated COPD patient, we get LVI_2= 318. For the successfully treated patient, we get LVI_2= 202. This shows that our non-dimensional index LVI_2 can enable effective decision-making to wean off a COPD patient from the mechanical ventilator.

Limitations: Objectively speaking, the non-dimensional LVI_2 has an excellent value for indicating the successful discontinuation of mechanical ventilation. Regarding limitations, we have to study and analyze many subjects in an extensive study to establish the ranges of LVI_2forintubated COPD patients and successfully weaned patients. In the future, an app will also be developed to enable precision diagnostics.

Conclusion

In this paper, we have developed a Lung Ventilatory Index (LVI) based on a lung ventilation model to assess lung function in COPD patients requiring mechanical ventilation because of acute respiratory failure. Then we have also developed a novel non-dimensional index LVI_2 for the same purpose, and have shown how this index can be collectively employed to decide on extubating a patient. Such a nondimensional index can enable precision medical diagnostics, and can help to develop interventional guidelines for assessing COPD therapy in intensive care unit settings.

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