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Effects of Body Position and Esophageal Balloon Placement on Lung Pressure-Volume Curves in Young Adults: A Double Exponential Model

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Abstract

Background: Changes in body position are associated with changes in functional residual capacity, elastic recoil pressure, and total lung capacity (TLC). Exponential analysis over the entire range of the lung inflation-expiratory pressure-volume (P-V) curve has not been studied using the esophageal balloon technique. **Objective:** A twin exponential fitting model was applied to the expiratory and inspiratory limbs of lung P-V data in healthy young adults in seated and supine postures using a modified exponential analysis. **Methods:** P-V curves were recorded between residual volume and TLC using the esophageal balloon technique in seated and supine positions in 10 healthy, non-smoking young adults. Data points were obtained in both postures with the balloon placed at 5, 10, and 15 cm above the cardia. A modified "double exponential" model was used to fit the data and transform it into a function, enabling its use as a linear regression technique. **Results:** Key findings included: a) curvilinearity of the P-V curve was greater during deflation than during inflation at volumes ≥ 51% TLC in both postures, particularly with esophageal pressure recorded at the 5 cm and 15 cm esophageal levels, b) the position of the inflation curve was shifted to the right at volumes ≥ 51% TLC in both postures regardless of the esophageal level, but not at volumes < 51% TLC, and c) at all esophageal levels and body positions, correspondence of recorded data points with respect to theoretically computed P-V points based on the twin exponential fit was excellent, with mean r^2 ranging between 96.9% and 99.7%. **Conclusions:** Using a modified inflation-deflation double exponential model permits accurate extrapolation of the P-V curve over a data range normalized according to TLC. Physiologically meaningful variables derived from the curve-fitting model better characterize the curve over its full range.

Keywords

Esophageal Balloon Technique, Exponential Analysis, Half-Inflation Pressure, Postural Change, Pressure-Volume Curve, Static Lung Compliance

1. Introduction

Body position and level of the esophageal balloon used to estimate pleural pressure influence lung pressure-volume (P-V) characteristics [1]-[3]. In general, with a supine posture, the P-V curve shifts to the right but remains parallel to the curve in an upright position, a finding attributed to the compression of the esophagus by mediastinal structures [3]. Because of the curvilinearity and static or quasi-static nature of the P-V curve, it is difficult to define pulmonary elasticity (inverse of compliance) over the entire range of total lung capacity (TLC). Exponential analysis of the P-V curve is also less influenced by patient age, effort, and lung size [4]-[6].

Defining P-V relationships below 50% total lung capacity (TLC) by exponential analysis has been problematic because of the effects of closing volume and alveolar dec-recruitment in the lower portion of the curves, such as in ARDS and chronic obstructive pulmonary disease [7]. Applying the exponential analysis to the lower and upper portions of the curves has been described in healthy individuals [8], smokers, and persons with lung disease [9]-[18]. In addition, most studies have applied exponential analysis only to the deflation portion of the P-V curve. Specifically, there is a research gap in not exploring the entire inflation-expiration P-V curve in different postures, particularly with esophageal pressure measurements.

The main objective of this study was to apply exponential analysis to inspiratory and expiratory P-V curves generated in young, healthy individuals in seated and supine postures to better define compliance over the entire volume range, using modifications of the methods of Pengelly [6] and Kraemer *et al.* [19] We constructed separate exponential curves for the upper and lower portions of the curve to better fit the raw data. In addition, to analyze alterations in regional P-V characteristics occurring with postural change, measurements were made with the esophageal balloon placed at 3 different levels in the esophagus. Previous studies have shown maximum compliance values for a given P-V curve at the lowest esophageal levels related to regional alveolar expansion with respect to total lung volume [2] [3].

2. Methods and Materials

Ten nonsmoking healthy subjects [mean (SD) age 29.4 (4.1) years] were recruited from hospital allied health personnel. Their anthropometric and physiologic data are shown in **Table 1**. None had ever smoked or had a history of a respiratory disorder. Following approval from the institutional review committee of Rancho Los Amigos National Rehabilitation Center, subjects signed an informed consent to participate in the experiment. Forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1) were measured in sitting and supine postures with a 9 L Collins spirometer (Boston, MA). Total lung capacity (TLC) and functional residual capacity (FRC) were measured by helium-dilution technique (Pulmo-Lab, model 5300, CardioPulmonary Instruments, Houston, TX). Residual volume (RV) was derived by subtracting VC from TLC. In healthy individuals, RV and TLC do not change by more than 5% and 7%, respectively, upon assuming the supine position [20] and were, for practical purposes, assumed to be the same in both postures. Esophageal pressure (Pes) was measured with a polyethylene catheter-latex balloon system. The balloon was 5 cm in length, 3.5 cm in circumference when inflated, and 0.06 mm in thickness, and was sealed over a polyethylene catheter (i.d. 1.4 mm, length 94 cm) connected to a Validyne MP 45-1 pressure transducer (Northridge, CA). The volume-pressure curve of the balloon-catheter system was flat within a range of 0.2 mL and 5 mL volumes. Mouth pressure (Pm) was measured with a similar catheter connected at one end to a side port on the mouthpiece and at the other end to an identical pressure transducer. The Pes and Pm systems were tested with a sine-wave pressure generator and were found to exhibit a flat frequency response of up to 22 cycles/sec with no phase lag between them. Volume changes were measured by integration (Gould Brush integrator, Cleveland, OH) of a flow signal obtained with a heated No. 3 Fleisch pneumotachograph. All signals were amplified and recorded on a 4-channel chart recorder (Gould Brush 2400). The volume signal was also displayed in real-time on a 510 Tektronix oscilloscope. Transpulmonary pressure (Ptp) was obtained by subtracting Pes from Pm.

Table 1. Anthropometric and physiologic data in 10 subjects.

Age, yr	Sex, M/F	Ht, cm	Wt, kg	FVC, L, sitting/supine		TLC, L sitting/supine		FRC, L sitting/supine		RV, L sitting/supine	
29.5 ± 4.1	8/2	173 ± 12	75 ± 14	5.2 ± 1.3	5.1 ± 1.3	6.9 ± 1.9	6.7 ± 1.9	3.6 ± 1.2	2.5 ± 0.9	1.6 ± 0.7	1.6 ± 0.8

Values represent mean ± SD. FVC: Forced Vital Capacity; TLC: Total Lung Capacity; FRC: Functional Residual Capacity; RV: Residual Volume.

Procedure

Following topical anesthesia of the nasal mucosa with lidocaine, the balloon was passed transnasally into the stomach and then gradually withdrawn until a negative deflection of Pes was recorded during inflation. The balloon was then withdrawn to 5, 10, or 15 cm above the gastroesophageal junction, where at each level, a series of pressure and volume readings were recorded. The level of the balloon within the esophagus was chosen at random. The volume of air in the balloon was 0.5 mL and was checked frequently during the course of the experiment.

The study was performed in seated and supine positions. In each posture and each esophageal level, the subject generated the P-V curves by watching the tracing on the oscilloscope. To monitor the tracings in supine position, the subject watched the oscilloscopic tracing reflected from a mirror mounted above his head. The occlusion test was used to validate the esophageal balloon technique as a means of measuring pleural pressure [21]. After 5 minutes of quiet breathing in either posture, the subject performed 3 inspiratory vital capacity (VC) maneuvers (to maintain consistent volume history) while watching the oscilloscope. Upon reaching the peak of the third VC maneuver, the lung was deflated to residual volume (RV) in a stepwise manner, keeping the glottis open at all times. After reaching RV, the direction was reversed, with the lungs inflating to TLC in a similar stepwise manner. Subjects held their breath for 1 - 2 seconds at each of 10 - 15 steps in each limb of the P-V curve. We found that, on average, this number of steps was within the tolerance range of breath-holding for our subjects. Measurements of Pes were not made during periods of esophageal contractions.

3. Data Analysis

Pressure-volume curves during inflation and inflation were constructed from data points obtained in the seated and supine position with the balloon placed at one of three esophageal levels (5, 10, and 15 cm above the cardia). Volume was expressed as %VC, and lung elastic recoil, Pst(L), as the negative of Pes. To avoid bias by a disproportionate number of values in either the upper or lower part of the P-V range, we surveyed all of the curves to determine where the best "cut off" point would be, above and below which an exponential function could be fitted. In all cases, this point, which also corresponded to the point of inflection, was located between 50% and 60% TLC, depending on the presence and number of data points in this region. We attempted to use equal numbers of points in each portion of the curve. In 4 subjects, data point fitting was difficult in the high-volume range because of the wide spread of Pst(L) points over a small volume range, particularly in the supine position. In 2 of these subjects, there was also difficulty in fitting data points in the lower limb of the curve.

The "double exponential" model used to fit the data is derived from the form described by Pengelly [22], modified by Colebatch *et al.* [4], and is expressed by:

$$V = V_o\,[1 + K_o \exp(K_1 P)] \text{ for } V < Vd \quad (1)$$

$$V = V_o\,[1 - K_o \exp(-K_1 P)] \text{ for } V > Vd \quad (2)$$

where V is the lung volume in liters, P is Ptp(L) in cm H_2O, Vd is the volume at the point of inflection, and V_o, K_o and K_1 are constants representing theoretical minimum or maximum volume, the ratio of the volume at the half inflation pressure, h, to the volume difference from V_o to V_o at zero transpulmonary pressure, and the elastic property of the lung (*i.e.*, convexity of the curve), respectively. The half-inflation or half-deflation pressure, h, was determined as a means of defining the position of the inflation or deflation curves with respect to the pressure axis and was defined as the pressure change required to inflate or deflate the lung from any given volume halfway to its maximum or minimum volume, respectively [16]. Note in Equation (1) that the signs are chosen to make the constants positive, and any constant of the same notation in one of the equations can have a value different from its corresponding value in the other equation. Equation (1) can be transformed logarithmically to:

$$\ln (V/V_o - 1) = K_1P + \ln K_o \text{ for } V < Vd \quad (3)$$

$$\ln (1 - V/V_o) = -K_1P + \ln K_o \text{ for } V > Vd \quad (4)$$

that is, V is transformed to a new function [$\ln (V/V_o - 1)$ or $\ln (1 - V/V_o)$] so that a linear regression technique can be applied to estimate the constants. However, there is an unknown parameter, V_o, on the left side of Equations (3)-(4), which necessitated repeating the computation by trial and error until the best fit was found [4] [6] [11] [23]. Vd was chosen to be the volume at the data point closest to, but not higher or lower than 50% TLC (depending on the lower or upper part of the curves, respectively), known to give the best fitting results [6]. Data points only in the range lower than Vd were used in the estimation for Equations (3) and vice versa.

The program was created in FORTRAN IX using a mini-computer (PDP-11/34, Digital Equipment Corporation). RV and TLC were used as the initial V_o in Equations (3)-(4), respectively. For each V_o, the other constants, K_1 and K_o, and the squared correlation coefficient, r^2, were calculated. V_o was then increased or decreased by an initially selected increment in such a way that r^2 increased. When r^2 reached a maximum value, the increment in V_o was halved, and the computation was repeated until the increase in r^2 in two subsequent computations reached 0.0001, at which point the process was stopped. Estimated $\ln K_o$ was converted back to K_o by taking its exponent, while V_o was divided by TLC/100 to obtain volume in terms of %TLC in Equations (3)-(4). We found this method of curve-fitting to be more practical than previously described techniques [9] [10] [13] because of the simplicity of its equations and the short computing time of the present method.

As long as the estimated exponentials can be assumed to represent the true P-V characteristics of the lung, static lung compliance (Cst(L)) at any volume level is calculated by differentiating Equation (1) as follows:

$$Cst(L) = dV/dP = K1 (V - Vo) \text{ for } V < Vd \quad (5)$$

$$= K_1 (V_o - V) \text{ for } V > Vd \quad (6)$$

Cst(L) was normalized to lung size by converting it to specific compliance (Csp(L) = Cst(L)/lung volume), where lung volume was selected to be 80% - 85% of VC and 18% - 20% of VC in seated and supine postures, respectively. In supine posture, VC is approximately 18% - 20% VC [20]. To express it as an index of stiffness comparable to h, Cst(L) was converted to specific elastance, Esp(L) = 1/Csp(L) [6].

Statistical Analyses

Physiologic variables were expressed as mean ± SD. Differences amongst variables at different body positions and esophageal levels were computed by analysis of variance.

4. Results

4.1. Inflation and Deflation Curves: Effects of Body Position and Esophageal Level

Figure 1 shows inflation and deflation curves obtained in sitting and supine positions with the balloon placed at 3 different esophageal levels in subject no. 1. In 5 of 6 curves, the exponential curves fit the raw data well. The highest portions of the curves above the points of inflection shifted to the right in the supine posture with the balloon at 5 and 10 cm above the cardia. Moreover, the effect of moving the balloon to a more cephalad position in the esophagus resulted in a shift of both the deflation and inflation curves to the right, indicating an increase in elastic recoil. As can be seen in Table 2, this finding was, in most instances, reflected in both postures by an increase in the Ptp at TLC with the balloon placed more cephalad. The exception was at 10 cm in the supine position, a finding likely related to gravitational pressure from the heart.

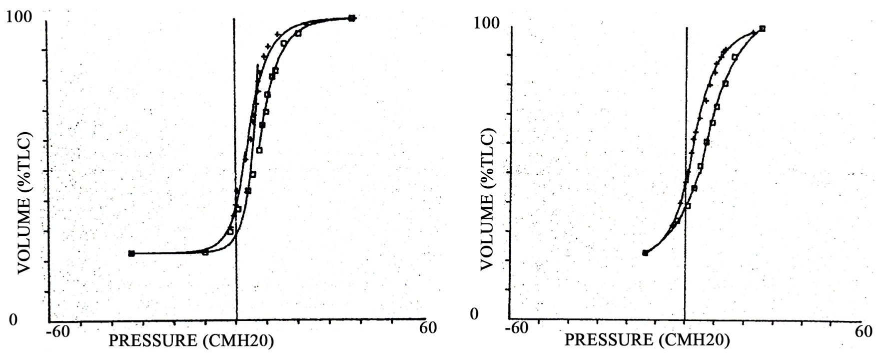

Figure 1. Pressure-volume curve in 2 subjects, nos. 1 (top) and 2 (bottom), seated with balloon position at 10 cm above the cardia. Lines represent the calculated exponential curves. Crosses and squares represent experimentally measured deflation and inflation points, respectively.

Table 2. Variables of curve-fitting exponential analysis and regression constants of inflation and deflation data.

	DEFLATION											
Vd	≥51% TLC						<51% TLC					
Posture	SIT			SUP			SIT			SUP		
Balloon level (cm above cardia)	5	10	15	5	10	15	5	10	15	5	10	15
V_o (% TLC)	106.4 (14.6)	105.5 (9.6)	101.4* (2.0)	99.8** (3.3)	100.6** (6.9)	108**† (7.1)	23.1 (4.5)	22 (5.4)	22.7 (4.3)	22.4 (4.5)	23.7 (4.4)	20.6 (8.1)
K_o (cm H_2O^{-1})	0.76 (0.27)	0.67† (0.20)	0.93 (0.27)	0.77 (0.22)	0.66 (0.23)	0.58† (0.10)	1.08 (0.47)	1.28 (0.67)	0.78†† (0.34)	1.19 (0.58)	1.19 (0.75)	1.07†† (0.58)
K_1 (cm H_2O^{-1})	0.164 (0.119)	0.117 (0.04)	0.173 (0.154)	0.183 (0.074)	0.141 (0.08)	0.081†† (0.017)	0.172 (0.057)	0.156 (0.079)	0.121† (0.063)	0.151 (0.06)	0.184 (0.064)	0.162 (0.097)
$P_{L}max$ (cm H_2O)	26.3 (7.2)	30.7 (8.3)	37.4†† (11.6)	28.9 (6.4)	27 (8.0)	29 (7.5)						
h (cm H_2O)	6.21 (4.13)	7.08 (4.29)	6.32 (2.08)	4.44 (1.89)	5.96 (2.26)	8.95†† (1.98)	4.55 (1.94)	5.72 (3.00)	7.77† † (4.71)	5.26 (1.87)	4.17 (1.35)	6.18 (4.71)

Continued

r^2 (%)	98.98 (1.17)	98.98 (1.07)	99.69 (0.22)	98.4 (1.8)	98.96 (1.35)	99.39 (0.69)	99.71 (0.47)	99.47 (1.00)	98.76 (1.15)	98.39 (3.65)	99.5 (6.4)	99.38 (0.89)
	INFLATION											
Vd	≥51% TLC						<51% TLC					
Posture	SIT			SUP			SIT			SUP		
Balloon level (cm above cardia)	5	10	15	5	10	15	5	10	15	5	10	15
V_o (% TLC)	103.8 (6.8)	101.9 (4.3)	117.2†† (26.3)	120.6 (3.3)	124.3 (6.9)	123.9 (7.1)	20.5 (4.5)	18.8 (5.4)	21.8 (4.3)	22.4 (8.1)	23.7 (4.5)	20.6 (4.4)
K_o (cm H_2O^{-1})	0.99 (0.26)	1.08 (0.75)	1.22 (0.82)	0.78 (0.14)	0.81 (0.47)	0.81 (0.24)	1.47 (1.73)	1.60 (1.35)	0.63†† (0.29)	1.21 (0.83)	1.47 (0.75)	1.04†† (0.58)
K_1 (cm H_2O^{-1})	0.111 (0.082)	0.118 (0.055)	0.088* (0.038)	0.119 (0.223)	0.082* (0.058)	0.052††** (0.017)	0.131* (0.056)	0.157 (0.102)	0.135 (0.052)	0.136 (0.055)	0.136* (0.063)	0.148 (0.134)
$P_L$max (cm H_2O)	25.8 (8.9)	28.9 (6.0)	37.1†† (10.2)	23.9 (7.4)	23.4 (4.0)	26.1 (4.3)	-	-	-	-		
h (cm H_2O)	29.51 (46.9)	9.56 (11.1)	12.15 (13.6)	49.57 (60.8)	13.88†† (11.7)	64.36 (92.4)	6.46 (3.56)	6.27 (3.57)	6.67 (4.65)	5.98 (2.72)	6.11 (2.61)	7.22 (4.2)
r^2 (%)	97.75 (2.75)	98.99 (1.04)	99.26 (0.79)	96.85 (3.57)	97.84 (2.74)	98.76 (0.74)	99.69 (0.44)	98.16 (2.52)	99.47 (1.13)	99.28 (0.99)	98.44 (2.28)	98.87 (1.21)

Values are expressed as mean (SD). †$p < 0.05$, ††$p < 0.01$, differences amongst variables within each group according to balloon levels, analysis of variance. *$p < 0.05$, **$p < 0.01$, differences amongst K_1 between deflation and inflation curves at corresponding esophageal levels, analysis of variance. Abbreviations: V: lung volume in liters; P_L: maximum Pst(L) in cm H_2O; Vd: volume at the point of deflection; V_o: constant representing theoretical minimum or maximum volume; K_o: constant describing the ratio of the volume at the half inflation pressure; h: to the volume difference from V_o to V_o at zero transpulmonary pressure; K_1: constant describing the elastic property of the lung (*i.e.*, convexity of the curve); r^2: correspondence of recorded data points with respect to the theoretically computed P-V points based on the twin-exponential fit.

Table 2 lists the physical and regression constants of the inflation and deflation portions of the P-V curve in the 10 subjects, seated and supine. Variables relevant to the derived exponential P-V curves have been separated according to those obtained at ≥51% TLC and those derived at <50% TLC. Note that during deflation, V_o, the derived maximal theoretical volume, was within 8% of the actual TLC at Vd ≥ 51% TLC at all esophageal levels in both postures, whereas the minimal theoretical value was 21% - 23% of TLC at Vd < 50% TLC. Of greatest interest, the shape constant K_1, defining curvilinearity, during deflation at volumes ≥ 51% TLC in most instances exceeded values during inflation at corresponding esophageal levels in both postures, reflecting the greater downward concavity in this region. Differences in K_1 between deflation and inflation were less apparent at volumes < 51% TLC in supine posture, again a likely consequence of dependent airway closure. Most mean values of K_1 at volumes ≥ 51% TLC tended to be lower than those at <51% TLC at all esophageal levels in both positions, consistent with the increased curvilinearity (with opposite concavity) of the lower portion of the P-V curve. The exceptions were during deflation at the 15 cm level in seated posture and at the 5 cm level in supine position, where K_1 was greater than their corresponding seated and supine values, respectively, indicating a "straightening" of the curve in these conditions. At the 15 cm level, regional lung volume remains closer to maximal inflation with an increase in Pst(L). By contrast, at the 5 cm level, the difference in curvilinearity can be accounted for by gravitational effects of the heart and "closing volume" which displaces Ptp more to the left (*i.e.*, less positive value) for a unit volume change below FRC [3] [10]. In both postures at the 5 cm esophageal level, the mean K_1 during deflation was greater than during inflation at both above and below 50% TLC ($p < 0.05$), reflecting the more acute pressure changes occurring during deflation.

4.2. Effect of Esophageal Level on K_1

The esophageal level also influenced K_1. At TLC ≥ 51%, in the supine posture, during both inflation and deflation, K_1 decreased in magnitude (by more than 50%) with the balloon moving from 5 cm to 15 cm above the cardia, indicating flattening of this portion of the curve with an increase in end-inspiratory Ptp in regions farther from the diaphragm, findings similar those reported by Milic-Emili *et al.* [3] This change was not apparent while seated or at volumes < 51% TLC, reflecting greater curvilinearity related to end-expiratory lung compression occurring in the supine position.

4.3. Influence of Esophageal Level on Transpulmonary Pressure

Transpulmonary pressure at half lung volume, h, was greatest at all esophageal levels during inflation in both postures at ≥51% TLC. It averaged 1.5 to 9 times the Ptp at corresponding esophageal levels in both postures at <51% TLC. These findings reflect the greater separation of the curves at high lung volumes and convergence of both curves at lower lung volumes due to closing volume.

The highest elastic recoil pressures were recorded at the 15 cm esophageal level in seated posture ($p < 0.025$), reflecting increasingly negative pleural pressures and alveolar expansion at a more cephalad esophageal level.

4.4. Curve Fitting

In nine of 10 patients, there were sufficient data points to construct inflation and deflation curves from peak to minimum lung volume. In a tenth subject, insufficient data points were available during inflation to construct complete P-V curves. In 5 subjects, data point fitting was difficult in the high-volume range because of a wide spread of Pst(L) points over a small volume range, particularly in the supine position. In 2 of these subjects, there was also difficulty in fitting data points in the lower limb of the curve. Five patients exhibited good overlap (that is, merging) of both inflation and deflation curves at their respective inflection points, and TLC was chosen to be between 50% and 60%. In 4 subjects, the overlaps were suboptimal above or below the inflection points in either the inflation or deflation curve.

In curves with acceptable data points, at all esophageal levels and in both body positions, the correspondence of recorded data points with respect to the theoretically computed P-V points based on the twin-exponential fit was excellent, with mean r^2 ranging between 96.9% and 99.7% (Table 2).

4.5. Half Inflation Pressure, h, and Its Relation to Specific Elastance, Esp, L, with Postural Change

We found statistically significant relations between h and specific elastance, predominantly in inflation curves at all lung volumes and lower esophageal levels, especially at the 10 cm level (Table 3). Amongst deflation curves, the only correlative significance was found in seated posture at the 10 cm esophageal level ($p < 0.03$).

Table 3. Regression constants (r), coefficients of determination, and significance of correlation between h and Esp, L at different esophageal levels, lung volumes, and postures.

Deflation curves (≥51% VC)						
	Sitting			Supine		
Esoph. level (cm)	5	10	15	5	10	15
n	10	9	10	10	9	8
Intercept	21.9	13.66	37.6	103.9	7.89	61.4
Slope	1.57	3.29	2.67	−8.22	4.71	−2.14
r	0.27	0.72	0.16	−0.213	0.54	−0.56
p	NS	**0.03**	NS	NS	NS	NS
Inflation curves (≥51% VC)						
	Sitting			Supine		
Esoph. level (cm)	5	10	15	5	10	15
n	9	8	9	10	9	9
Intercept	38.2	0.16	37.9	44.4	29.1	64.2
Slope	−0.16	0.004	0.55	−0.11	0.71	−0.02
r	−0.58	0.81	0.55	−0.67	0.78	−0.32
p	NS	**0.01**	NS	**0.03**	**0.015**	NS
Deflation curves (<51% VC)						
	Sitting			Supine		
Esoph. level (cm)	5	10	15	5	10	15
n	10	9	10	10	9	9
Intercept	7.54	3.51	9.07	−0.71	21.37	7.85
Slope	2.07	1.94	0.21	3.13	−0.6	1.06
r	0.58	0.63	0.46	0.56	−0.01	0.62
p	NS	NS	NS	NS	NS	NS
Inflation curves (<51% VC)						
	Sitting			Supine		
Esoph. level (cm)	5	10	15	5	10	15
n	9	8	9	10	8	8
Intercept	12.2	6.53	4.39	13.22	5.34	3.62
Slope	1.03	1.72	2.5	10.96	2.82	2.84
r	0.71	0.87	0.98	0.43	0.81	0.94
p	**0.03**	**0.006**	**<0.001**	NS	**0.01**	**<0.001**

h, half-inflation pressure; Esp, L, specific elastance.

5. Discussion

To our knowledge, this is the first description of the application of exponential analysis to both inspiratory and expiratory lung pressure-volume curves in seated and supine spontaneously breathing healthy young individuals using the esophageal balloon technique. In addition, the curves were constructed while placing the esophageal balloon at 3 different esophageal levels to assess changes in curve parameters at different effects on the measurement of lung mechanics. Key findings included: a) curvilinearity of the P-V curve was greater during deflation than during inflation at volumes ≥ 51% TLC in both postures, particularly with Pes recorded at the 5 and 15 cm esophageal levels, b) the position of the inflation curve, as reflected by h, was shifted to the right at volumes ≥ 51% TLC in both postures regardless of the esophageal level, but not at volumes < 51% TLC, and c) at all esophageal levels, in both postures, the fit of recorded data points was excellent with respect to the theoretically computed P-V points based on the twin-exponential fit.

Pressure-volume curve fitting using mathematical models permits more accurate extrapolation of the curve over a selected data range. To enable comparisons between curves obtained amongst subjects under different conditions (such as body position and esophageal level, or disease states), volume data are normalized according to TLC [4]. In this study, we assumed that in normal subjects, TLC was within 100-200 mL of the maximal volume V_o for the purpose of defining the curves as exponential functions [6] [22]. In some cases, complete data points were not available. As Venegas *et al.* [24] point out in their sigmoidal analysis of P-V curves, however, in most cases, it may not be desirable to obtain complete data points that reach the upper and lower asymptotes of the curve. As individual data sets rarely reach exact maximum pressure, TLC values are derived by curve-fitting. Physiologically meaningful variables derived from the curve-fitting model better characterize the P-V over its full range.

5.1. Effects of Changes in Posture and Esophageal Balloon Placement

Supine position moved the P-V curve up and to the left at every balloon position, findings also reported by Milic-Emili *et al.* [3]; mean values of Ptp (= Pm − Pes) were 2 - 3 cm H_2O lower than in seated posture. In some of our subjects, lung volumes were lower than 20% VC, and Ptp decreased disproportionately in the supine position, likely reflecting mediastinal effects and closing volume. Pleural pressure recordings can also be distorted at higher esophageal levels, likely due to traction on, or compression of, the esophagus by mediastinal structures, notably the trachea [3].

The issue of pleural pressure (Ppl) measurement and its relation to regional lung mechanics and body posture bears an important influence on our findings. The indirect measurement of Ppl is based on the principle that when the regional static distribution of gas and the intrinsic static mechanical properties are known, the regional distribution of Ppl can be determined. Chest wall deformations during maximal muscle contractions, such as when performing TLC and RV maneuvers, can alter Ppl swings from those that are generated during quiet tidal breathing [7]. Such deformations are less likely to occur while seated, where lung weight influences regional differences in Ppl.

5.2. Curvilinearity as Expressed by K_1

Our values of K_1 (**Table 2**) are like those in previously described healthy young individuals (assuming a balloon level of 10 cm in a seated position); mean K_1 was 0.106 and 0.073 for deflation and inflation, respectively [11] [15]. The curve's variables (of greatest importance being K_1, representing curvature) also correlate with changes in pulmonary elasticity with aging and smoking [5] [9] [11]-[14] [16] [25]-[28].

5.3. Relationship of h to Specific Elastance

We found a significant relationship of h to Esp, L that occurred most often during inflation curves in both postures. Eight of 12 associations were statistically significant, 3 of 6 at >50% VC and 5 of 6 at <50% VC. All but one exhibited a positive relationship; the only negative association occurred at the supine 5 cm esophageal level, most likely because of the distorting effects of closing volume and mediastinal factors [3]. The explanation for why the relationship is more robust during inflation is likely related to a more circular rib cage adopted during inflation, resulting in a more uniform distribution of pleural pressure than during deflation [1] [7] [29] [30]. The exception would be at regions close to the diaphragm where pleural pressure swings are greater in magnitude than corresponding mouth pressure swings, as shown by the "occlusion test" [2] [21].

Because the magnitude of both elastance and compliance depends on lung volume while h is independent of lung volume [31] [16], correction for Est, L was made by expressing elastic recoil as specific elastance, Esp, L = Est, L x lung volume [6]. Our findings indicate that the relationship found between h and Esp, L at any lung volume estimates its slope at that volume, at least during inflation at most esophageal levels.

5.4. Comparison of Curve Fitting Using Different Mathematical Models

We found our method of curve-fitting to be more practical than previously described techniques [9] [15] [23] [32] because of the simplicity of its equations and short computing time. There have been few attempts to define the P-V curve in its lower as well as upper portions in humans using either the exponential or sigmoidal method [4] [24] [26] [27] [33]. Colebatch *et al.* [4] used a single exponential function best fitted to static inflation-deflation pressure-volume data above FRC by an iterative least-squares analysis in 12 of 43 awake subjects (the other 31 subjects underwent deflation analysis only). Ferreira *et al.* [26] derived data only from sigmoidal inflation curves in anesthetized and paralyzed patients with idiopathic pulmonary fibrosis. Harris *et al.* [27] analyzed only sigmoidal inflation curves in 10 mechanically ventilated patients with acute respiratory distress syndrome. Paiva *et al.* [22] demonstrated that a single sigmoid mathematical model applied only to the expiratory limb of P-V curves allowed reporting of volumes and pressures by their actual values (rather than by visual fit) and would allow the fitting of the whole P-V curve. However, the model of Paiva *et al.* [22] was constructed based on P-V data obtained only above FRC, and while theoretical data under FRC obtained by sigmoid analysis were added to the curve, the authors conceded the difficulty of fitting data points under FRC. These problems were attributed to the quasi-static method of constructing the curves and measurements of Pes. Using the exponential technique, similar conclusions were reached by Kraemer *et al.* [19], who studied the elastic behavior of lungs in healthy children at volumes above FRC, and by Collie *et al.* [23] in anesthetized sheep.

Our twin-exponential model incorporating inspiratory and expiratory limbs showed a close fit to experimentally obtained pressure-volume data over the entire range of lung volume, even at low lung volumes. This approach may be compared to other P-V curve models. Murphy and Engel [8] present a detailed comparison of different equations used to fit P-V data. While the exponential method of Salazar and Knowles [16] has been widely used to characterize the inflation and deflation limbs of normal and diseased lungs, data, including the low range of lung volumes, is poorly fitted by their equation [6], particularly in conditions exhibiting alveolar de-recruitment and airway closure. To compensate for this poor fitting at low lung volumes, various polynomial equations have been employed to improve curve fits [9] [11], but they incorporate increased numbers of parameters that provide little physiologic relevance [27]. While we used the modified Salazar and Knowles [16] exponential curve to describe the inflation and deflation limbs above and below their respective inflection points, its close fit to the experimentally recorded points attests to its adaptability in at least young, healthy individuals. Exponential model equations provide close approximations in high and low-pressure regions, and their parameters are influenced by the characteristics of the P-V curve [34].

5.5. Comments on Methodology: Strengths and Limitations

The novel aspect of our investigation is its application of the exponential approach in seated and supine postures using the esophageal balloon technique. We attempted to derive a greater degree of "realism" in our curves by combining a number of technical methods: a) the use of 2 separate exponential functions above and below FRC during both inflation and deflation, allowing increased concordance between actual data points and the exponential analysis; b) we measured Pes with the glottis open at each quasi-static step, rather than measuring the Ptp by having subjects relax against a closed valve, thus avoiding errors associated with compression and expansion of alveolar gas, upper airway, and cheeks [35]; and c) our method of analysis also avoided the disadvantage of an inflection point related to airway closure which may lead to under or overestimation of K_1 and overestimation of Vmax [11] [23].

The main limitation in this analysis is the use of identical mathematical functions (except for the reversal in signs) for the upper and lower portions of the inflation and deflation curves. This approach assumes that the curvilinearity of the upper and lower parts are mirror images of (symmetrical with respect to) each other. However, as shown by our data (K_1 in particular), they are not identical. Harris *et al.* [27] and Venegas *et al.* [24] used a simple sigmoidal equation that closely corresponded to the inflation and deflation limbs of experimental and diseased states and was symmetrical above and below the inflection point, which may not be the case in diseased lungs, or with postural change as was the case in this study. As Venegas *et al.* [24] state, it may be necessary to modify the sigmoidal equation to fit data sets that extend further onto both asymptotes. Paiva *et al.* [22] proposed a sigmoidal model that fits better than the exponential relationship described by Salazar and Knowles [16] but also assumed a lower asymptote of lung volume of zero, which may not be zero in diseased lungs.

Finally, this study was conducted in young, healthy (mostly male) adults and may not apply to infants and small children. In a study of curves in newborn mammals (and a review of the same in human infants), Saetta and Mortola [36] showed that the monoexponential fitting reflected only a small portion of the P-V curve, with the K value being higher than in adult mammals. This was explained by the airspace per unit of lung mass being smaller than in adults of corresponding species, that is, exhibiting a decreased compliance. Conversely, aging and/or disease induce collagen and elastin-related changes in mechanical properties, specifically the slope and hysteresis area enclosed by P-V curves in diseases such as emphysema and fibrosis [5], in part related to percolation and lung tissue viscoelasticity [37]. Future studies in this area may consider expanding the age and sex distribution. The application of this twin exponential approach needs to be further investigated in older individuals and in disease states.

Our measurements were obtained by analog means with the use of pressure transducers, an oscilloscope, and a chart recorder, while curves were constructed by computer. Modern electronic devices, including analog to digital converters with appropriate anti-aliasing filters and solid-state pressure transducers, are likely to increase the efficiency of such measurements and computation. Time, however, was not an issue for the completion of this study. Instead, careful attention was paid to the recordings obtained and subsequent computations to minimize errors in precision.

6. Conclusion

We constructed separate exponential curves for the upper and lower portions of the lung P-V curve to better fit raw data derived by the esophageal balloon technique. This method facilitates the analysis of alterations in regional P-V characteristics occurring with postural changes and with the esophageal balloon placed at 3 different levels in the esophagus. The curvilinearity of the P-V curve was greater during deflation than during inflation at volumes ≥ 51% TLC in both postures, particularly with Pes recorded at the 5-cm and 15-cm esophageal levels. At all esophageal levels, in both postures, the fit of recorded data points can be excellent with respect to the theoretically computed P-V points based on the twin-exponential fit. A twin-exponential model applied during inflation and deflation facilitates defining the elasticity of the lung over its range. Whereas Cst, L correlates with the alveolar volume at which the breath is held, K_1 is independent of this variable and is, therefore, a more useful index for comparing distensibility in different postures and disease states. The relationship of h to Esp, L was closest most often during inflation in both postures and likely related to a more uniform distribution of pleural pressure than occurs during deflation. This approach has the potential to be applied to disease states where most previous analyses have primarily focused on the mechanical properties during lung deflation and lung volumes above FRC.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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