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Effect of pleural effusion on respiratory mechanics, and the influence of deep inflation, in dogs

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ABSTRACT: We wished to study how pleural effusion affects dynamic mechanics of the lung and the chest wall. We also determined if these changes could be reversed by deep lung inflations.

Pleural effusion was produced by saline infusion into the pleural space. During the infusion and over the following 2 hours, dynamic elastance and resistance of the lungs, the chest wall and the whole respiratory system were recorded.

Dynamic elastance and resistance of the lung increased significantly during fluid loading and were partially, and only transiently, reversed by deep inflations. Dynamic elastance and resistance of the chest wall were little affected by these procedures.

Thus, pleural effusion can have significant effects on dynamic elastance and resistance of the respiratory system (Ers, Rrs). The transient nature of the change in lung parameters after deep inflation suggests that therapies based on periodic lung inflations may be of little benefit to patients with this condition.
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Pleural effusions are a very common clinical entity. To date, investigations of the effects of pleural effusions on lung function have concentrated on quantifying the changes which occur in gas exchange, lung volume [1–4], or forced expiratory flow rates [2, 4]. A few studies have examined the alterations in static elastance of the respiratory system which occur as a result of pleural effusion [2–4]. However, none have assessed changes in dynamic elastance (E) and resistance (R) that accompany pleural effusion. These dynamic properties of the respiratory system, which may differ markedly from its static properties, are obviously more relevant during breathing.

The purpose of the present study was to investigate the changes in the dynamic mechanical properties of the canine respiratory system and its components, the lung and chest wall, produced by the progressive development of pleural effusion. We also sought to determine the extent to which such changes could be reversed by deep lung inflations, in order to discern the therapeutic effectiveness of such a manoeuvre.

Methods

Six mongrel dogs, weighing 18–25 kg were anaesthetized with pentobarbital sodium (25 $mg \cdot kg^{-1}$ *i.v.*) and maintained with an hourly dose of 10–15% of the initial dose. The dogs were positioned supine, tracheostomized and a cannula was inserted in the airway (ID 20 mm).

Tracheal pressure (Ptr) was measured by a piezoresistive pressure transducer (ICS 12 002 g 8051610, SPR Control Systems Ltd, Rexdale, Ontario, Canada) at a lateral tap in the cannula. A heated Fleisch No. 2 pneumotachograph was connected to the cannula for the measurement of tracheal flow ($\dot{V}$). The pressure drop across the pneumotachograph was measured by a piezoresistive pressure transducer (MicroSwitch 163PC01D36, Honeywell, Scarborough, Ontario, Canada). A three-way valve was connected to the pneumotachograph to allow occlusion of the airway during the occlusion test (see below). Pleural pressure (Poes) was measured with a thin latex balloon, 5.5 cm long and sealed over one end of a thin polyethylene catheter (88 cm long, 1.7 cm ID). The other end of the catheter was connected to another ICS pressure transducer. The balloon was filled with 0.7 ml of air, which placed it on the flat portion of its volume pressure curve.

All signals were passed through 8 pole Bessel filters (902LPF, Frequency Devices, Haverhill, MA, USA) with their corner frequencies set at 30 Hz. They were then sampled at 100 Hz with a 12-bit analogue-to-digital converter (DT2801 A, Data Translation, Marlborough, MA, USA) and stored on computer. All data were collected using LABDAT software (RHT-InfoData Inc., Montreal, Quebec, Canada).

The oesophageal balloon was positioned 10 cm above the oesophageal sphincter and the occlusion test was performed at functional residual capacity (FRC) and FRC+500 ml [5]. The slope of Poes *vs* Ptr, obtained during a spontaneous breathing effort, did not vary more than 5% from unity in any dog at either lung volume. We have previously shown that the changes in Poes and Ptr during an occlusion test are even closer after paralysis than during spontaneous breathing efforts [6]. However, the ability of the oesophageal balloon to accurately measure changes in pleural pressure with an effusion in place is controversial [3, 7, 8]. Therefore, we tested the accuracy of Poes as a measure of pleural pressure in a similar manner to that described in our previous investigations, in two paralysed dogs with unilateral pleural effusion. Specifically, the dogs were tracheostomized and an oesophageal balloon placed 10 cm above the gastro-oesophageal junction. Each dog was placed in a plethysmograph, paralysed with pancuronium bromide, and ventilated. The occlusion test was performed by occluding the airway and measuring Ptr and Poes, while the pressure around the animal was oscillated by injecting and withdrawing 2 *l* of air from the plethysmograph. This caused Ptr and Poes to oscillate quasi-sinusoidally, with an amplitude of 1 kPa and a frequency of 0.08–0.28 Hz. We then infused saline into the pleural space, until we obtained the same maximum volume per kg used in the dogs reported in this paper. The oscillation test was then repeated. The slope of Ptr *vs* Poes did not vary more than 2% between the control and effusion states. Therefore, we are confident that Poes accurately reflected mean pleural pressure in the investigations reported here.

Dogs were paralysed with a bolus of pancuronium bromide (2 mg) and paralysis maintained by 2 mg hourly doses thereafter. The three-way valve was removed from the pneumotachograph and a Harvard ventilator (model 618, Harvard Apparatus, Southnatick, MA, USA) connected in its place. The dogs were mechanically ventilated with a tidal volume of 15 $ml \cdot kg^{-1}$ at a frequency of 20 $breaths \cdot min^{-1}$. A polyethylene catheter was inserted into either the right or left pleural space, at the level of the seventh or eighth intercostal space. The catheter was sutured in place and air was evacuated from the pleural space using an underwater sealed suction apparatus.

Just prior to saline infusion, three deep inflations were given. A deep inflation was accomplished by occluding the expiratory port of the ventilator for three consecutive breaths, which raised transpulmonary pressure to approximately 3 kPa. Saline was then infused into the pleural space in 60 ml increments, given each minute, until an effusion of 60 $ml \cdot kg^{-1}$ body weight had been administered. Ptr, Poes and $\dot{V}$ were measured continuously for 3 min prior to, during, and 10 min following loading of the effusion. They were also measured for 40 s every 5 min over the next 2 h. Following loading of the effusion, three deep inflations were given every 20 min, immediately after a data collection period.

At the termination of the experiment we opened the chests of two of the dogs and removed the pleural effusion using a 60 ml syringe. In both cases we recovered at least 90% of the effusate.

Data Analysis

Forty second segments of Ptr, Poes and $\dot{V}$ following each increment in effusate were isolated from the continuous data record. Volume (V) was calculated by numerical integration of $\dot{V}$. A small constant was added to $\dot{V}$ prior to integration so that the resulting V had no baseline drift. The segments were divided into individual breaths, the breaths superimposed and the data ensemble averaged [9]. Similar ensemble averaging was performed on the data collected in discrete 40 s samples in the 2 h period following fluid loading. We then fitted the equation:

$$P = E \times V + R \times \dot{V} + K$$

to each ensemble averaged data set by multiple linear regression in order to calculate elastance (E) and resistance (R) of the respiratory system (RS), lung (L) and chest wall (CW), where RS = L + CW. K (constant) is the value of pressure when V and $\dot{V}$ are both zero. Of course, these model parameters do not characterize the respiratory system perfectly, but they do embody the great majority of its elastic and dissipative properties during regular mechanical ventilation [10]. P was represented by Ptr, Poes or Ptr-Poes (Ppt), yielding E_{RS} and R_{RS}, E_{CW} and R_{CW} and E_L and R_L, respectively.

In all cases, the equation $P = E \times V + R \times \dot{V} + K$ accounted for at least 98% of the variance in the dependent variable P as indicated by the coefficient of variation.

All data were analysed using ANADAT data analysis software (RHT-InfoDat Inc., Montreal, Quebec, Canada).

Results

Figure 1 shows changes in E_{RS}, E_{CW} and E_L during baseline until the end of effusate loading for each dog studied. Figure 2 illustrates the changes in R for the same time period in the same dogs. In all cases, there are steady increases in E_{RS}, E_L, R_{RS} and R_L. There are much smaller decreases in E_{CW} and R_{CW}. Changes in E_{RS} and R_{RS} are very similar in shape and amplitude to those observed for the lung. Table 1 presents the percentage changes in E and R from baseline values produced by effusate loading for each dog. In all cases the changes in E and R for the RS, L, and CW were significant at $p<0.05$.

Figures 1 and 2 demonstrate an abrupt decrease in E and R in dog no. 4 at 15 min after initiation of loading. Examination of the corresponding Ptr signal revealed a sudden increase in the baseline and a decrease in the amplitude of the pressure swing.

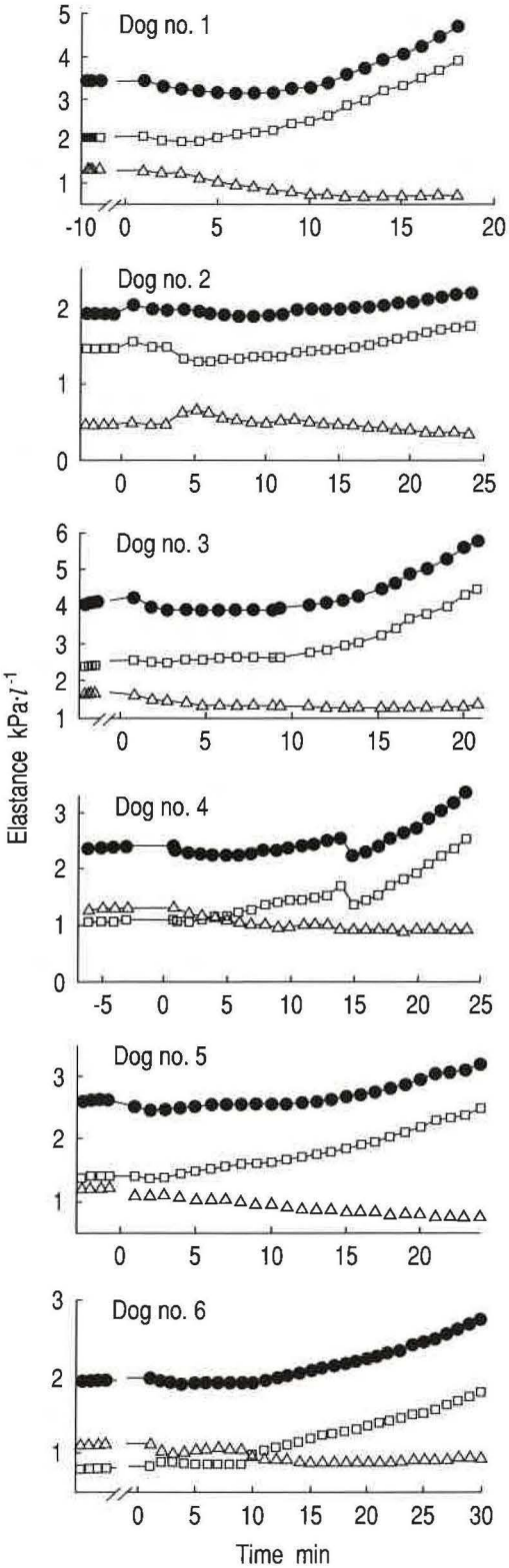

Fig. 1. – ERS (●), EL (□) and ECW (Δ) plotted against time. "0" time indicates the initiation of effusate loading, which is complete at the end of each plot. Points before initiation of loading are baseline data. (In dogs no. 1, 3 and 6 the break on the abscissa is used because baseline data were measured 8–10 min prior to initiation of loading which would unnecessarily extend graph). ERS, EL and ECW: elastance of the respiratory system, lung and chest wall, respectively.

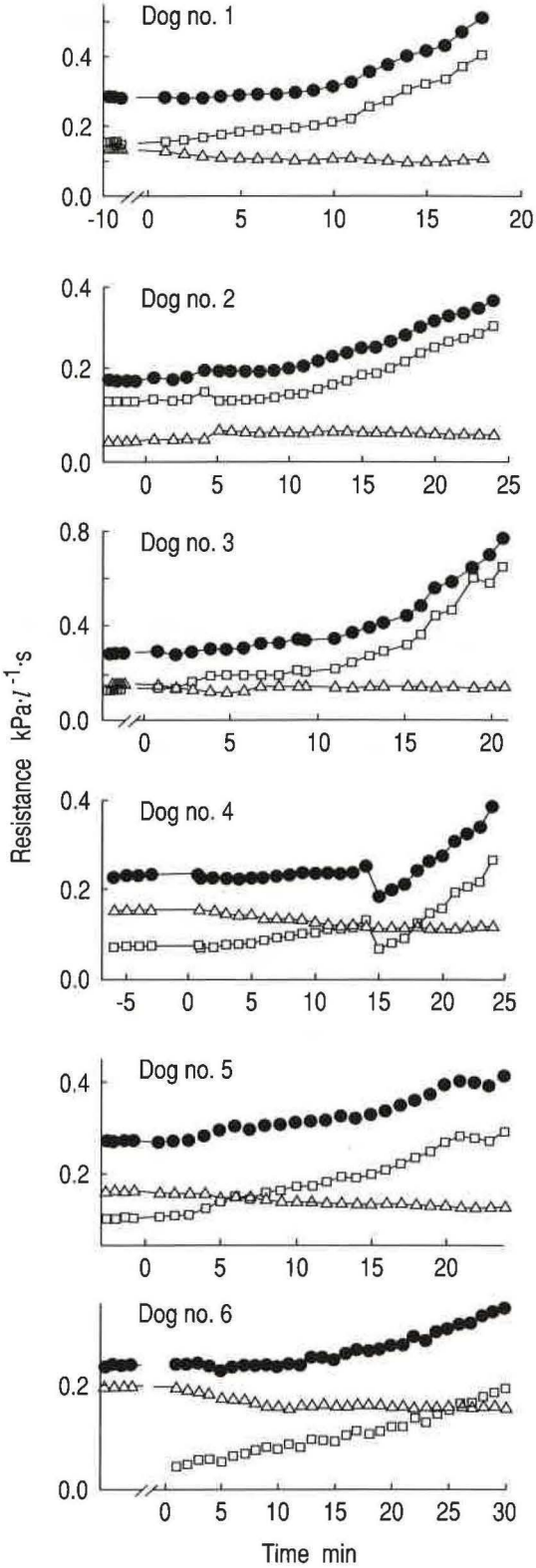

Fig. 2. – RRS (●), RL (□) and RCW (Δ) plotted against time. "0" time indicates the initiation of effusate loading, which is complete at the end of each plot. Points before initiation of loading are baseline data. (In dogs no. 1, 3 and 6 the break on the abscissa is used because baseline data were measured 8–10 min prior to initiation of loading which would unnecessarily extend graph). RRS, RL and RCW: resistance of the respiratory system, lung and chest wall, respectively.

Table 1. – Changes in E and R during effusate loading

Dog no.	E_{RS}	E_L	E_{CW}	R_{RS}	R_L	R_{CW}
1	34	64	-52	57	93	-26
2	17	23	-8	66	77	19
3	34	61	-21	91	135	-25
4	32	79	-44	52	114	-25
5	7	56	-52	40	88	-33
6	34	75	-18	-25	133	37
Mean	26	60	-32	47	107	-9
SD	12	20	19	39	24	29

Data are expressed as a percentage of baseline values. All changes are significant at $p<0.05$. E_{RS}, E_L and E_{CW}: elastance of the respiratory system, lung and chest wall, respectively; R_{RS}, R_L and R_{CW}: resistance of the respiratory system, lung and chest wall respectively.

patterns of change in E and R were similar to those of the other dogs examined.

Figure 3 illustrates the changes in E and R which occurred 45–120 min following loading of the effusion and includes the effects of three deep inflations for a representative dog. These data illustrate the immediate, marked decreases in E_{RS} and E_L and the small decreases in E_{CW} resulting from deep inflations. These decreases were followed by returns towards original values. R_{RS} and R_L also decreased following deep inflations, whilst R_{CW} was little affected. Again, the resistances increased toward original values following the deep inflations.

Table 2 presents the percentage changes in E and R produced by deep inflations in all dogs studied. The lung rather than the chest wall was primarily affected by deep inflations in all cases.

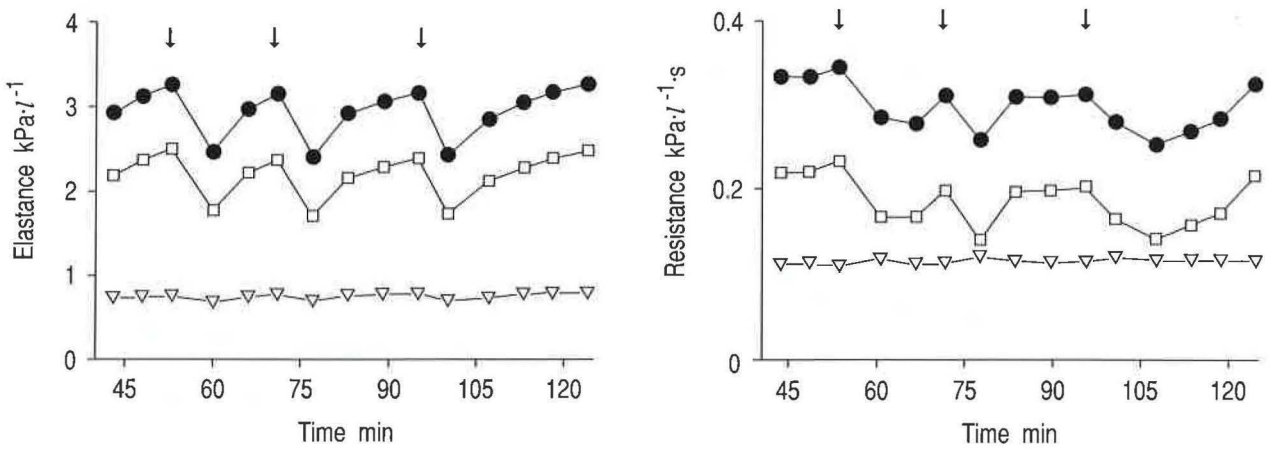

Fig. 3. – Elastance and resistance for dog no. 5 against time from the initiation of loading of effusate. ↓ : administration of a total lung capacity (TLC) manoeuvre; ●: respiratory system data; □: lung data; ▽ : chest wall data.

Table 2. – Changes in E and R with deep inflations

Dog no.	E_{RS}	E_L	E_{CW}	R_{RS}	R_L	R_{CW}
1	29 (1)	35 (1)	15 (0.1)	17 (6)	21 (7.5)	4.5 (2.6)
2	26 (1.7)	29 (2.1)	13 (1)	36 (2.1)	40 (2.1)	17 (3)
3	28 (8.5)	31 (9.9)	12 (2.3)	36 (6.4)	47 (6.4)	9 (2.5)
4	38 (3)	49 (3.8)	6 (2)	50 (3.8)	71 (3.6)	4 (2.7)
5	23 (1)	29 (1.5)	2 (0.58)	32 (3.6)	45 (5.3)	2 (1)
6	17 (2.1)	24 (2.5)	2 (1.8)	6 (5.5)	14 (6.1)	5 (3.6)
Mean	27	33	8	30	40	7
SD	7	8.7	5.6	15.6	20.3	5.4

Data are expressed as a percentage of end-loading values and are the means of the data points recorded immediately following three deep inflations given between 15 and 120 min post-loading. Numbers in parentheses are the standard deviations of the points. For abbreviations see legend to table 1.

This apparent abnormality in pressure measurement resolved spontaneously at the end of the recording period and was not observed at any other time. We suspect that this may have been due to the formation of a fluid bubble at the opening to the tracheal cannula side port. Despite this anomaly in Ptr the

Discussion

Effusate loading of the pleural space produced progressive changes in the dynamic E and R of the lung and chest wall in the animals studied (figs 1 and 2, table 1). Following the completion of loading, the

courses of these changes were stable, apart from transient reversals induced by deep inflations (fig. 3). This indicates that the changes in E and R during fluid loading are not due solely to the accrual of atelectasis as a result of regular ventilation over the recording period. These results, therefore, demonstrate that pleural effusion can create significant changes in the dynamic mechanical properties of the respiratory system, and that the extent of the changes is closely related to the volume of the effusion.

EL increased steadily throughout effusate loading (fig 1). This was probably due to a combination of parenchymal distortion, which occurs as the lung rotates around its long and transverse axes during effusate loading [3, 11, 12], and to a decrease in FRC as dependent lung regions are displaced by the fluid [1]. The decrease in FRC can occur as a result of airspace closure, or a uniform decrease in volume throughout the lungs. For example, several investigators using animal models have reported an increase in static EL at very low lung volumes, whilst noting that airspaces remained open, even at negative transpulmonary pressures [13–16]. On the other hand, research on humans has demonstrated impaired oxygen exchange in the presence of pleural effusion, which is indicative of some degree of airspace closure [17, 18, 4]. In reality, there is probably a combination of the above phenomena, which could potentially result in significant regional inhomogeneities of ventilation, and so cause an increase in dynamic elastance *via* the mechanism described by OTIS *et al.* [19].

MEAD and COLLIER [20] described a decline in compliance associated with airspace closure in dogs ventilated for several hours without periodic deep inflations. In the present study, we found sudden marked decreases in EL, followed by slower returns toward original values in response to deep inflations (fig. 3). Similar results have been described for quasi-static elastance following a period of low volume breathing [15] and for dynamic elastance determined from normal FRC or above [21, 22]. The decreases in EL may be explained either by stress adaptation of the lung tissues, recruitment of previously closed airspaces, or a combination of the two phenomena [11]. Although previous work has demonstrated that the lung and chest wall exhibit a similar degree of stress adaptation in response to moderate changes in lung volume at normal FRC [23], we found deep inflations produced much smaller changes in Ecw than EL (fig. 3). This suggests that airspace recruitment may have been responsible for the marked transient decreases in EL that occurred in response to deep inflations in the present study. On the other hand, LUDWIG *et al.* [22] and LORING *et al.* [21] observed large changes in EL in response to deep inflations from normal FRC, where pre-existing airspace closure is presumed absent. Therefore, it is still possible that our results are a reflection of a severe volume dependence of stress adaptation of lung tissue. In any case, our results (fig. 3) clearly show that the effects of deep inflations on mechanics following fluid loading of the pleural space are only transitory and that the changes induced by the loading itself are stable over 2 h.

Figure 2 demonstrates a steady increase in RL as mean lung volume decreases below FRC during effusate loading. This is in contrast to the work of LUDWIG *et al.* [22] who demonstrated a positive dependence between mean lung volume and RL. Previous work has established that at low ventilation frequencies, such as the one used in this study, tissue and not airway properties are the principal determinants of RL [24, 22]. However, all of these previous measurements were made at mean lung volumes at or above normal FRC. It is possible that airways contribute significantly more to RL at volumes below FRC, thus explaining the contradiction between our work and that of LUDWIG *et al.* [22]. However, the decrease in lung volume induced by the effusion in the present study probably affected the peripheral more than the central airways and, thus, would not have significantly increased airway resistance. We also observed a decrease in RL in response to deep inflations which neither LORING *et al.* [21] nor LUDWIG *et al.* [22], operating at mean lung volumes at or above normal FRC, demonstrated. This supports the notion that the development of airspace closure below normal FRC, temporarily removed by deep inflations, may have contributed significantly to the increase in RL that we observed with effusate loading.

Figure 1 and table 1 show a decrease in Ecw during effusate loading. KRELL and RODARTE [3] also reported decreases in Ecw associated with an increase in chest wall volume during fluid loading of the pleural space. Their findings are consistent with those of Barnas (personal communication), who demonstrated a decrease in Ecw with a decrease in mean lung volume. Such evidence supports our opinion that chest wall volume increased during effusate loading in the present study.

It is interesting to note that in dogs, unlike humans, the pleural space is incomplete and communicates bilaterally [25]. Therefore, it is possible some of the effusate could have crossed the mediastinum, resulting in a bilateral, not unilateral, effusion in the dogs that we studied. The fact that we were able to recover at least 90% of the effusate by evacuation *via* the chest tube, suggests that much of the effusion remained unilaterally distributed. In any case, we are interested in the behaviour of the respiratory system with pleural effusion and the exact distribution of the effusion is not pivotal to our findings.

In summary, the results of our study suggest that changes in respiratory system, lung and chest wall volume during effusate loading of the pleural space alter the dynamic E and R of these structures. It also appears that breathing at mean lung volumes below normal FRC may change the relative extents to which airways and tissues contribute to EL and RL. In particular, our data suggest that airspace closure may be an important determinant of the changes in lung mechanics that we observed. Deep inflations, which may act to dissipate airspace closure, were only able to

transiently reverse the observed changes in E_L and R_L. Furthermore, it suggests that a measure, such as mask continuous positive airway pressure (CPAP), which raises mean lung volume over prolonged periods of time, may be a more effective treatment for this patient population.

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