

Elastic recoil changes in early emphysema

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ABSTRACT An attempt was made to determine if emphysema and static lung recoil were related in a group of 65 excised human lungs. We studied 23 normal lungs, 24 lungs with an emphysema score of 5 or less, and 18 lungs with an emphysema score greater than 5. A comparison of the percentage of predicted elastic recoil revealed that both emphysema groups were significantly different from normal lungs. In addition, the total lung capacities were significantly different between the three groups. In the group with an emphysema score greater than 5 we found a linear negative correlation between the extent of emphysema and percent of predicted elastic recoil at 90% total lung capacity ($r = -0.696$, $p < 0.01$). We found a negative correlation between the percentage of predicted elastic recoil and the lung volume ($r = -0.612$, $p < 0.01$). We conclude that a significant loss of elastic recoil and a significant increase in total lung capacity occurs in the early stages of emphysema.

It is generally believed that the anatomical destruction of pulmonary tissue in emphysema is closely related to the functional loss of elastic recoil. Thurlbeck^{1,2} has challenged this concept in recent articles and presents an alternative hypothesis that emphysema and elastic recoil are related only coincidentally. If the traditional view is correct and emphysema and elastic recoil are related as cause and effect, a good correlation between elastic recoil and emphysema should be present.

Methods

Excised human lungs were obtained from necropsies performed at either Colorado General Hospital or the Denver Veterans Administration Hospital. Lung specimens were chosen which appeared free of significant disease other than emphysema. Lungs that were later found on microscopic examination to have any pathological process other than emphysema that involved greater than 10% of the lung were eliminated from the study. This experimental protocol was completed within 48 hours of death or of cessation of mechanical ventilation in the case of cadaveric transplant donors.

Lungs were cannulated and inflated with air.

Leaks were repaired by ligature. Only specimens that could be made airtight were used in this study. The lungs, while floating on a bed of normal saline, were inflated three times with air to a pressure of 20 to 22 cm of H₂O and allowed to deflate passively. A static pressure-volume curve was constructed by inflating the lung with air to 20 cm H₂O and deflating by removing air in 2 cm H₂O pressure decrements. Pressure was measured on a U-tube water manometer. Thirty seconds at each pressure measurement were allowed to ensure equilibration. Minimal volume, the volume of gas remaining in the lung at zero transpleural pressure, was determined by water displacement and subtracting the volume of the tissue, assuming the specific gravity of lung tissue to be 1.0.

The pressure-volume curves were corrected for gas compression. Total lung capacity (TLC) was calculated by assuming that the left lung represents 45% and the right lung 55% of the total lung volume. The total lung capacity was expressed as a percent of predicted total lung capacity, using the predicted values of Goldmark and Becklake³ for females and the values of Boren *et al*⁴ for males.

The lungs were fixed in inflation at a pressure of 20 cm H₂O with 1.8% neutral buffered glutaraldehyde and sectioned sagittally at 10 mm intervals. The lungs were studied histologically using the methods of Mitchell *et al*.⁵

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An emphysema score was established for each lung by a modification of the method of Thurlbeck *et al.*,⁶ using a series of 20 standardised photographs representing differing degrees of destruction. The score for the degree of destruction was increased by 5, 10, or 20 points, respectively, if mild, moderate, or severe fenestration of alveolar walls in grossly normal portions of lung was noted microscopically. Only five of the 65 cases studied were altered by the fenestration reading. All specimens were scored independently of the other studies.

Results

The lungs were divided into three groups based on the amount of anatomical emphysema present. The normal group consisted of 23 lungs without any discernible emphysema by gross or microscopic observation. The emphysematous lungs were divided into two groups, one with emphysema score of trace to 5, and the other with score greater than 5. The greater than 5 group ranged from a score of 10 to 85 with a mean of 39.7 ± 4.9 SEM. The sex and age distribution of each group is shown in table 1. Because of obvious age differences among the groups studied, we have expressed elastic recoil as a percentage of predicted recoil at specific volumes of total lung capacity (Pst(l) x, where $x = \%$ total lung capacity). We have used the

Table 1 Sex and age distribution of three groups studied

	Normal	Trace-grade 5 emphysema	> Grade 5 emphysema
Men	14	17	16
Women	9	7	2
Total	23	24	18
Age (yr)	33.0 ± 15.9	47.8 ± 14.6	65.4 ± 12.7

Table 2 Percentage of predicted static lung recoil \pm SEM

%TLC	Normal	\leq Grade 5 emphysema	> Grade 5 emphysema
After data of Knudson <i>et al.</i> ⁷			
50	44.3 ± 2.9	$29.2 \pm 2.6^*$	$16.0 \pm 1.8^{*\dagger}$
60	48.9 ± 2.8	$34.9 \pm 2.4^*$	$22.0 \pm 2.2^{*\dagger}$
70	54.0 ± 2.7	$42.6 \pm 2.2^*$	$27.7 \pm 2.2^{*\dagger}$
80	59.5 ± 2.3	$49.9 \pm 1.9^*$	$36.1 \pm 1.9^{*\dagger}$
90	64.8 ± 1.7	$58.1 \pm 1.5^*$	$49.8 \pm 1.6^{*\dagger}$
From Bode <i>et al.</i> ⁸			
50	56.0 ± 3.0	$42.2 \pm 3.2^*$	$38.2 \pm 6.1^*$
60	55.8 ± 2.4	$46.2 \pm 2.5^\ddagger$	$40.2 \pm 4.8^*$
80	62.2 ± 2.1	$56.0 \pm 1.7^\ddagger$	$45.8 \pm 2.3^{*\dagger}$

* Different from normal $p < 0.01$.

† Different from \leq grade 5 emphysema $p < 0.01$.

‡ Different from normal $p < 0.05$.

Table 3 Percentage of predicted h value \pm SEM (after Turner *et al.*¹¹)

Normal	\leq Grade 5 emphysema	> Grade 5 emphysema
54.3 ± 2.6	$43.5 \pm 2.9^\ddagger$	$28.2 \pm 6.3^*$

* Different from normal $p < 0.01$.

† Different from normal $p < 0.02$.

data of Knudson *et al.*⁷ and of Bode *et al.*⁸ for predicted Pst(l).

By one-way analysis of variance,⁹ the elastic recoil was decreased in the trace-grade 5 group compared to the normal group ($p < 0.01$) at all volumes studied and in the grade 5 or greater group was statistically different from normal and the trace-grade 5 group ($p < 0.01$) at all volumes examined when using regression curves obtained from the data of Knudson *et al.*,⁷ (table 2). When using the prediction data of Bode *et al.*,⁸ the two emphysema groups were statistically different from normal at Pst(l) 50, 60, and 80% of total lung capacity (table 2). Only at Pst(l) 80% was the greater than 5 emphysema group significantly different from trace-grade 5 emphysema group.

The expiratory pressure-volume curves were fitted with a single exponential function after the method of Salazar and Knowles.¹⁰ To correct for age we have used the data of Turner *et al.*¹¹ A multiple comparisons test reveals a significant difference when comparing the two emphysema groups with the normal lungs ($p < 0.03$) (table 3). Surprisingly, there was no significant difference between the two emphysema groups.

The total lung capacities were different for each group (fig 1). An analysis of variance shows that the percentage predicted TLC differed significantly ($p < 0.02$) between the three groups.

In order to gain some insight into the relationship of emphysema and elastic recoil, we correlated the extent of emphysema against Pst(l) x in the greater than grade 5 emphysema group of lungs. There was a negative correlation which was significant ($p < 0.05$) at Pst(l) 80, 90% of TLC using the data of Knudson *et al.*⁷ for predicted data. The plot of the data at Pst(l) 90% is shown in fig 2.

When the volume of the lungs expressed as a percentage of predicted TLC is related to elastic recoil as a percentage of predicted using the regression curves of Knudson *et al.*⁷ there is a significant correlation ($p < 0.05$) at Pst(l) 50 and 90% of TLC. The plot of the data at Pst(l) 90% is shown in fig 3.

Our data were also compared with Niewoehner *et al.*¹² by obtaining α_1 which describes the elastic

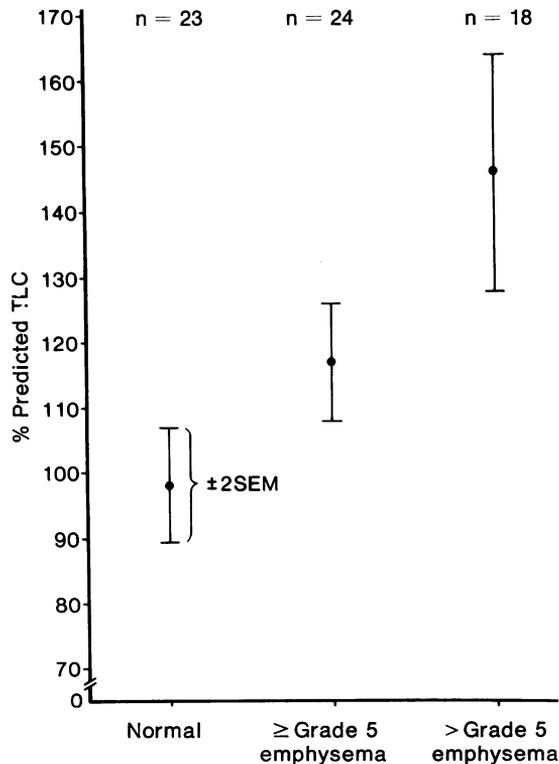


Fig 1 Mean percentage predicted total lung capacity \pm SEM is shown for the three lung groups examined ($p < 0.02$ between all three groups).

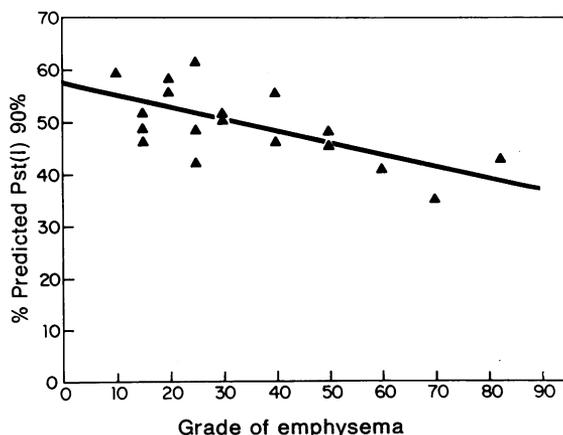


Fig 2 Percentage of predicted elastic lung recoil at 90% total lung capacity after Knudson *et al*⁷ is plotted against the score of emphysema for the > 5 emphysema group ($r = -0.696$, $p < 0.01$, $\blacktriangle = > \text{grade } 5 \text{ emphysema}$).

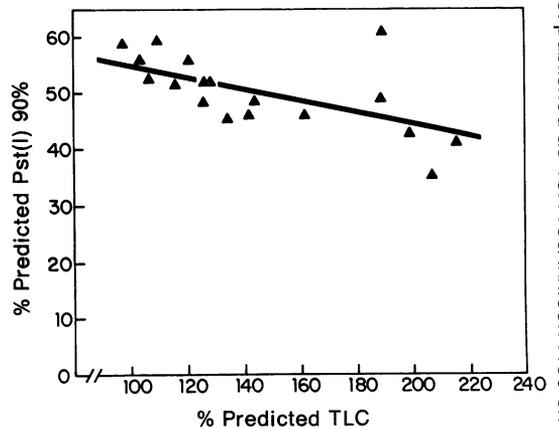


Fig 3 Volumes of the lungs as a percentage of predicted total lung capacity (TLC) is plotted against elastic recoil as a percentage of predicted elastic recoil at 90% total lung capacity ($r = -0.612$, $p < 0.01$, $\blacktriangle = > \text{grade } 5 \text{ emphysema}$). The predicted recoil values are after Knudson *et al*.⁷

properties of a lung independent of lung size, (fig 4). Nine of the greater than 5 emphysema groups and 14 of the less than grade 5 emphysema group were below the 2 SEE for normal lungs.

Discussion

Frank and associates found that older subjects demonstrated less lung elastic recoil¹³ than younger subjects.¹⁴ Permutt and Martin,¹⁵ however, concluded that there was no change of elastic recoil of the lung with age. Other studies since then have concluded that the decrease in lung elastic recoil is a function of aging^{7 8 11 16 19} in living subjects as well as studies of excised normal human lungs.¹² A decrease in elastic recoil has also been shown to be associated with advanced anatomical emphysema²⁰⁻²² as well as in mild emphysema from excised lungs.¹² Our study would support these earlier observations but raises the question whether emphysema is the sole cause of the loss of elastic recoil in addition to normal aging.

The data we obtained from the excised lungs are comparable with data from live subjects. We have compared the Pst(l) 50% obtained from all lungs against the transpulmonary pressure at 50% of the total lung capacity reported by Turner *et al*¹¹ (fig 5). All of the points fall at or below the regression line, and all but three are within the -2 SEE. Although the data

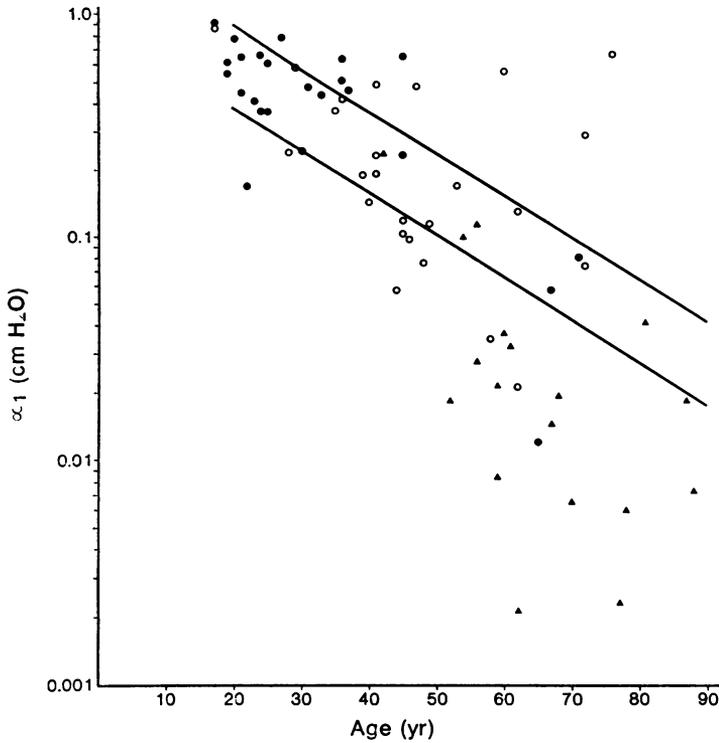


Fig 4 Semilogarithmic plot of α_1 related to age in all lungs studied (● = normal, ○ = \leq grade 5 emphysema, ▲ = $>$ grade 5 emphysema). Solid lines represent 2 SEE of the mean for normal lungs reported by Niewoehner *et al.*¹²

Turner and associates¹¹ included smokers and former smokers and therefore may contain data from subjects with mild emphysema. The purpose of this comparison is to demonstrate that the values we obtained are within limits seen in living subjects. These data are also similar to values obtained by Niewoehner *et al.*¹² from ex-

cised normal human lungs.

The low elastic recoil in excised lungs when compared to intact lungs suggests that excised lung TLC may be greater than in vivo TLC. Examination of the TLC of the normal lungs we have examined would indicate that our measurements of TLC agree very well with predicted

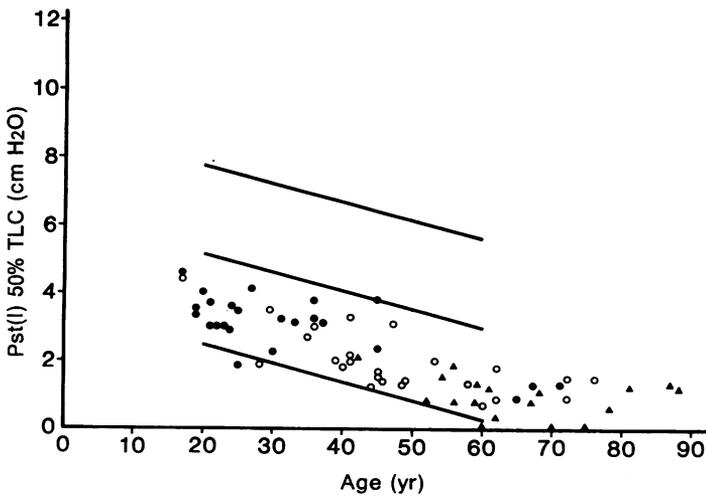


Fig 5 Comparison of elastic lung recoil at 50% total lung capacity and age, symbols as in fig 4. Solid lines are the mean and \pm SEE of Turner *et al.*¹¹

values. Thurlbeck concluded from a study of the comparison of TLC of human lungs fixed at necropsy with formalin at transpulmonary pressure of 25 cm of water were similar to their TLC assessed radiologically.² That study included lungs without emphysema as well as lungs with emphysema ranging from a score of 1 to greater than 65. Niewoehner and associates¹² have commented that excised lung pressure volume characteristics may more realistically describe the properties of the lung since chest wall characteristics and oesophageal balloon error are eliminated.

Since there is a difference in the sizes and volumes of the lungs we have studied, we have also used the method of Niewoehner and associates¹² which expresses the elastic properties of a lung independent of lung size and volume, α_1 (fig 5). Our study would support the observations of Niewoehner *et al*¹² that pressure-volume curve differences can be detected in mild emphysema and this difference is caused by elastic characteristics.

Our study tested the hypothesis that mild emphysema can be detected by pressure-volume curves by comparing elastic recoil data from normal subjects with lungs with only minimal anatomic emphysema—that is, grade 5 or less—compared in turn to a group with various degrees of advanced emphysema. We found that the group with minimal emphysema did have reduced elastic recoil compared to normal subjects when we expressed the static lung recoil as a percentage of predicted. It would thus appear from our data that changes in elastic recoil occur early with anatomical emphysema.

If emphysema and elastic recoil are related as cause and effect then a good correlation between the amount of emphysema and the loss of elastic recoil should be present. Linear correlations made between the grade of emphysema and the percentage of predicted elastic recoil at Pst(1) 90% did reveal a significant negative correlation ($r = -0.696$), but this correlation was not as strong as one would have expected if the loss of elastic recoil was directly related to the extent of emphysema. The predicted elastic recoil used for these correlations were after Knudson *et al*.⁷

Thurlbeck has speculated that since mean linear intercept was increased in a group of excised human lungs with mild emphysema compared with normal lungs, but the mean alveolar surface area corrected for an arbitrary lung volume of five litres was not altered, this suggested an increased lung volume.²³ More recently he has suggested that a change in lung volume

in patients with equivocal or mild degrees of anatomical emphysema could account for the mechanical property changes described with age in living subjects.² The data from the present study would support Thurlbeck's notion—that is to say, the increase in lung volume in the group with minimal emphysema is out of proportion to the extent of emphysema. The greater volume of the lungs noted at a given distending pressure must be derived from altered elasticity.

Although we found differences in percentage predicted TLC among the three groups examined the possibility remained that excised human lungs demonstrate an increase in percentage predicted TLC with age. Since age differences were present in the groups studied we tested the normal group with respect to percentage predicted TLC and age. No significant correlation was found ($r = 0.13$, $p > 0.05$). It is therefore possible that changes in elastic recoil and lung volume may precede the development of emphysema as judged by light microscopy. The greater than grade 5 group did show a correlation with the percentage predicted TLC and score of emphysema ($r = 0.618$, $p < 0.01$). This agrees with Thurlbeck's data.²

The cause of changes in elastic recoil in adult human non-emphysematous lungs is yet to be fully understood. Previous chemical analysis of lung elastin content of human lungs have demonstrated either an increase or constant amount of elastin in aging lungs.²⁴⁻²⁷ Recent studies in aging mice however, suggest that lung elastin content decreases with age.²⁸ Those authors believed that pseudoelastin could account for the findings in human lungs where elastin content was found to be increased or remained constant with age. This suggests that elastin in human lungs may decrease with age.

A study of elastic fibres of normal human lungs and lungs with mild emphysema, 1-10% by point count, demonstrate that no differences in total fibre length and diameter exist.²⁹ This would indicate that loss of elastic recoil is not the result of a simple loss of elastic fibres.

Our results show that elastic recoil in lungs with minimal emphysema is reduced and the total lung capacity is increased when compared to normal subjects. Since these changes are out of proportion to the degree of emphysema present we conclude that the loss of elastic recoil is not caused entirely by emphysema. Our results suggest that emphysema and elastic recoil are not related as cause and effect and that they may be related only coincidentally.

This notion is also consistent with the concept

and studies of Laros and associates³⁰ that elastic recoil may be altered by subtle changes in elastic junctions, connections, and abnormalities in the ground substance of the connective tissue of the lung.

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