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Pulmonary function of patients with spontaneous pneumothorax in relation to the extent of emphysema-like changes

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The aim of the present study was to analyse pulmonary function parameters of patients with spontaneous pneumothorax (SP) in relation to the extent of emphysema-like changes (ELCs). Pulmonary function tests were performed in 85 patients with unilateral SP, 6 weeks after video-assisted thoracoscopy (VAT). In 63 patients, thoracic computer tomography (CT) was obtained. An ELCs score, based on findings of CT and VAT, was used to quantify ELCs, ranging from 0 (expressing no ELCs) to 3 (expressing extensive ELCs). Emphysema-like changes were detected during VAT in 74% of patients, of which 70% were considered larger than 2 cm. An ELCs score ≥ 2 was found in 27 patients. Clinical characteristics of the patients grouped according to thoracoscopical findings and ELCs score did not differ, except for age. Patients with large ELCs were significantly older than patients without ELCs or small ELCs ($P=0{\cdot}0009$). In patients with large ELCs and ELCs score ≥ 2, increased mean percentages of predicted total lung capacity and decreased diffusing capacity (*K*CO) were found. None of the patients exhibited all pulmonary function criteria of emphysema, in contrast to 43% of the patients with an ELCs score ≥ 2. *K*CO was the only pulmonary function parameter which was decreased in smokers, especially in patients with large ELCs or ELCs score ≥ 2. Static lung compliance (C_{stat}) was the only pulmonary function parameter which was increased in patients with recurrent SP. The authors concluded that *K*CO is related to smoking behaviour and ELCs in patients with SP. C_{stat} is the only parameter which is increased in patients with recurrent SP. The discrepancy between pulmonary function and macroscopical parenchymal changes could be explained by the fact that not all patients with SP are old enough at presentation to show all signs of emphysema with pulmonary function testing. On the other hand, it might be possible that ELCs in SP cause different pulmonary function abnormalities than in centriacinar or panacinar emphysema.

Introduction

Spontaneous pneumothorax (SP) is defined as presence of air in the pleural cavity resulting from spontaneous rupture of the pulmonary parenchyma and visceral pleura. The exact pathogenesis of SP is unknown, but it is supposed that blebs and bullae play an important role, since they are nearly always found during surgery, not only in the affected lung (1–3) but also on the contralateral side (4–6). These blebs and bullae, also known as emphysema-like changes (ELCs), have also been demonstrated by computer tomography (CT) (7–9). The histopathological substratum of ELCs is known as distal acinar or paraseptal emphysema (10–12).

The peak incidence of SP is found in patients of 20–40 years of age. Until the presentation of SP, most of these patients do not have any pulmonary complaints (13). As in emphysema, smoking is a risk factor for the development of SP (14–16). It can be hypothesized that the demonstration of ELCs in SP is an initial sign of emphysema, although other clinical features may never become apparent, or not until several decades later.

As yet, no study of pulmonary function parameters has revealed sufficient evidence that SP is an early sign of pulmonary emphysema (17–20). However, the

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histopathology of the lung parenchyma or the macroscopical aspects of the visceral pleura were not studied in any of these reports. The aim of this prospective study was to analyse pulmonary function parameters of patients with SP, in relation to the presence and extent of ELCs demonstrated on thoracic CT scanning and during video-assisted thoracoscopy (VAT).

Materials and Methods

PATIENTS

From December 1991 to December 1994, all patients with unilateral SP were treated with VAT. Prior to VAT, thoracic CT scans were performed for the detection of large bullae to decide whether bullectomy would be necessary. Six weeks after VAT, patients underwent pulmonary function testing and serum α1-antitrypsin (α1AT) measurement.

Patients with known pulmonary disease were excluded from the study.

THORACIC COMPUTER TOMOGRAPHY

Prior to CT scanning, complete re-expansion of the affected lung was obtained by pleural drainage. Computer tomography scans were performed during maximal inspiration using a Siemens Somaton Plus CT scan (slice thickness 1 cm, 137 kV, 180 mAs).

VIDEO-ASSISTED THORACOSCOPY

Video-assisted thoracoscopy was performed during general anaesthesia with double lumen intubation and multiple ports of entry. Details of the operation technique and results of this approach have been published previously (21,22). Complete collapse of the lung was obtained in all cases. The appearance of the visceral pleura was judged as being normal or showing ELCs. If no ELCs were present, pleurodesis was performed by talc poudrage. Emphysema-like changes were considered small if they consisted of blebs or bullae smaller than 2 cm. Patients with small ELCs were treated with electro-cautery of ELCs and pleurodesis with talc poudrage. Emphysema-like changes were considered large if bullae were larger than 2 cm. Patients with large ELCs were treated with bullectomy by a stapling device (Autosuture Multifire EndoGIA® 3·5), and pleurodesis by pleural scarification. Vacuum drainage was continued until air leakage had ceased and the lung had been completely re-examined.

QUANTIFICATION OF EMPHYSEMA-LIKE CHANGES

In order to quantify the extent of ELCs, a scoring system (named ELCs score) based on findings of thoracic CT scanning and VAT was used. On CT, the absence of ELCs was scored 0; the presence of ELCs was scored 1; the unilateral presence of ELCs was scored 0, and the bilateral presence of ELCs was scored 1. During VAT, the absence of ELCs or presence of small ELCs were scored 0, the presence of large ELCs was scored 1. The ELCs score was calculated by adding the scores of CT and VAT. The ELCs score ranged from 0 (expressing absence of ELCs) to 3 (expressing presence of extensive ELCs). Patients were divided into two groups, consisting of patients with an ELCs score of less than 2 (<2) and of patients with a ELCs score of 2 or more (≥ 2).

PULMONARY FUNCTION TESTING

Forced expiratory volume in 1 s (FEV_1) and vital capacity (VC) were recorded using a pneumotachometer (Masterlab, Jaeger, Wurzburg). Parameters of diffusing capacity [*D*LCO), *D*LCO/VA (*K*CO)] were obtained using the single breath CO test, corrected for haemoglobin according to Cotes *et al.* (23) (Masterlab, Jaeger, Wurzburg). Total lung capacity (TLC), residual volume (RV) and airway resistance (*R*AW) were measured by using whole body plethysmography (Masterlab, Jaeger, Wurzburg). The lung compliance was measured by plotting the quasistatic volume–pressure curves using a latex oesophageal balloon and an expiratory shutter. The static lung compliance (C_{stat}) was calculated between FRC and FRC+0·5 l (24). All testing and calibration procedures were performed in accordance with the recommendations of the EGKS and European Respiratory Society (23–25). Normal predictive values for VC, FEV_1, TLC, RV, C_{stat} and parameters of diffusing capacity were taken from elsewhere (23–25).

Pulmonary function parameters were expressed as mean percentages of predicted.

STATISTICS

Analysis of patient characteristics and pulmonary function parameters were performed using one-way analysis of variance, unpaired *t*-tests for continuous variables and chi-square tests for categorical variables.

The correlation between two continuous variables was calculated by using Pearson's correlation coefficient. A P value of $\leq 0{\cdot}05$ was considered statistically significant.

Results

PATIENTS

From December 1991 to December 1994, 98 patients were admitted to the authors' hospital with

Table 1 Patient characteristics, grouped according to the thoracoscopical findings

	No ELCs	Small ELCs	Large ELCs	*P*
Mean age ± SD	25·6 ± 6·4	27·5 ± 10·0	37·1 ± 15·1	0·0009*
Sex (m/f)	13/5	19/4	37/7	0·54†
Recurrent SP	28%	30%	23%	0·77†
Smokers	67%	78%	61%	0·38†
Cigarettes smoked per day ± SD	12·1 ± 9·1	18·6 ± 14·1	12·6 ± 13·0	0·15*

P, significance of one-way analysis of variance* and Chi-square test†; SD, standard deviation; m, male patients; f, female patients; SP, spontaneous pneumothorax; ELCs, emphysema-like changes.

unilateral SP. Pulmonary function tests could be obtained in 85 patients 6 weeks after VAT. Patient characteristics grouped according to the thoracoscopical findings are shown in Table 1. Emphysema-like changes were detected during VAT in 74% (63 of 85 patients) of the patients, of which 70% (44 of 63 patients) were considered large. The mean age of the patients was 32·1 ± 12·4 years. The male:female ratio was 4·3:1. Sixty-seven percent of the patients were smokers and 26% had a recurrent SP at presentation. No differences in clinical characteristics, except age, existed between patients with large ELCs and patients without ELCs or with small ELCs. Patients with large ELCs were significantly older compared to patients without ELCs or with small ELCs ($P=0·0009$).

In 63 patients, thoracic CT scanning was performed prior to VAT. Emphysema-like changes were detected on CT in 56% (35 of 63 patients) of the patients, of which 46% (16 of 35 patients) were located bilaterally. One patient without ELCs on the affected side showed ELCs on the contralateral side. In 33% (21 of 63 patients) of the patients, large ELCs were demonstrated both on CT and during VAT. In 21% (13 of 63 patients) of the patients, no ELCS could be demonstrated on CT and during VAT. Based on these findings, 43% (27 of 63 patients) of the patients had an ELCs score ≥ 2.

In 47 patients, serum α1AT levels could be measured. Three (6%) of these patients showed a slightly decreased level.

ANALYSIS OF PULMONARY FUNCTION TEST PARAMETERS

Static lung volumes showed increased VC in 5% (four of 83 patients), increased TLC in 3% (two of 75 patients) and increased RV in 17% (13 of 75 patients) of the patients. Dynamic lung volumes showed decreased FEV_1 in 19% (16 of 83 patients) of the patients. Diffusing capacity parameters showed decreased *D*LCO in 37% (25 of 67 patients) and decreased *K*CO in 40% (27 of 67 patients) of the patients. C_{stat} was increased in 32% (16 of 50 patients) and *R*AW in 16% (10 of 63 patients) of the patients.

None of the patients showed all pulmonary function criteria of emphysema. Decreased *K*CO in combination with increased C_{stat} was seen in 16% (seven of 43 patients), with increased RV in 10% (seven of 67 patients) and with increased TLC in 3% (two of 67 patients) of the patients. One patient had decreased *K*CO in combination with both increased TLC and C_{stat}.

When analysing the effect of smoking on mean percentages of predicted pulmonary function parameters, TLC was significantly higher in smokers (95·8 ± 14·7%) than in non-smokers (88·1 ± 10·6%) ($P=0·02$). However, the number of patients with increased TLC was equally divided among smokers and non-smokers. Mean percentage of predicted *K*CO was significantly decreased in smokers (83·4 ± 13·3%) compared to non-smokers (75·9 ± 13·6%) ($P=0·05$). The number of cigarettes smoked per day was significantly correlated with the decrease of mean percentage of predicted *K*CO ($r=0·31$; $P=0·01$). All other pulmonary function parameters did not differ between smokers and non-smokers, and showed no correlations with the number of cigarettes smoked per day.

Patients with recurrent SP showed significantly increased mean percentage of predicted C_{stat} (110·2 ± 38·5%) compared to patients with first time SP (88·1 ± 24·6%). All other pulmonary function parameters did not differ between patients with recurrent SP and first-time SP.

Table 2 shows the mean percentages of predicted pulmonary function parameters of patients with SP, according to the thoracoscopical findings. Patients with large ELCs showed significantly decreased *K*CO (73·8 ± 11·0%) compared to patients with small or no ELCs (81·9 ± 15·2%) ($P=0·01$). Total lung capacity

Table 2 Mean percentages of predicted (± standard deviation) of pulmonary function parameters of patients with spontaneous pneumothorax, grouped according to the thoracoscopical findings

	No ELCs	Small ELCs	Large ELCs	*P*
FEV_1 (83*)	94·9 ± 11·4	91·0 ± 15·6	95·4 ± 16·2	0·54
VC (83*)	93·0 ± 14·3	87·2 ± 13·9	95·5 ± 4·1	0·10
FEV_1/VC (83*)	103·0 ± 10·8	104·8 ± 12·4	100·2 ± 11·5	0·30
TLC (72*)	85·2 ± 8·6	85·9 ± 11·8	96·0 ± 14·2	0·04
RV (72*)	85·2 ± 30·6	83·1 ± 12·9	98·9 ± 29·5	0·19
RV/TLC (72*)	99·0 ± 37·8	97·7 ± 27·1	95·0 ± 19·6	0.39
*R*AW (63*)	91·1 ± 33·1	91·0 ± 30·6	87·1 ± 41·3	0·91
*D*LCO (67*)	85·9 ± 15·2	87·6 ± 18·3	86·8 ± 17·7	0·97
*K*CO (67*)	79·0 ± 13·3	85·3 ± 16·8	73·8 ± 11·0	0·02
C_{stat} (50*)	104·9 ± 32·3	75·3 ± 13·8	91·9 ± 29·0	0·06

P, significance of unpaired *t*-test; *number of patients who underwent that specific pulmonary function test; FEV_1, forced expiratory volume in 1 s; VC, vital capacity; TLC, total lung capacity; RV, residual volume; *R*AW, airway resistance; *D*LCO, transfer factor; *K*CO, transfer factor per unit lung volume; C_{stat}, lung compliance at TLC, ELCs, emphysema-like changes.

was significantly increased in patients with large ELCs (95·8 ± 14·7%) compared to patients with small or no ELCs (88·1 ± 10·6%) ($P=0·02$), although the number of patients with increased TLC was not significantly different between the two groups.

Table 3 shows the mean percentages of predicted pulmonary function parameters according to the ELCs score, based on findings of CT and VAT. Patient characteristics and number of cigarettes smoked per day were not significantly different between patients with an ELCs score ≥2 and patients with an ELCs score <2. In patients with an ELCs score ≥2, significantly increased mean percentage of TLC ($P=0·006$) and decreased mean percentage of C_{stat} ($P=0·05$) were found compared to patients with an ELCs score <2. In patients with an ELCs score ≥2, mean percentages of VC and RV tended to be increased ($P=0·10$) and mean percentages of *K*CO tended to be decreased in patients with an ELCs score ≥2 ($P=0·07$). In smoking patients, *K*CO was significantly lower in patients with an ELCs score ≥2 (70·4 ± 14·6%) than in patients with an ELCs score <2 (78·8 ± 10·8%) ($P=0·05$). This latter finding could not be demonstrated in non-smoking patients. Other pulmonary function parameters did not show differences between patients with an ELCs score ≥2 and patients with an ELCs score <2.

Table 3 Mean percentages of predicted (± standard deviation) of pulmonary function parameters of patients with spontaneous pneumothorax, grouped according to the emphysema-like changes (ELCs) score based on findings of thoracic computed tomography scanning and video-assisted thoracoscopy

	ELCs score <2	ELCs score ≥2	*P*
FEV_1 (61*)	94·0 ± 14·0	96·7 ± 17·2	0·51
VC (61*)	91·5 ± 13·9	97·7 ± 14·8	0·10
FEV_1/VC (61*)	103·5 ± 12·1	99·2 ± 13·0	0·19
TLC (52*)	88·1 ± 11·3	99·0 ± 15·8	0·006
RV (52*)	87·0 ± 23·5	101·6 ± 35·9	0·10
RV/TLC (52*)	101·5 ± 30·0	94·7 ± 23·7	0·36
*R*AW (46*)	80·4 ± 28·8	90·4 ± 45·7	0·39
*D*LCO (53*)	85·3 ± 14·3	88·5 ± 20·3	0·52
*K*CO (53*)	80·5 ± 13·4	73·5 ± 13·6	0·07
C_{stat} (38*)	101·3 ± 28·7	81·2 ± 33·5	0·05

P, significance of unpaired *t*-test; *number of patients who underwent that specific pulmonary function test; FEV_1, forced expiratory volume in 1 s; VC, vital capacity; TLC, total lung capacity; RV, residual volume; *R*AW, airway resistance; *D*LCO, transfer factor; *K*CO, transfer factor per unit lung volume; C_{stat}, lung compliance at TLC.

Discussion

In the past, several studies have reported different results concerning the analysis of pulmonary function parameters in patients with SP (17–20). However, evaluation of histopathology of the lung parenchyma or macroscopical aspect of the visceral pleura formed no part of these studies.

In the present study, it was possible to compare pulmonary function parameters with macroscopical changes of the visceral pleura and pulmonary parenchyma. As far as age and smoking behaviour were concerned, they were comparable with the earlier published reports (17–20). The number of patients

with decreased α1AT levels was not significantly different from other findings (20).

Previously, decreased diffusing capacity parameters were demonstrated in 25–86% of patients with SP (17,18,20). The present study confirms this finding, showing a decreased *K*CO in 40% of patients, with a mean decline of 22·5% of predicted. Patients with large ELCs detected during VAT showed larger reduction of *K*CO compared to patients without or with small ELCs. Decreased diffusing capacity parameters have been reported in apparently healthy smokers caused by decrease of the gas exchanging surface, due to destruction of alveolar walls (26–28). This was also confirmed in the present study, showing a decrease of mean percentages of predicted *K*CO in smoking patients and a significant correlation with the number of cigarettes per day. Because the percentage of smokers and the number of cigarettes smoked per day did not differ between the patients without ELCs, with small and with large ELCs, one must conclude that the reduction of *K*CO not only reflects the smoking behaviour of the patients but also the presence and size of the ELCs found during VAT in patients with SP.

The incidence of SP has been reported to be higher in smokers and patients with ELCs (14–16). In the present study, 33% of patients did not smoke. In these patients, the presence and size of ELCs was not significantly different from patients who smoked. Previously, the authors did not demonstrate any relation between the occurrence of recurrent pneumothoraces and the presence of ELCs found during VAT (29). Hence, the relation between the smoking habit of the patients and the increased risk of contracting a pneumothorax seems to be independent of the presence of ELCs. This is also supported by the fact that *K*CO was not significantly different between patients with first-time and recurrent SP. The static lung compliance was the only parameter which was significantly higher in patients with recurrent SP.

In order to quantify both subpleural and intrapulmonary ELCs, a scoring system based on findings of thoracic CT scanning and VAT was used. Previous studies reported detection of ELCs with CT in up to 80% of the patients with unilateral SP in the affected lung and in 31% of the patients on the contralateral side (7–9). In the present study, ELCs were found with CT in 56% of patients. A comparable percentage of patients with large ELCs (51%) was seen during VAT. However, in only 33% of patients, ELCs were detected both by CT and VAT. The discrepancy in detection of ELCs between CT and VAT can be explained by several reasons. On one hand, CT demonstrates not only sub-pleural ELCs but also intrapulmonary ELCs which can not be detected by VAT. On the other hand, small ELCs can remain undetected on CT using 10 mm slices in case they are localized in an area just between two slices. Therefore, the authors decided to use 2 cm as the cut-off point for the detection of ELCs on CT and during VAT.

Using the scoring system of ELCs, a reduction of *K*CO was also demonstrated in patients with extensive subpleural and intra-pulmonary ELCs, especially in smokers. Therefore, *K*CO is a good pulmonary function parameter to quantify smoking behaviour and ELCs in patients with SP.

In the present study, increased mean percentages of TLC were found in patients with extensive subpleural and intrapulmonary ELCs. However, a reliable explanation of this finding can not be given because the patients underwent different kinds of treatment, influencing the static lung volumes in different manners.

None of the patients exhibited all pulmonary function criteria of emphysema in contrast to 43% of the patients who showed an ELCs score ≥ 2. On the one hand, the discrepancy between pulmonary function and macroscopical pulmonary changes could be explained by the relatively young age of the patients, since previous reports demonstrated that aging resulted in a homogeneous enlargement of the alveolar air spaces (30,31). These changes preceded emphysema and were responsible for loss in lung elasticity. Additional destruction of pulmonary parenchyma occurred in smokers, resulting in emphysema (32). These histopathological changes are reflected by the decline of pulmonary function occurring between 23 and 35 years (33). On the other hand, it might be possible that ELCs in SP cause different pulmonary function abnormalities than in centriacinar or panacinar emphysema.

A follow-up study over several decades analysing pulmonary function parameters of patients with SP and healthy volunteers will be needed to answer the question whether more patients with SP will develop clinical emphysema compared to the healthy volunteers.

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