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Impaired lung compliance and $D_{L,CO}$ but no restrictive ventilatory defect in sarcoidosis

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ABSTRACT: Sarcoidosis is a systemic granulomatous disease with predominant manifestation in the lungs, often presenting as interstitial lung disease. Pulmonary function abnormalities in sarcoidosis include restriction of lung volumes, reduction in diffusing capacity of the lung for carbon monoxide ($D_{L,CO}$), reduced static lung compliance ($C_{L,s}$) and airway obstruction. The aim of the present study was to assess various lung function indices, including $C_{L,s}$ and $D_{L,CO}$, as markers of functional abnormality in sarcoidosis patients.

Results from 830 consecutive patients referred for lung function tests with a diagnosis of sarcoidosis (223 in stage I, 486 in stage II and 121 in stage III) were retreospectively analysed. The mean±SD age of the patients was 40±11 yrs; 18% were active smokers and 24% were former smokers.

Normal total lung capacity was found in 772 (93%) patients. Of these cases, 24.5% had a low $C_{L,s}$ and 21.5% had a low $D_{L,CO}$. At least one abnormality was observed in 39.3% of these patients, whereas, in restrictive patients, this figure was 88%. Airway obstruction was present in 11.7% of cases.

Lung volumes usually remain within the normal range and measurement of either $C_{L,s}$ or $D_{L,CO}$ often reveal impaired lung function in sarcoidosis patients, even when their lung volumes are still in the normal range; these two measurements provide complementary information.

KEYWORDS: Diffusion capacity, lung compliance, pulmonary function tests, restriction, sarcoidosis

Sarcoidosis is a systemic granulomatous disease of unknown aetiology characterised by the formation of granulomas in the lungs and intrathoracic lymph nodes [1]. In progressive sarcoidosis, cellular infiltrates in the lung transform into fibrotic changes, causing interstitial lung disease (ILD) [2, 3].

Sarcoidosis forms part of a group of ILDs which are characterised by diverse clinical and histopathological manifestations, sharing a common basic pattern of functional impairment. The basic mechanism of lung function impairment is assumed to be decreased lung compliance (lungs become stiffer, less compliant) so that the static expiratory pressure–volume (P–V) curve of the lung is shifted downwards and to the right compared with normal subjects. The P–V curve is contracted along its volume axis, as both total lung capacity (TLC) and vital capacity decrease [4, 5]. The transpulmonary pressure near TLC is increased, which reflects the greater mechanical advantage of the diaphragm, the force-generating capacity of which is enhanced at the diminished lung volume in ILD. Static lung compliance ($C_{L,s}$), measured from the P–V curve, is one of the parameters that reflect the mechanical properties of the lung tissue, but it is rarely measured in clinical settings. Figure 1 shows an example of $C_{L,s}$ measurement in a patient with sarcoidosis and a low TLC.

An increased alveolar–arterial oxygen tension gradient and resting hypoxaemia also occur with more severe ILD [6]. The arterial carbon dioxide tension is usually normal but may be reduced at rest in a proportion of patients due to alveolar hyperventilation [6]. The diffusing capacity of the lung for carbon monoxide ($D_{L,CO}$) is characteristically reduced in ILDs, and to a greater extent

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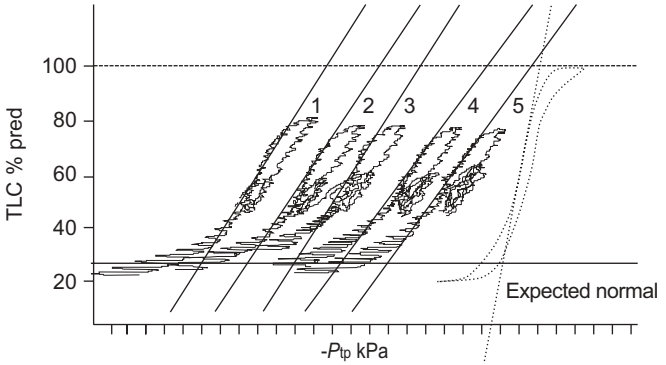

FIGURE 1. An example of a set of five pressure–volume curves in a patient with sarcoidosis and restriction of lung volumes. The slopes of the tangents on the expiratory limbs of the curves represent static lung compliance ($C_{L,s}$). ·····: expected normal $C_{L,s}$ (3.62 L·kPa^{-1}); —: predicted residual volume; ---: predicted total lung capacity (TLC). The patient's $C_{L,s}$ was very low. -P_{tp}: negative transpulmonary pressure.

than the TLC at which it is measured [7]. Spirometry and $D_{L,CO}$ measurements are recommended tests in the initial evaluation of the magnitude of functional lung involvement, but the prognostic value of $D_{L,CO}$ in sarcoidosis is poor [1, 8].

Although a restrictive ventilatory defect, characterised by the reduction in static lung volumes, and impaired gas exchange, expressed as reduced $D_{L,CO}$, are classically considered the most prevalent pattern of lung function abnormality in ILD, airway obstruction has also been reported [7, 9–13].

The National Tuberculosis and Lung Diseases Research Institute (Warsaw, Poland) serves as the regional referral centre for patients with sarcoidosis and other ILDs. All patients with chronic interstitial markings on chest radiographs or lung computed tomography (CT) scans seen by their pulmonary specialists are referred to the pulmonary function testing (PFT) laboratory for measurement of lung volumes, single-breath $D_{L,CO}$ and $C_{L,s}$. This practice provided the opportunity to describe patterns of lung function abnormality from a much larger group of patients with sarcoidosis than previously reported [7, 9, 10, 12–16]. One study reported a comparable number of subjects, but PFT results were not reported [17].

The main purpose of the present investigation was to describe lung function abnormalities and determine the rates of lung function impairment expressed as reduced $D_{L,CO}$ and/or reduced $C_{L,s}$ in patients with sarcoidosis, especially those with no volume restriction.

This study was approved by the local Ethics Committee (National Tuberculosis and Lung Diseases Research Institute).

METHODS

The study group consisted of 830 patients with sarcoidosis (387 females and 443 males, all Caucasian) referred consecutively for PFT evaluation, at the time of diagnosis or during follow-up, over a period of almost 4 yrs. Only the first result was considered if the patient was assessed on more than one occasion; usually, this was the initial PFT evaluation, and so the majority of patients were not being treated at the time of the present investigation. In the majority of cases (85%), the diagnosis was confirmed by histopathological examination. In most cases, endobronchial biopsy was performed, but mediastinoscopy, transbronchial biopsy, video-assisted thoracoscopy or open-lung biopsy were also used. In a minority of patients with no histopathological confirmation (15%), clinical features, such as Löfgren's syndrome, regression of the disease without treatment and exclusion of other causes of hilar lymphadenopathy, were used to establish the diagnosis of sarcoidosis with a high degree of confidence, in agreement with the European Respiratory Society (ERS)/American Thoracic Society (ATS) 1999 statement on sarcoidosis [1]. Radiographic stages were defined in accordance with the same statement [1]. The study group characteristics are presented in table 1.

All patients underwent a standard evaluation that included history, physical examination, chest radiography, spirometry and flow–volume curve, whole-body plethysmography, $C_{L,s}$ and single-breath $D_{L,CO}$. All treated patients were asked not to use any inhalers $\leqslant$24 h before the tests. ERS guidelines were followed for all lung function measurements [18, 19]. All PFTs were performed using a MasterScreen system (software version 4.65; Jaeger, Würzburg, Germany).

Semi-static lung compliance was measured from quasi-static expiratory *P–V* curves using the standardised oesophageal pressure method [19]. Details are provided in the online supplementary material. This measurement is routine procedure in our laboratory (Lung Function Laboratory, National Tuberculosis and Lung Diseases Research Institute, Warsaw, Poland; ~1,000 measurements annually) and is only sporadically refused by patients. Adverse effects (*e.g.* nasal and throat bleeds, vomiting and nausea) occur a few times a year and are not threatening. In general, this procedure is safe for patients.

Reference equations for spirometry were taken from the study of FALASCHETTI *et al.* [20] and those for lung volumes and $D_{L,CO}$ from the ERS guidelines [18, 21]. For $C_{L,s}$, reference values taken from COLEBATCH *et al.* [22] were used. $D_{L,CO}$ results were

TABLE 1 Characteristics of patients with sarcoidosis stratified by disease stage

	Stage I	Stage II	Stage III	p-value
Subjects n	223	486	121	
Females %	45.7	45.9	51.2	0.54
Age yrs	39.1 (24–64)	40.1 (24–63)	43.7 (24–63)	0.001
Smoking status %				
Active smoker	13.5	21.6	14.9	0.001
Ex-smoker	18.4	25.1	31.4	0.001
Never-smoker	68.2	53.3	53.7	0.001
Ever-smokers n	71	227	56	
Smoking exposure pack-yrs	4.5 (0.2–20.0)	6.0 (0.5–45.0)	7.5 (0.5–40.0)	0.01

Age data are presented as mean (95% CI) and smoking exposure data as median (95% CI).

corrected for haemoglobin concentration [23]. Following the ATS/ERS 2005 guidelines, the lower limit of normal (LLN) was set at the level of the 5th percentile (or mean - 1.645 SD) of each reference population [24]. Results were expressed as percentage predicted, as is conventional; however, as the mean predicted value falls with age and the scatter does not fall proportionately, percentage predicted leads to an age-, height- and sex-related bias. Therefore, standardised residuals (SR = (observed – predicted)/residual SD) [18], which are free of such bias, were also calculated. Data are presented as mean (95% CI). For each disease stage, the percentage of subjects whose pulmonary function index was below the LLN was also calculated.

Statistical analysis

Differences between the various disease stages were analysed using the general linear model ANOVA, with pulmonary function expressed as percentage predicted or SR as the outcome variable, disease stage and sex as predictors, and age, height and smoking exposure expressed as daily tobacco consumption, years smoked or pack-years as confounding variables. Levene's test did not disclose inhomogeneity of variance. A p-value of <0.05 was regarded as significant. Group comparisons were made using paired t-tests for independent samples to clarify whether significant differences detected with ANOVA translated into significant differences between all groups; applying Bonferroni correction, a p-value of <0.017 was considered significant. The Chi-squared test was used to test for differences in the prevalence of observations below the LLN. Statistical analyses were performed using STATISTICA, version 8.0 (StatSoft, Inc., Bedford, UK).

RESULTS

The mean $\pm$SD age of the patients was 40.3 $\pm$ 10.9 yrs (range 19–75 yrs). There were 223 (26.9%) patients in stage I, 486 (58.6%) in stage II and 121 (14.6%) in stage III of the disease. Only six cases were classified as stage IV and their lung function indices were not statistically different from those patients in stage III, and so they were included in stage III for the present analysis.

Analysis of variance revealed that, after taking into account age, height and sex, disease stage was a significant ($p<0.01$) predictor for all PFT indices, except the forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC) and residual volume/TLC ratios, and forced expiratory flow at 25–75% FVC ($FEF_{25-75\%}$). Smoking variables were only related to $D_{L,CO}$. The most frequent PFT abnormalities in all patients were reduced $C_{L,s}$ (27.8%) and reduced $D_{L,CO}$ (25.7%) (table 2).

Only 58 of the 830 patients with sarcoidosis had a low TLC (the classic pattern of restriction). In this restrictive group of patients, $D_{L,CO}$ and $C_{L,s}$ were reduced in 81 and 72.4% of cases, respectively, at least one abnormal finding being observed in 88% of these patients. Another 33 patients showed a reduced FVC but normal TLC (a nonspecific pattern). Of the 772 patients with normal lung volumes, figure 2 shows those with a low $D_{L,CO}$ and/or low $C_{L,s}$. The distributions of $D_{L,CO}$ and $C_{L,s}$ results in the 772 patients are presented in figure 3, showing a shift towards abnormally low values.

Airflow obstruction (FEV_1/FVC <LLN) was detected in 97 (11.7%) patients. Using ATS/ERS guidelines to grade severity [24], obstruction was mild (FEV_1 >70% pred) in the majority (n=77), moderate in 15 patients and severe in four patients. The mean duration of smoking in the 153 current smokers and 201 former smokers was 9.0 yrs.

In the 772 patients with a TLC within normal limits, $C_{L,s}$ identified more subjects with abnormal lung compliance than did $D_{L,CO}$ (24.5 (189 out of 772) *versus* 21.5% (166/772), but the difference (3%-points, 95% CI 0.072– -0.012) was nonsignificant (Chi-squared test). The detailed distribution of patients with different types of lung function disturbances, stratified according to stage of disease, is presented in table 3 (and figures in the online supplementary material).

The patient characteristics of those with normal $D_{L,CO}$ and normal $C_{L,s}$ (n=476) were compared with those with abnormal $D_{L,CO}$ and/or abnormal $C_{L,s}$, irrespective of a restrictive ventilatory defect. A reduced $C_{L,s}$ was more frequently observed in females and in older patients (table 4). Ever-smokers with a greater number of pack-yrs of smoking exposure were more likely than other patients to exhibit a low $C_{L,s}$ and low $D_{L,CO}$.

DISCUSSION

The lung function measurements in this large group of patients with pulmonary sarcoidosis revealed that only 7% presented with restriction of lung volumes, despite parenchymal involvement visible on the chest radiograph in approximately three-quarters of these patients (stages II–IV). Previous investigators have also reported normal lung volumes in the majority of patients with stage I or II sarcoidosis [15, 26]. The cause of a restrictive ventilatory defect in sarcoidosis patients may be more complex and respiratory muscle weakness should also be considered [27].

$D_{L,CO}$ and $C_{L,s}$ tests were much more sensitive than lung volumes in detecting functional disturbances in sarcoidosis. This corroborates findings from previous smaller studies [1, 16, 28–30]. When only hilar lymphadenopathy is seen on the chest radiogaph (stage I sarcoidosis), parenchymal involvement is present in some patients and is often noted on high-resolution lung CT scans [31]. This may explain the low $D_{L,CO}$ and $C_{L,s}$ in the present patients with stage I sarcoidosis (low $D_{L,CO}$ in 13% and low $C_{L,s}$ in 17%). In previous studies, a reduced $C_{L,s}$ was frequently observed in ILD patients with reduced lung volumes [32–36]. However, in only one study was lung compliance measured in patients with ILD but normal lung volumes [37]. In the present study, $C_{L,s}$ was abnormally low in 72.4% of patients with lung volume restriction (TLC < LLN). The proportion of findings of abnormal $D_{L,CO}$ and $C_{L,s}$ correlated well with the clinical staging of the disease (table 2), underlining that these indices reflect clinically relevant disease-related lung damage.

$D_{L,CO}$, a measure of gas transfer in the lungs, is highly dependent upon pulmonary vascular blood volume. Therefore, a low $D_{L,CO}$ usually suggests alveolitis or vasculitis in sarcoidosis patients [38, 39]. Other causes of a low $D_{L,CO}$ (*e.g.* emphysema or marked uneven ventilation distribution) cannot explain the findings in the present patients. However, a low $C_{L,s}$ may not be due solely to parenchymal pathology. Fibrotic changes or infiltrates in the airway walls may stiffen the bronchi, which act as a supporting frame for lung tissue; thus pathological changes in small airways may contribute to apparent lung stiffness.

TABLE 2 Pulmonary function test results from all 830 patients with sarcoidosis, stratified by disease stage

	Stage I	Stage II	Stage III
Subjects n	223	486	121
FVC			
% pred	102.7 (73.9–127.5)	98.0 (72.7–122.2)	90.2 (56.2–112.4)
SR	0.22 (-1.88–2.30)	-0.15 (-2.25–1.71)	-0.78 (-3.42–0.98)
Subjects with low FVC %	4.0	8.2	19.8
FEV_1			
% pred	100.8 (71.4–128.3)	95.4 (64.3–120.9)	88.2 (50.8–113.9)
SR	0.07 (-2.21–2.46)	-0.38 (-2.89–1.78)	-1.0 (-4.11–1.09)
Subjects with low FEV_1 %	8.1	15.8	25.6
FEV_1/FVC			
%	80.5 (70.3–91.0)	79.6 (63.8–92.7)	79.5 (64.7–94.1)
SR	-0.32 (-2.34–1.26)	-0.44 (-2.95–1.55)	-0.37 (-2.82–1.97)
Subjects with obstruction %	6.3	13.2	15.7
$FEF_{25–75\%}$			
% pred	87.9 (40.8–137.6)	81.8 (32.5–138.9)	74.0 (27.5–137.3)
SR	-0.50 (-2.48–1.78)	-0.72 (-2.64–1.79)	-1.02 (-2.99–1.69)
Subjects with reduced $FEF_{25–75\%}$ %	13.5	23.0	28.9
TLC			
% pred	107.2 (82.4–134.2)	103.7 (77.7–129.7)	97.1 (62.3–121.3)
SR	0.62 (-1.7–2.97)	0.31 (-2.14–2.57)	-0.30 (-3.01–1.77)
Subjects with low TLC %	2.7	5.3	21.5
VC			
% pred	111.8 (84.1–144.5)	107.0 (78.5–138.7)	100.0 (60.6–128.2)
SR	0.92 (-1.50–3.30)	0.52 (-2.12–2.81)	-0.08 (-2.81–1.94)
Subjects with low VC %	1.8	3.9	15.7
RV/TLC			
% pred	92.0 (57.3–124.0)	95.9 (64.3–130.8)	98.4 (63.9–142.0)
SR	-0.40 (-2.13–1.37)	-0.21 (-2.00–1.66)	-0.1 (-2.19–2.19)
Subjects with high RV/TLC %	1.3	2.9	5.8
$D_{L,CO}$			
% pred	92.4 (69.9–118.4)	87.1 (59.4–113.5)	77.9 (42.4–105.7)
SR	-0.60 (-2.42–1.41)	-0.97 (-3.13–1.12)	-1.63 (-4.03–0.51)
Subjects with low $D_{L,CO}$ %	13.0	26.7	44.6
$C_{L,s}$			
% pred	77.6 (42.7–127.6)	69.6 (34.8–110.0)	62.4 (17.6–112.4)
SR	-0.88 (-2.35–0.97)	-1.19 (-2.69–0.35)	-1.50 (-3.23–0.45)
Subjects with low $C_{L,s}$ %	17.0	29.2	42.1
$C_{L,s}$ reference values#			
% pred	86.1 (53.0–126.9)	77.9 (41.5–116.9)	70.5 (24.9–119.6)
SR	-0.73 (-2.79–1.47)	-1.15 (-3.25–0.88)	-1.55 (-3.79–1.07)
Subjects with low $C_{L,s}$ %	21.5	33.5	46.3

Values are expressed as mean (95% CI), unless otherwise stated. FVC: forced vital capacity; % pred: % predicted; SR: standardised residual; FEV_1: forced expiratory volume in 1 s; $FEF_{25–75\%}$: forced expiratory flow at 25–75% FVC; TLC: total lung capacity; VC: vital capacity; RV: residual volume; $D_{L,CO}$: diffusing capacity of the lung for carbon monoxide; $C_{L,S}$: static lung compliance. #: reference values from BEGIN *et al.* [25].

Patients with both low $C_{L,s}$ and low $D_{L,CO}$ were more likely to exhibit airway obstruction, perhaps because of more widespread disease involving both parenchyma and airways. They were also more likely to be ever-smokers with more pack-years of smoking exposure (table 4). ANOVA revealed no relation between PFT results and smoking status (including ever-/never-smokers as categorical predictor and pack-years of smoking as continuous predictor). Differences were found between ever-smokers and never-smokers, and were statistically significant, but only for TLC and $D_{L,CO}$; however, they were too small to be clinically important. Interestingly, lung function indices attributed to airway obstruction (which are expected to be affected by smoking) were comparable between ever- and never-smokers (table in online supplementary material). This observation is in agreement with some data suggesting that smoking may even play a protective role in sarcoidosis [40, 41].

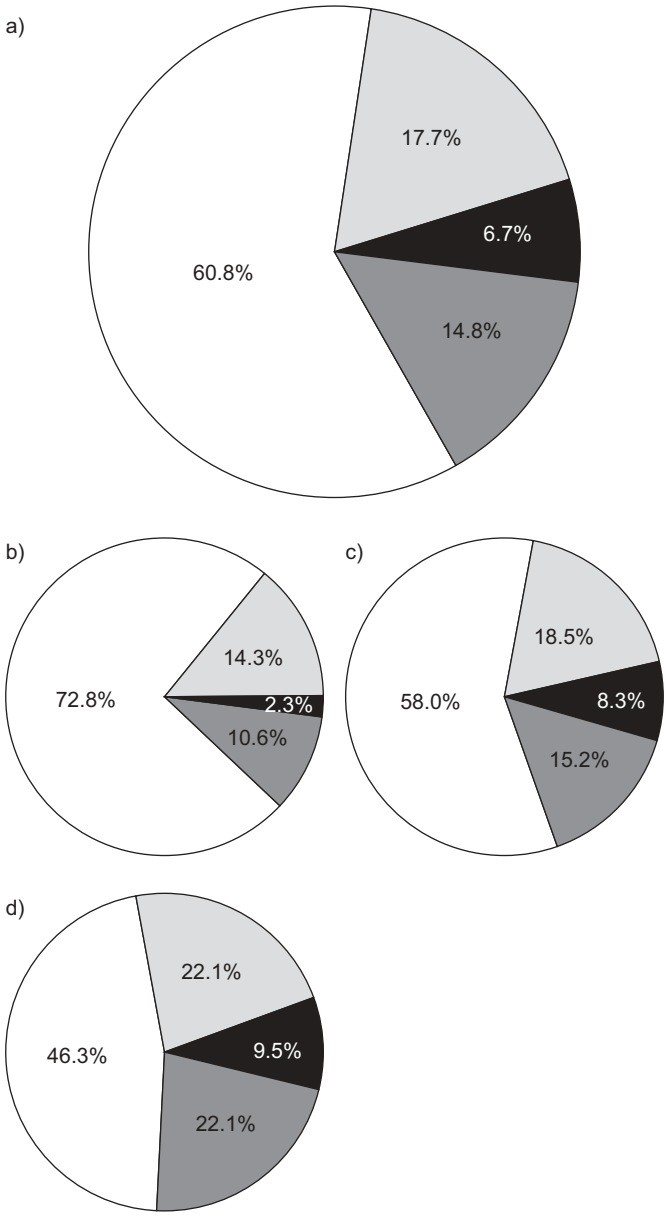

FIGURE 2. Distribution of abnormally low static lung compliance ($C_{L,s}$; ▫), abnormally low diffusing capacity of the lung for carbon monoxide ($D_{L,CO}$; ■), both low $C_{L,s}$ and low $D_{L,CO}$ (■), and normal $C_{L,s}$ and $D_{L,CO}$ (□) in patients without restriction of lung volumes in a) all subjects (n=772), and in groups stratified by stage of sarcoidosis: b) stage I (n=217), c) stage II (n=260) and d) stage III (n=95).

$C_{L,s}$ was most frequently reduced in females (35.9 *versus* 20.7%). This finding is independent of the choice of reference equations; using those from BEGIN *et al.* [25], the prevalence was 36.4 and 28.5%, respectively. Older patients were also more likely than younger patients to show a low $C_{L,s}$, perhaps because long-standing disease causes more fibrosis.

Airway obstruction is more common in sarcoidosis than in other ILDs. Approximately 6% of the present patients in stage I and 13–16% of those in stages II and III exhibited a low FEV1/FVC; however, statistical analysis (ANOVA) did not confirm the relationship between this index and stage of disease. These rates are lower than those reported by others, perhaps because

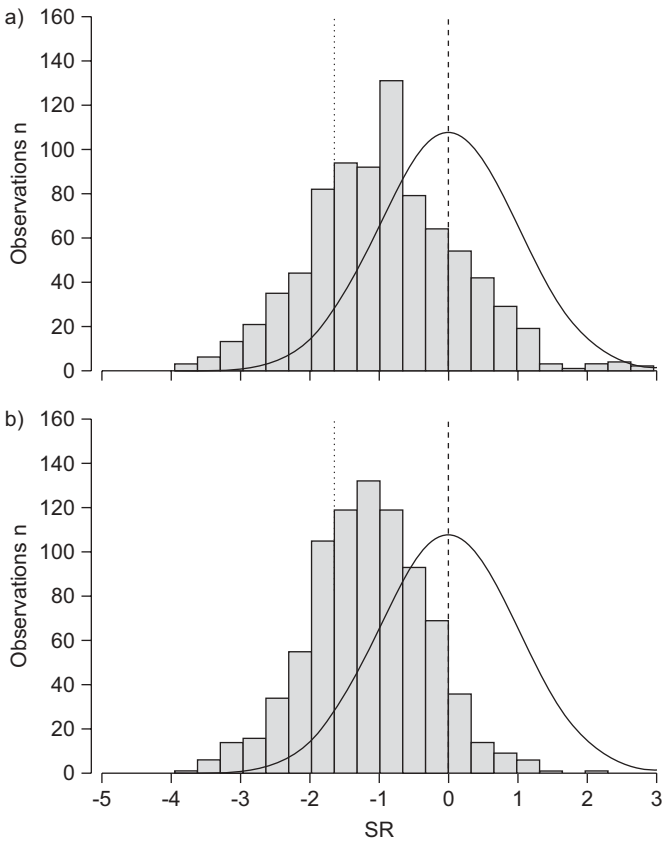

FIGURE 3. Distribution of a) diffusing capacity of the lung for carbon monoxide and b) static lung compliance in 772 patients with sarcoidosis but normal lung volumes. ·····: lower limit of normal (LLN); -----: predicted values based on the standardised residuals (SR). ——: expected normal distribution for healthy adults.

of differences in the definition of airway obstruction [42, 43]. Judged by a low $FEF_{25-75\%}$, as was done in previous studies, airway obstruction was about twice as prevalent as when using FEV1/FVC. However, current ATS/ERS guidelines for the interpretation of PFTs discourage using $FEF_{25-75\%}$ to define airway obstruction [24]. Moreover, the physiological meaning of a low $FEF_{25-75\%}$ in sarcoidosis patients is unclear. Other studies may have used FEV1/FVC <0.70 to define airway obstruction, but this causes considerable misclassification [24, 44].

Study limitations

The present study was a retrospective, cross-sectional analysis based on the group of sarcoidosis patients seen in the laboratory over a 4-yr period. The number of cases required to demonstrate significant differences was not established beforehand. The numbers of cases in each group and proportion of them reflects the real distribution of patients in our laboratory and hospital.

Ideally, statistical analyses would have made use of matched controls; however, this was not feasible for this study, thus reference values were used. The reference values for the various PFTs that were performed did not come from a single source, but relate to different samples of healthy subjects. Thus the predicted values and LLNs from each of these studies may have caused some misclassification of abnormality rates in the

TABLE 3 Prevalence of abnormal static lung compliance ($C_{L,s}$), diffusing capacity of the lung for carbon monoxide ($D_{L,CO}$) or both in patients in whom total lung capacity was within normal limits

	Stage I	Stage II	Stage III	Total
Normal $C_{L,s}$ and $D_{L,CO}$	158 (72.8) [33.7]	267 (58.0) [56.9]	44 (46.3) [9.4]	469 [100]
Low $C_{L,s}$	31 (14.3) [22.6]	85 (18.5) [62.0]	21 (22.1) [15.3]	137 [100]
Low $D_{L,CO}$	23 (10.6) [20.2]	70 (15.2) [61.4]	21 (22.1) [18.4]	114 [100]
Low $C_{L,s}$ and $D_{L,CO}$	5 (2.3) [9.6]	38 (8.3) [73.8]	9 (9.5) [17.3]	52 [100]
Total	217 (100)	460 (100)	95 (100)	772 (100) [100]

Data are presented as n (% stage total) [% condition total].

present patients. Predicted values for $C_{L,s}$ are poorly established and the present techniques may not have exactly matched those used by the reference study. We chose the predicted values of COLEBATCH *et al.* [22] because they were based on the highest number of healthy subjects (83 males and 40 females) and included information about the scatter of the results (SD). However, the present findings on lung compliance are, to a minor extent, influenced by such a choice. Using the prediction equations of BEGIN *et al.* [25] (based on only 40 healthy males and 26 healthy females), somewhat higher percentages of an abnormally low $C_{L,s}$ were obtained in all groups. Additional reference values for $C_{L,s}$ based on an even higher number of subjects have recently been published [45], but they were limited to males and did not include variance data and could, therefore, not be used in the present study. If the true LLN range for $C_{L,s}$ were lower for the present patients (or the true LLN for TLC were higher), the number of abnormal (decreased) $C_{L,s}$ measurements would have been overestimated.

The use of specific $C_{L,s}$ (*e.g.* $C_{L,s}$/functional residual capacity ratio) has the potential advantage that it can be regarded as a parameter of lung mechanics that is independent of lung volume. However, only very limited reference value data are available. Moreover, the large majority of patients exhibited normal lung volumes, so adjusting for lung volume would have had limited impact on the results.

Quasi-static expiratory *P–V* curves were used to assess $C_{L,s}$ (slow expiration from TLC, without interruptions forced by a shutter). This may lead to underestimation of $C_{L,s}$ in patients with increased airway resistance, particularly if airflow is not very low [19]. However, airway obstruction with increased airway resistance (>0.35 kPa·L^{-1}·s) occurred in only eight cases (<1% of the group) and expiratory flow during measurements was low (0.3 L·s^{-1}). Moreover, the comparative studies in some patients showed good agreement between semi-static lung compliance and $C_{L,s}$ (online supplementary material).

TABLE 4 Characteristics of 830 patients with sarcoidosis, stratified by diffusing capacity of the lung for carbon monoxide ($D_{L,CO}$) and static lung compliance ($C_{L,s}$) abnormality

	Normal $C_{L,s}$/normal $D_{L,CO}$	Low $C_{L,s}$	Low $D_{L,CO}$	Low $C_{L,s}$/low $D_{L,CO}$
Subjects n	476	141	123	90
Cases in stages I/II/III %	33.8/56.5/9.7	23.4/61.7/14.9	19.5/61.0/19.5	5.6/66.7/33.3
Females %	41.6	68.1	40.7	47.8
Age yrs	38.2±9.5	48.0±11.1	35.9±8.5	45.7±12.9
Weight kg	79.8±15.5	75.6±13.6	77.2±16.1	74.6±14.8
Height cm	172.0±9.3	163.2±8.8	174.6±9.3	167.3±11.0
Ever-smokers %	40.7	35.5	54.5	47.8
Smoking exposure# pack-yrs	7.5±8.1	9.6±9.9	8.6±9.0	15.7±18.0
FVC % pred	103.9±11.3	95.2±12.4	93.4±10.8	78.4±12.2
VC % pred	112.3±13.9	108.2±17.2	100.9±12.9	87.5±15.7
TLC % pred	108.4±11.8	102.1±11.7	99.7±12.9	86.2±14.1
RV/TLC % pred	92.9±16.1	98.1±16.2	95.4±20.0	103.1±20.6
FEV_1/FVC %	80.0±6.4	79.6±6.7	80.2±7.2	78.6±8.2
Subjects with abnormal FEV_1/FVC %	11.1	7.8	12.2	20.0
$FEF_{25–75\%}$ % pred	88.1±25.6	78.8±29.1	81.6±25.6	63.4±31.1
Subjects with abnormal $FEF_{25–75\%}$ %	14.9	22.7	23.6	50.0

Data are presented as mean±SD, unless otherwise stated. FVC: forced vital capacity; % pred: % predicted; VC: vital capacity; TLC: total lung capacity; RV: residual volume; FEV_1: forced expiratory volume in 1 s; $FEF_{25–75\%}$: forced expiratory flow at 25–75% FVC. #: ever-smokers only.

This was a cross-sectional study of patients at various stages of disease. Some patients may have had above-average PFT results before the onset of disease, and, despite having lost lung function, the test results may have remained within normal limits. Measurement of change in lung function over a prolonged period would be more sensitive in such cases.

We believe that lung function assessment in sarcoidosis patients should include $C_{L,s}$ measurement as a method of evaluation of the mechanical properties of the lungs, as it discloses abnormalities in pulmonary function that are not detected by measurement of lung volumes and $D_{L,CO}$. $C_{L,s}$ and $D_{L,CO}$ concern different aspects of respiratory pathophysiology, and they complement, rather than overlap, each other in revealing lung function disturbances at all stages of the disease. The functional abnormalities are likely to reflect parenchymal involvement and correlate well with clinical staging, but further studies are required in order to assess the prognostic value of a low $C_{L,s}$ in patients with sarcoidosis.

STATEMENT OF INTEREST

None declared.

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