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RESPIRATORY PHYSIOLOGY

Comparison Between Cardiopulmonary Exercise Testing Parameters and Computed Tomography Findings in Patients with Thoracic Sarcoidosis

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Abstract
Background Cardiopulmonary exercise testing (CPET) is a safe and clinically useful method to assess functional capacity and to follow disease progression and the response to treatment in several clinical conditions.
Aim We set out to determine the relationship between outcome measures of CPET and high-resolution computed tomography (HRCT) findings in thoracic sarcoidosis.
Methods A cross-sectional study was carried out in which 42 nonsmoking outpatients (22 females; median age = 46.5 years) were evaluated. All the patients underwent pulmonary function tests (PFTs) and CPET. By using CPET, the most probable causes of exercise limitation were separated into respiratory mechanics ($n = 25$) and cardiovascular ($n = 17$). By using HRCT, the following patterns were recorded: predominant nodules ($n = 18$), predominant ground-glass opacity ($n = 10$), and predominant traction bronchiectasis and honeycombing ($n = 14$).
Results Although significant differences have been shown for both PFT parameters and CPET results, only the latter were able to distinguish between patients with ground-glass opacity and patients with traction bronchiectasis and honeycombing on HRCT. A statistically significant difference was found for peak VO_2, breathing reserve, and $P(A\text{-}a)O_2$ when patients with predominant traction bronchiectasis and honeycombing were compared to patients with other HRCT patterns ($p < 0.0001$). There was no statistical difference among the patterns with abnormal CPET and the patterns of abnormalities on HRCT ($p > 0.05$).
Conclusion The functional capacity assessed by CPET was strongly influenced by HRCT patterns in sarcoidosis. Patients with traction bronchiectasis and honeycombing have lower exercise capacity measured by CPET.

Keywords Sarcoidosis · Exercise · Respiratory function tests · Respiratory mechanics · Tomography · X-ray computed

Introduction

Sarcoidosis is a multisystemic disorder of unknown cause. Although it potentially can affect any organ system, the involvement is more frequent in mediastinal and pulmonary sites, occurring in more than 90% of cases. The diagnosis is established when clinicoradiological findings are supported by histological evidence of noncaseating epithelioid cell granulomas [1].

In thoracic sarcoidosis, pulmonary function tests (PFTs) and imaging methods are the most used exams during the follow-up and evaluation of the therapeutic response. PFTs are important to measure initial lung impairment and to provide a baseline to assess improvement or deterioration of the lung disease [1]. With regard to imaging methods, a

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chest radiograph still holds a prominent position in the initial evaluation and monitoring of patients with sarcoidosis. Although the diagnosis of the disease is suspected when there is an abnormal chest radiograph, about 5–10% of patients with thoracic sarcoidosis have a normal chest radiograph [2].

The advent of computerized tomography (CT), especially high-resolution computerized tomography (HRCT), was a breakthrough in the study of interstitial lung diseases. It is considered the best method of evaluating the extent of thoracic sarcoidosis and has proven superiority in the detection of adenopathy and subtle parenchymal disease when compared to chest radiograph [3]. Although CT provides a superior pictorial assessment of disease pattern and extent, HRCT findings have been shown not to correlate well with pulmonary function abnormalities at rest in sarcoidosis patients [4, 5]. Remy-Jardin et al. [4] reported low, although statistically significant associations between the specific HRCT findings of sarcoidosis and PFTs outcomes. Muers et al. [5] found that reticular and fibrotic abnormalities on HRCT scan correlated modestly with physiological aberrations, but mass opacities or confluence did not.

In practice, cardiopulmonary exercise testing (CPET) should be considered when specific questions remain unanswered after consideration of basic clinical data, including history, physical examination, chest radiographs, and PFTs. However, the use of CPET in patient management is increasing with the understanding that PFTs cannot reliably predict exercise performance and functional capacity and that, furthermore, overall health status correlates better with exercise tolerance than with resting measurements [6]. CPET abnormalities may result from the reduced capacity of any system involved with oxygen transport (heart, lung, systemic circulation, and pulmonary circulation) or its utilization (muscle) [7]. In interstitial lung disease a spectrum of respiratory (mechanical and pulmonary gas exchange) and cardiovascular abnormalities can be observed, which may reflect differences in disease severity [6]. In sarcoidosis there is some evidence suggesting that impaired gas exchange during exercise might be important in estimating the extent and severity of the disease [8, 9]. Because sarcoidosis can affect any thoracic structure, it is likely that the CPET results better correlate with the HRCT abnormalities than do PFT variables [9]. Since the association between HRCT patterns and exercise performance is not well established in sarcoidosis, this characterization could provide relevant information for the clinical management of these patients. Additionally, the literature lacks information on the clinical utility and understanding of CPET in patients with sarcoidosis [6]. Therefore, we sought to determine the relationship between outcome measures of the CPET and HRCT findings in a sample of patients with thoracic sarcoidosis.

Materials and Methods

Patients

This is a cross-sectional study with a convenience sample. The subjects were recruited from the Pneumology Service of Pedro Ernesto University Hospital and evaluated for study inclusion on the basis of having a clinical diagnosis of thoracic sarcoidosis, with biopsy confirmation. Subjects with a history of smoking and a medical history or laboratory findings of concomitant respiratory, cardiac, or neuromuscular disease were excluded from the study. The protocol was approved by the Research Ethics Committee of the University of the State of Rio de Janeiro and written informed consent was obtained from all participants.

Measurements

Each pair of chest radiographs was examined by two pulmonologists using the following classification: stage 0, no radiographic abnormalities; stage 1, bilateral hilar adenopathy without parenchymal abnormalities; stage 2, bilateral hilar adenopathy with interstitial parenchymal infiltrates; stage 3, interstitial parenchymal infiltrates without hilar adenopathy; and stage 4, cicatricial changes [10].

All CT examinations were performed using a high-resolution scanner (GE HiSpeed Advantage, General Electric Medical Systems, Milwaukee, WI, USA); 1-mm-thick slices, at 1.5-s intervals and increased by 10 mm; image reconstruction with a 512 × 512-pixel matrix, using a high-resolution algorithm; 1000-HU width window; and −700-HU medium window level. The HRCT images were evaluated for the presence and distribution of the signs by two radiologists [11, 12]. Additionally, they classified the CT scans according to the predominant pattern, as follows: grade 1 = predominant nodules, grade 2 = predominant ground-glass opacity, and grade 3 = predominant traction bronchiectasis and honeycombing. The same two radiologists interpreted the chest radiographs and HRCT images and reached a consensus on the final classification.

Pulmonary function tests were performed within 2 weeks of the CT scan examination in all patients and consisted of spirometry and single-breath diffusing capacity for carbon monoxide (DLco). Measurements were carried out using the Collins Plus Pulmonary Function Testing Systems (Warren E. Collins, Inc., Braintree, MA, USA), following the American Thoracic Society's standards for the procedure and interpretation [13]. Maximum voluntary

ventilation (MVV) was performed by coaching the patients to hyperventilate as vigorously as possible for 10 s, aiming for a minimum frequency of 80 breaths/min while the mobilized volume was recorded in liters per minute [14]. Results were expressed in percent of the predicted values for the Brazilian population [15, 16].

Each subject performed symptom-limited maximal exercise testing using an electrically braked cycle ergometer connected to the Collins Plus Pulmonary Function Testing System (Warren E. Collins, Inc.). After 5 min of data collection at rest, subjects pedaled for 3 min at 60 rpm without resistance, after which the work rate (WR) was incremented by 10–25 W each minute. The WR increment for each ramped exercise test was individualized based on each patient's pretest activity level, with the objective of achieving 8–12 min of progressive exercise before stopping [17]. Heart rate (HR) was monitored continuously using a 12-lead electrocardiogram monitor (Marquette Electronics, Milwaukee, WI, USA), and blood pressure measurements by sphygmomanometer (Hewlett Packard, Andover, MA, USA) were obtained every 2 min throughout exercise and recovery. Oxygen saturation (SpO_2) was monitored noninvasively with a fiber-optic earpiece oximeter (Nonin Medical, Plymouth, MN, USA). Oxygen desaturation during exercise was defined as a reduction of oxygen saturation of more than 4% from baseline values [18]. Oxygen uptake (VO_2), carbon dioxide output (VCO_2), minute ventilation (VE), and related variables were calculated breath-by-breath. Arterial blood gas and lactate levels were measured by blood gas analyzer (Roche Diagnostics, São Paulo, SP, Brazil) at rest and at the end of exercise (peak performance) using samples taken from an indwelling radial arterial line. Breathing reserve was calculated as the difference between measured resting MVV and the peak VE, expressed as a percentage of MVV [1 – (VE/MVV) × 100]. Heart rate reserve (HRR) was calculated as the difference between peak and resting heart rate [(220 − age) − peak HR]. The VO_2 at the estimated lactate threshold ($VO_2\theta L$) was obtained by using both the modified V-slope and the ventilator methods [8]. Oxygen alveolar pressure (PAO_2) was estimated by the alveolar air equation, using $PaCO_2$ and the recorded respiratory exchange ratio (VCO_2/VO_2 or RER) values. The alveolar-arterial oxygen pressure gradient [$P(A\text{-}a)O_2$] was obtained by the difference between the estimated PAO_2 and measured PaO_2 [19], and the results were compared with those predicted by Neder et al. [20] for the adult Brazilian population. Two pulmonologists categorized the CPET results according to the type of limitation as follows: (1) possible respiratory mechanics limitation and (2) possible cardiovascular limitation [17, 19].

Data Analysis

The data were analyzed using the SAS v6.11 software (SAS Institute, Inc., Cary, NC, USA). The results were expressed as the median and interquartile range values, or frequencies (percentage). According to data distribution (verified by the Kolmogorov–Smirnov test), comparisons between CT grades (predominant nodules, predominant ground-glass opacity, and predominant traction bronchiectasis and honeycombing) and functional variables were performed using the nonparametric Kruskal–Wallis test (nonparametric analysis of variance) followed by Dunn's multiple comparisons post-test. Categorical variables were compared using the Mann–Whitney U-test. Differences were considered significant when $p < 0.05$.

Results

Fifty-seven patients were evaluated. Fifteen were excluded for history of smoking (10), concomitant respiratory disease (2), cardiac disease (2), and neuromuscular disease (1). The range of time from diagnosis of sarcoidosis in the 42 outpatients was 1–360 months. Thirty-three patients (78.6%) received corticosteroids alone or in combination with immunosuppressive therapy, while 9 patients (21.4%) did not receive any therapy.

Demographic data, PFT parameters, and CPET results are summarized in Table 1. Twenty-four patients (57.1%) had abnormal spirometric results: obstructive impairment was identified in 14 (33.3%), restrictive in 7 (16.7%), and mixed (obstructive plus restrictive) in the remaining 3 patients (7.1%). The DLco was at the lower limit of normality in 16 patients (38.1%). With respect to outcome measures of CPET, 37 of 42 patients (88.1%) failed to reach at least 80% of their predicted peak VO_2. Arterial oxygen desaturation occurred with exercise in 20 patients (47.6%), while breathing reserve less than 25% was observed in 17 patients (40.5%). Fifteen patients (35.7%) had $P(A\text{-}a)O_2 > 35$ mmHg. Thirty of 42 patients (71.4%) showed low oxygen pulse (VO_2/heart rate) at peak exercise (< 80% of predicted). Seventeen patients (40.1%) had $VO_2\theta L < 40\%$ predicted peak VO_2, while only three patients had HRR < 15 beats/min.

Five patients (11.9%) had stage 1 chest roentgenograms, 9 (21.4%) had stage 2, 23 (54.8%) had stage 3, and 5 (11.9%) had stage 4. With respect to HRCT scan, all patients had lung parenchyma abnormalities. Nodules and consolidation were detected in 31 (73.8%) and 10 (23.8%) cases, respectively. Traction bronchiectasis and honeycombing were noticed in 17 cases (40.5%). Other CT findings were ground-glass opacity in 23 patients (54.8%), linear opacity in 34 (81%),

Table 1 Demographic data, pulmonary function parameters, and outcome measures of the cardiopulmonary exercise testing

Variables	Values
Demographic characteristics	
Age (years)	46.5 (39–53)
Sex (female)	22 (52.4)
Pulmonary function parameters	
FVC (% predicted)	95.5 (82–105)
FEV_1 (% predicted)	90 (73–101)
FEV_1/FVC (%)	78.5 (74–84)
DLco (% predicted)	93.5 (79–103)
Cardiopulmonary exercise testing results	
Peak VO_2 (l/min)	0.95 (0.77–1.09)
Peak VO_2 (% predicted)	56.5 (33–65)
$VO_2\theta L$ (%)	41.5 (30–55)
RER max	1.24 (1.11–1.33)
O_2 pulse max (ml/beats/min)	8.51 (7.15–9.87)
O_2 pulse max (% predicted)	61.3 (51.3–81.1)
HRR (beats/min)	47 (34–54)
BR max (breaths/min)	41 (34–56)
Breathing reserve	45.6 (13.9–62.6)
P(A-a)O_2 (mmHg)	18.6 (15–36)
Δ SpO_2 (%)	2.5 (1–7)
Δ blood lactate (mmol/L)	1.86 (1.13–3.21)
Possible mechanical respiratory limitation	25 (59.5)
Possible cardiac limitation	17 (40.5)

Data are presented as median (interquartile range) or number (%)

FVC forced vital capacity, *FEV_1* forced expiratory volume in 1 second, *DLco* carbon monoxide diffusing capacity, *Peak VO_2* peak oxygen uptake, *$VO_2\theta L$* % peak VO_2 at the estimated lactate threshold, *RER max* maximum respiratory exchange ratio (VCO_2/VO_2) at peak exercise, *O_2 pulse max* maximum oxygen pulse (VO_2/heart rate) at peak exercise, *HRR* heart rate reserve, *BR max* maximum respiratory rate at peak exercise, *P(A-a)O_2* alveolar-arterial oxygen pressure gradient at peak exercise, *Δ SpO_2* % difference between peak and resting oxygen saturation, *Δ blood lactate* difference between peak and resting blood lactate

and mediastinal or hilar adenopathy in 26 patients (61.9%). Predominant sites of lesions were the upper and middle zones (76.2%) and posterior zones (66.7%). CT appearances were categorized as grade 1 (predominant nodules) in 18 patients, grade 2 (predominant ground-glass opacity) in 10 patients, and grade 3 (predominant traction bronchiectasis and honeycombing) in 14 patients.

Table 2 shows the comparison between the functional variables and HRCT patterns. There was no statistical difference between the type of limitation (respiratory mechanics or cardiovascular) and the patterns of abnormalities on HRCT ($p > 0.05$). Although significant differences have been shown for both PFT parameters and CPET results, only outcome measures of CPET were able to distinguish between CT grades 2 and 3 (Figs. 1, 2).

Discussion

In our study, the HRCT images were classified according to the predominant pattern. The most common tomographic pattern was the predominance of nodules (grade 1), representing coalescent, noncaseating sarcoid granulomas [21]. In general, PFTs and CPET results were close to normal only for patients with CT grade 1. When compared to patients with CT grades 2 and 3, these patients showed statistical differences in some variables of CPET. Indeed, some studies established no relationship between the presence of nodules on HRCT and decline in lung function at rest [22, 23]. Moreover, Akira et al. [24] found that the parenchymal abnormalities in most sarcoidosis patients with a predominant nodular pattern disappeared or decreased in size on long-term follow-up CT scans.

In this investigation, patients with predominance of a ground-glass opacity pattern (CT grade 2) showed intermediate values in the functional variables compared to patients with CT grades 1 and 3. Interestingly, only the CPET results were able to differentiate patients with CT grades 2 and 3, showing the higher sensitivity of the physiological measurements obtained during exercise (Table 2). Although ground-glass opacity pattern has been postulated to represent alveolitis, the CT scan–pathological correlation of this finding in sarcoidosis patients has demonstrated the presence of either granulomas or fibrosis [21]. If ground-glass opacity is seen only in lung regions also showing significant HRCT findings of fibrosis, such as traction bronchiectasis or honeycombing, it is most likely that fibrosis will be the predominant histologic abnormality. Thus, a ground-glass opacity pattern may be a result of fibrosis below the limits of the HRCT scan technique resolution [24]. Interestingly, Alhamad et al. [11], comparing sarcoidosis patients with and without ground-glass opacity, found a shorter walking distance for the former in the 6-min walk test (6MWT).

Our results showed that patients with predominance of traction bronchiectasis or honeycombing (CT grade 3) have major changes in functional capacity. A statistically significant difference was observed for peak VO_2, breathing reserve, and P(A-a)O_2 when patients with CT grade 3 were compared to patients with CT grades 1 and 2 ($p < 0.0001$). Interestingly, Alhamad et al. [11], in evaluating the 6MWT in sarcoidosis patients, observed a significant difference in the product of the walking distance and SpO_2 when comparing patients with and without lung fibrosis. Indeed, the presence of traction bronchiectasis or honeycombing is generally associated with a poor prognosis, with increased morbidity and mortality [24].

When comparing CT patterns, we did not observe a significant difference between patients with possible respiratory mechanics limitation and patients with possible

Table 2 Comparison between functional variables and computed tomography patterns

Variables	Grade 1 (predominant nodules, $n = 18$)	Grade 2 (predominant ground-glass opacity, $n = 10$)	Grade 3 (predominant traction bronchiectasis and honeycombing, $n = 14$)	p value
Pulmonary function parameters				
FVC (% predicted)	104 (95–108)	87.5 (76–96)	85 (71–97)	0.007*†
FEV_1 (% predicted)	97.5 (90–104)	79.5 (65–95)	76.6 (68–90)	0.005*†
FEV_1/FVC (%)	80 (74–85)	77 (72–81)	78 (75–86)	0.651
DLco (% predicted)	101.5 (97–108)	83.5 (71–102)	72.5 (59–93)	0.002*†
Cardiopulmonary exercise testing results				
Peak VO_2 (% predicted)	65 (60–70)	60 (37–62)	31.5 (31–33)	<0.0001*†‡
$VO_2\theta$L (%)	41.5 (34–53)	33 (26–44)	50.5 (31–58)	0.089
RER max	1.21 (1.09–1.33)	1.12 (1.05–1.26)	1.30 (1.21–1.37)	0.097
O_2 pulse max (% predicted)	63.6 (56.2–71.6)	52.4 (46.3–61.6)	74.7 (45.3–88.1)	0.203
HRR (beats/min)	43.5 (25–53)	45 (35–49)	49 (37–58)	0.570
BR max (breaths/min)	36 (32–41)	38 (27–44)	64 (50–66)	<0.0001†‡
Breathing reserve	62.1 (55.4–83.9)	50.1 (18.3–59.2)	11.9 (8.9–13.9)	<0.0001*†‡
P(A-a)O_2 (mmHg)	15.4 (11.8–17.7)	18 (15–34.5)	37.1 (34.1–43.4)	<0.0001*†‡
Δ SpO_2 (%)	1 (1–2)	1.5 (1–4)	10 (6–11)	<0.0001†‡
Δ blood lactate (mmol/L)	2.37 (1.18–3.53)	1.28 (0.73–1.91)	1.74 (1.02–3.48)	0.184
Possible mechanical respiratory limitation	12 (66.7)	4 (40)	9 (64.3)	0.432
Possible cardiovascular limitation	6 (33.3)	6 (60)	5 (35.7)	0.541

Data are presented as median (interquartile range) or number (%)

* Significant difference between grade 1 and grade 2

† Significant difference between grade 1 and grade 3

‡ Significant difference between grade 2 and grade 3

FVC forced vital capacity, *FEV_1* forced expiratory volume in 1 second, *DLco* carbon monoxide diffusing capacity, *Peak VO_2* peak oxygen uptake, *$VO_2\theta L$ %* peak VO_2 at the estimated lactate threshold, *RER max* maximum respiratory exchange ratio (VCO_2/VO_2) at peak exercise, *O_2 pulse max* maximum oxygen pulse (VO_2/heart rate) at peak exercise, *HRR* heart rate reserve, *BR max* maximum respiratory rate at peak exercise, *P(A-a)O_2* alveolar-arterial oxygen pressure gradient at peak exercise, *Δ SpO_2 %* difference between peak and resting oxygen saturation, *Δ blood lactate* difference between peak and resting blood lactate

cardiovascular limitation. Exercise requires a global and integrated response of the cardiovascular, respiratory, neuromuscular, and metabolic systems [9]. Because sarcoidosis is a multisystemic disorder, it is possible that several mechanisms are involved simultaneously in exercise limitation.

Even though only nonsmoking subjects were included in this study, the most common spirometric abnormality was airflow limitation ("pure" obstructive impairment plus mixed) in 17 patients (40.5%). Similarly, Harrison et al. [25] found airflow limitation in 61 of 107 patients (57%) with newly diagnosed disease. Airway obstruction in sarcoidosis may be attributed to various mechanisms, including narrowing of the bronchial wall because of granulomatous lesions or fibrosis scarring, compression by lymphadenopathy, airway distortion caused by pulmonary fibrosis, small airway disease, or bronchial hyperreactivity [26].

Another common functional abnormality found in our study was low DLco in 16 patients (38.1%). In sarcoidosis, the reduction of DLco may reflect impairments in gas exchange area, barrier thickness, or ventilation-perfusion-diffusion mismatching of the lung [23]. Interestingly, DLco has also been found to be fairly correlated with gas exchange abnormalities during exercise, and particularly to be the best predictive and sensitive index of a fall in PaO_2 [14].

Exercise capacity is often impaired in patients with thoracic sarcoidosis. A reduced peak VO_2 is usually the starting point in the evaluation of reduced exercise capacity. A low peak VO_2 can be due to multiple factors, including gas exchange across the lung, oxygen content of the blood, oxygen delivery to tissues, and oxygen uptake in the tissues. In our study, about 90% of the patients failed to reach at least 80% of predicted peak VO_2. Similarly, in a group of subjects with thoracic sarcoidosis, Gibbons et al. [16] found low peak VO_2 in 29 of the 35 studied patients.

In our study, over 40% of the patients showed a reduced breathing reserve and arterial desaturation, which are usually seen in patients with interstitial lung disease as sarcoidosis. Because most of our patients (66.7%) had radiographic stages 3 and 4, this may reflect limitation by

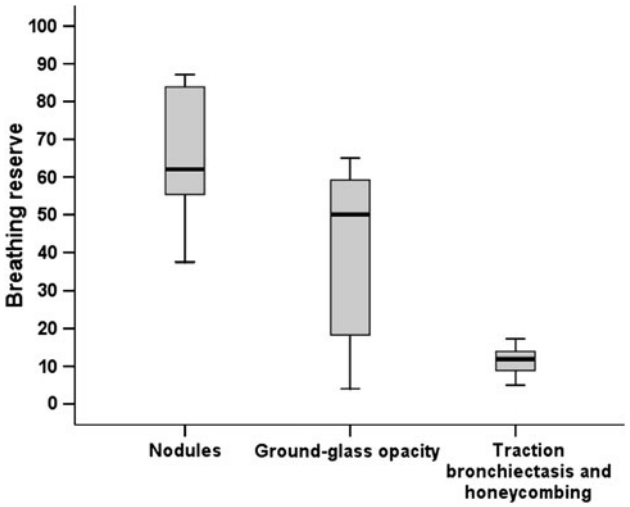

Fig. 1 Box plots (median, 1st and 3rd quartiles, minimum and maximum) of breathing reserve at peak exercise according to computerized tomography (CT) pattern (predominance of nodules, ground-glass opacity, or traction bronchiectasis and honeycombing). Significant differences ($p < 0.0001$) were found between the three CT patterns

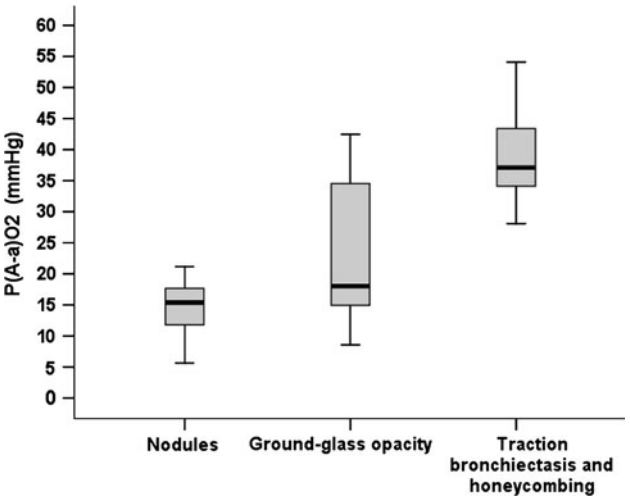

Fig. 2 Box plots (median, 1st and 3rd quartiles, minimum and maximum) of alveolar-arterial oxygen gradient [P(A-a)O_2] at peak exercise according to the computerized tomography (CT) pattern (predominance of nodules, ground-glass opacity, or traction bronchiectasis and honeycombing). Significant differences ($p < 0.0001$) were found between the three CT patterns

ventilatory mechanisms [27]. Moreover, respiratory mechanics abnormalities during CPET have been reported in up to 47% of sarcoidosis patients [17, 28].

During exercise in patients with interstitial lung disease, ventilation-perfusion ratio mismatching, diffusion limitation, and low mixed venous O_2 have been shown to contribute to the abnormally increased P(A-a)O_2 [6]. Abnormal widening of P(A-a)O_2 with exercise was detected in more than 35% of our sarcoidosis patients. At rest, the apical regions of the lung contribute relatively little to ventilation and gas exchange, but during exercise, apical pulmonary circulation is normally recruited and contributes significantly to the increase of the rate of gas exchange. Because the lesions of sarcoidosis favor the upper lobes of the lungs, lung function measured during exercise may have a higher sensitivity for detecting the presence and progression of parenchymal disease [29].

In 17 of 42 patients in the present study (40.1%), the $VO_2\theta L$ was low and the oxygen pulse at peak exercise was abnormal, suggesting a cardiocirculatory dysfunction. Using CPET to evaluate sarcoidosis patients with normal or mildly abnormal spirometry patterns, Sietsema et al. [17] found abnormal exercise results with reduced peak VO_2 and low $VO_2\theta L$. They concluded that many of these patients had unsuspected cardiocirculatory impairment. Although clinical evidence of myocardial involvement is present in only about 5% of sarcoidosis patients, unsuspected cardiac involvement may be found in up to 30% of cases at autopsy [18]. In the heart, noncaseating granulomas can involve the ventricular septum, papillary muscles, and/or free ventricular walls [29].

The present study had some limitations. First, we did not evaluate the extent of each CT pattern. However, the semiquantitative scoring systems used to assess the extent of the disease are of limited value in clinical practice [26]. Second, we did not directly determine cardiocirculatory status. As indicated by CPET results, it is possible that some patients had cardiac sarcoidosis or pulmonary hypertension, the latter resulting from granulomatous and fibrotic obliteration of the pulmonary capillary bed and/or arterial oxygen desaturation [18]. Finally, suboptimal effort alone could account for reduced peak VO_2. However, our patients were actively encouraged during exercise to reach a maximum, and they all showed blood lactate levels to be greater than 4 mmol/L and a respiratory exchange ratio greater than 1.15 [7].

In conclusion, the functional capacity assessed by CPET is strongly influenced by HRCT patterns in thoracic sarcoidosis. Patients with predominance of a traction bronchiectasis and honeycombing pattern have lower exercise capacity measured by CPET.

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