Original Article

Correlation Between the Degree of Air Trapping in Chest HRCT and Cardiopulmonary Exercise Test Parameters: Could HRCT be a Predictor of Disease Severity?

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See the pages 84 – 85

Abstract

Objective: The purpose of this study was to examine whether the degree of air trapping in high resolution computed tomography (HRCT) of patients with histories of sulfur mustard gas exposure during suspended full expiration correlated with various parameters of the cardiopulmonary exercise test as the gold standard for assessment of pulmonary function.

Methods: In this analytic study 75 male patients, each with a history of sulfur mustard gas exposure, were investigated. Each participant underwent an incremental cardiopulmonary exercise test, pulmonary function test and arterial oxygen saturation for hemoglobin measurement. For HRCT examination, both lungs were divided into three parts (upper, middle, and lower) and in each part images were separately observed from the involved area point of view (<25% = <6/24; $\geq$25% = $\geq$6/24).

Results: A total of 49.3% of the patients (37/75) had evidence of air trapping in over 25% of their lung segments. The mean age±SD in the patients with air trapping of ≥25% or <25% were 41.1±6.8 and 39.7±4.0 years, respectively (*P*=0.281). In our study there was no significant difference in pulmonary function test findings (FEV1, FVC and FEV1/FVC) between the two groups. There was no significant correlation with air trapping of ≥25% and any of the exercise test parameters. Also, no correlation was found between significant air trapping and exercise test findings in maximum exercise and anaerobic situations.

Conclusions: No correlation was found between HRCT and cardiopulmonary exercise test findings. HRCT is neither pathognomic of the disease nor a good predictor of disease severity but it might be suggestive of mustard lung injuries.

Keywords: air trapping, cardiopulmonary exercise test, high resolution computed tomography, sulfur mustard

Introduction

Air trapping seen on computed tomography (CT) scans is defined as “decreased attenuation of pulmonary parenchyma, especially in attenuation during expiration”.[1] Normally, during full expiration CT scans show a homogenous increase in pulmonary attenuation because the amount of air in the lung being scanned is reduced.[1,2] According to some reports, air trapping could be detected frequently in asymptomatic healthy subjects with normal pulmonary function and CT may be more sensitive than pulmonary function tests for detecting focal air trapping, whereas CT can detect small focal abnormalities that may be present when pulmonary function test results show normal findings.[3,4]

Air trapping on expiratory HRCT is the best indicator of bronchiolitis obliterans after lung transplantation with a sensitivity of 91%, specificity of 80% and accuracy of 85%, respectively.[5] Inhalation of mustard gas has been reported to cause chronic bronchitis, airway hyper reactivity, bronchiectasis, pulmonary fibrosis, and bronchiolitis obliterans.[6,7]

Our patients had histories of exposure to mustard gas, dyspnea on exertion and various degrees of air trapping on lung HRCT. The impact of air trapping on lung function and the relationship between the extent of air trapping and exercise capacity are unanswered questions. There are studies that have evaluated the correlation between air trapping and alterations in PFT results.[8,4] To our knowledge, this is the first study to examine the correlation between air trapping and cardiopulmonary exercise test (CPET) results.

The purpose of this study was to examine whether the degree of air trapping in HRCT of patients with histories of sulfur mustard gas exposure, during suspended full expiration correlates with various parameters of the CPET.

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Accepted for publication: 4 August 2010

Materials and Methods

Seventy five males with confirmed histories of exposure to mustard gas during the Iran-Iraq war who suffered from persistent respiratory complaints of shortness of breath, cough, and exercise intolerance were enrolled in this study. The inclusion criteria were as follows: documentation of sulfur mustard exposure by military officials; presence of exertional dyspnea; and presence of at least one segment with air trapping in lung HRCT. Patients older than 65 years and/or patients with known cardiovascular and systemic diseases or a history of smoking were excluded. The frequency of air trapping was measured by quantitative methods. This study was approved by the Ethics Committee of Baqiyatallah University of Medical Sciences. Informed consent was obtained from all patients.

Sulfur mustard exposure

Exposure to sulfur mustard was determined by documented development of blisters in the exposed areas of skin, transient visual deterioration and associated respiratory symptoms that lasted for several days. Due to the lack of complete documentation the duration, frequency, and extent of exposure to sulfur mustard were difficult to discern from the field records.

Pulmonary function test

All participants underwent spirometry (HI-801 Chest M.I. Spirometer, Tokyo, Japan) at the screening visit. The spirometer was calibrated using the device provided by the manufacturer. To assess pulmonary function, we measured forced expiratory volume in the first second (FEV1), forced vital capacity (FVC) and FEV1/FVC ratio.[8]

Cardiopulmonary exercise test

Exercise testing was done between 8:30 a.m. and 12:00 noon. Patients were encouraged to take their medications as usual. Each participant underwent an incremental exercise test according to the protocol of Wasserman et al. on an electrically-braked cycle ergometer (Sensor medics 2900).[9] Unloaded pedaling at a cycling speed of 60 rpm followed a three minute rest. The load was progressively increased by 15 watts/min. Cardiopulmonary data were continuous collected with a metabolic unit (CPX) including maximal heart rate (HRmax) and oxygen pulse (VO_2/HR). Arterial oxygen saturation for hemoglobin was measured by a pulse oximeter. The subjects were encouraged to cycle until discomfort (e.g., breathlessness) or exhaustion (e.g, muscular or general fatigue) or the appearance of an abnormal electrocardiogram.[9] At the termination of each exercise test, patients' symptoms were recorded (e.g., dyspnea, leg fatigue, chest pain, etc). Predicted maximal exercise data was set according to the Jones standards.[10] Predicted HRmax was calculated at 210 – [age×(0.65)].[9] The dyspnea index, expressed in percent, was calculated by dividing the minute ventilation by maximal voluntary ventilation (VE/MVV). Ventilatory reserve was defined as the difference between MVV and VE. The anaerobic threshold was determined by the V-slope method. Calibration of gas analyzers before each test was achieved using a tank of standard gas provided by the manufacturer (Sensor medics). All airflow and gas measurements were corrected for ambient temperature, barometric pressure and water vapor, and expressed in Body Temperature and Pressure Saturated (BTPS) units. Results of CPET were independently classified as indicating no, mild, moderate, or severe impairments based on the American Medical Association classification.[10] The pulmonary function test (PFT) and CPET data were expressed as mean values with one level of significance. The patient's effort was usually considered to be maximal if one or more of the following occurred:

1. Achievement of predicted peak oxygen uptake and/or a plateau was observed.
2. Predicted maximal work rate was achieved.
3. Predicted maximal heart rate was achieved.
4. Evidence of ventilatory limitation, e.g., exercise ventilation approached or exceeded maximal ventilatory capacity.

HRCT evaluation

HRCT examinations were obtained on one scanner (HiSpeed Advantage, General Electric Medical Systems; Milwaukee, WI).[11] Each HRCT examination consisted of five 1.0 mm collimation images obtained during both deep inspiration and full expiration, with the patient lying in a supine position. Images without contrast were obtained at the level of the aortic arch, midway between the aortic arch and tracheal diaphragm, and 1 cm above the right hemi diaphragm. All images were reconstructed using a high-spatial-resolution algorithm and displayed at standard (level -700, width 1500) and narrow (level -700, width 1000) lung window settings.[11] All chest HRCT scans were reviewed separately by two teams, each consisting of a pulmonologist and a radiologist. Both lungs were divided into three parts (upper, middle, and lower) and in each part, images were separately observed from the involved area point of view ($<25\% = <6/24$; $\geq 25\% = \geq 6/24$). A positive lobe was defined as one with the presence of any lesions such as bronchiectasis, air trapping, mosaic parenchymal attenuation, ground glass attenuation and secondary lobular abnormalities.[12] Inspiratory images were viewed before expiratory ones. Expiratory images were displayed at standard and narrow settings. These were directly compared to determine differences in conspicuity of air trapping. The criteria used to diagnosis the presence of air trapping were alteration of normal anterior posterior lobar attenuation gradients and/or lack of homogeneous increase in lung attenuation resulting in persistent areas of decreased attenuation.[11] The extent of air trapping was quantified and classified using the same system as defined for hyperlucent regions on inspiratory images, considering that limited air trapping has been reported in normal individuals. Presence of air trapping was considered indicative of bronchiolitis obliterans (BO) only if it exceeded 25% of the cross-sectional area of an affected lung on at least one scan level.[11]

Statistical analysis

The data were analyzed using SPSS software version 11.5. All the results are expressed as mean (standard deviation) and number (percent). Continuous variables were compared with the *t*-test. A *P* value of <0.05 was considered statistically significant.

Results

Among the 75 patients, 37 (49.3%) had air trapping in over 25% of their lung segments. The mean (SD) age in the significant air trapping group (>25%) and non-significant group (<25%) were 41.1 (6.8) and 39.7 (4.0) years, respectively (*P*=0.281). The patients were all male. The mean height and weight of the patients are shown in Table 1.

Tables 2 and 3 demonstrate the comparison of PFT and exercise test results with air trapping in HRCT images in both groups. There was no significant correlation between air trapping of ≥25% with any of the exercise test results or PFT findings. Also, no correlation was observed between significant air trapping and exercise test findings in maximum exercise and anaerobic situations.

Discussion

Air trapping is a pathophysiological term for the retention of excess gas in all or part of the lung at any stage of expiration, according to the definition proposed by the Nomenclature Committee of the Fleischner Society.[1] Results of the present study demonstrated no significant relation between the degree of Expiratory-HRCT air trapping and PFT or CPX findings; thus Expiratory-HRCT does not seem to be a reliable method to predict disease severity in SM induced respiratory disorders.

Recently, CT scans obtained at suspended full expiration have mainly been used to show air trapping in diseases such as bronchiectasis, emphysema, and asthma,[13,7] Langerhans cell histiocytosis,[14] chronic airway disease,[4,15] and pediatric pulmonary disease[16–18] in which the severity of disease is important for the clinicians. In many normal subjects, areas of air-trapping are visible on expiratory scans. In these regions, the lung does not increase normally in attenuation and appears relatively lucent. This appearance is most typically seen in the superior segments of the lower lobes or in the anterior middle lobe or lingula, or it involves individual pulmonary lobules, particularly in the lower lobes. As air trapping is present both in patients and the normal population, it may not be a reliable predictor of the disease itself or its severity.

Several authors have described the frequency of air trapping in subjects with normal pulmonary function. For example, in a study by Chen et al.[19] focal areas of air-trapping, including the superior segments of the lower lobes, were visible in 61% of patients having normal pulmonary function tests. In a study by Lee et al,[20] air-trapping was seen in 52% of 82 asymptomatic subjects with normal pulmonary function tests. The frequency of air-trapping also increased with age *(P*<0.05). Mastora et al.[4] recently reported air trapping in 155 (62.0%) of 250 volunteers. Although 214 of the 250 volunteers in that study had normal pulmonary function, air trapping was seen in a considerable number of the volunteers with normal pulmonary function.

Potential reasons for the high prevalence of air trapping in patients with normal pulmonary function are as follows: *(a)* extensive difference in local lung compliance or muscle tone of small air-ways without small-airway disorders or *(b)* presence of a small-airway disorder that is too mild to be detected by percent predicted MEF50% testing because such testing does not have adequate sensitivity for the detection of small-airway disorders.

Previous studies have compared PFT and HRCT,[2–5] but in our study we assessed the exercise test as a gold standard of the lung's ability to function. The second feature of our study used an air trapping cut off point of 25% of the cross-sectional area of an affected lung on at least one scan level as an indication of bronchiolitis obliterans and used this as a test to determine if pulmonary function is different when air trapping is more or less than this cut off point. This cut

Table 1. Body height and weight of patients in the two groups.

	Height [mean(SD)]/inches	Weight [mean(SD)]/lbs
Air trapping >25%	67.4 (2.8)	170.5 (23.6)
Air trapping <25%	68.1 (2.3)	172.1 (24.7)
P value	0.236	0.780

Table 2. Comparison of pulmonary function test in the two groups.

Index	Air trapping ≥25%		Air trapping <25%		PV
	Mean	SD	Mean	SD	
Spirometry findings					
Forced vital capacity (percent predicted)	99.1	15.0	95.6	12.9	0.282
FEV1 (percent predicted)	97.6	14.2	95.4	14.0	0.509
FEV1/FVC (%)	76.0	7.9	76.7	6.1	0.674

FEV1= forced expiratory volume in the first second; PV= pressure-volume

Table 3. Comparison of exercise test in the two groups.

Index	Air trapping ≥ 25%		Air trapping < 25%		PV
	Mean	SD	Mean	SD	
Cardiopulmonary exercise test findings					
Work at anaerobic threshold(AT) (watts)	68.39	18.16	63.37	26.41	0.346
VCo2 at AT (liter/minute)	0.89	0.22	0.83	0.32	0.339
Ventilation at AT (liter/minute)	33.43	8.28	30.57	11.79	0.234
Ventilation at AT (percent predicted)	28.69	8.32	27.15	12.30	0.533
Ventilatory equivalent of O_2 at AT (%)	37.47	7.92	36.34	6.22	0.496
Ventilatory equivalent of CO_2 at AT (%)	38.42	7.27	37.53	5.43	0.551
Heart rate at AT (beats/minute)	116.25	17.20	114.14	22.45	0.653
Heart rate at AT (percent predicted)	67.19	9.95	65.57	12.94	0.550
O_2 pulse at AT (liter/beat)	7.73	2.20	7.52	2.20	0.695
Heart rate at rest	91.94	24.96	85.54	13.02	0.172
Peak O_2 consumption (VO2)(mL/kg/minute)	22.31	5.58	23.27	4.71	0.421
Peak VO_2 (percent predicted)	61.62	11.47	61.39	12.82	0.936
Peak VO_2 (liter/minute)	1.76	0.31	1.79	0.33	0.658
Peak work rate	143.76	25.60	148.82	23.73	0.378
Peak work rate (percent predicted)	75.16	15.38	73.71	10.91	0.638
Anaerobic threshold (AT) (liter/minute)	1.17	1.65	1.50	3.93	0.644
Anaerobic threshold (percent predicted)	31.75	8.06	29.74	10.31	0.354
Peak heart rate	148.24	20.27	153.97	10.57	0.132
Peak heart rate (percent predicted)	85.68	10.87	88.38	5.50	0.181
O_2 pulse (liter/beat)	12.08	2.67	11.64	2.28	0.449
O_2 pulse (percent predicted)	84.68	22.69	77.68	14.23	0.116
Heart rate reserve	24.70	18.56	19.59	9.56	0.141
Maximal ventilation	81.33	17.86	82.79	16.83	0.717
Maximal ventilation (percent predicted)	69.59	14.05	71.18	17.19	0.663
Peak respiratory rate	39.70	8.40	37.87	9.81	0.388
Breathing reserve	34.86	13.55	31.89	18.48	0.436
VD/VT at rest	0.47	0.06	0.46	0.09	0.566
VD/VT at peak exercise	0.18	0.05	0.16	0.05	0.103
Arterial O_2 saturation at rest	97.34	1.33	97.46	1.02	0.676
Arterial O_2 saturation at peak exercise	96.23	2.38	96.22	1.86	0.980

VD/VT=ratio of dead space to tidal volume; PV=pressure-volume.

off point has been used as a predictor of disease severity in previous studies.[20, 21]

Some studies have reported HRCT as an appropriate method for evaluating disease severity, but we did not find any statistically significant difference in exercise test results between the two groups. In this study all the patients in both groups were symptomatic, the VO_2 in the exercise test was decreased and the ventilation at AT was increased which showed the increase in breathing frequency. In patients with toxic fume inhalation physical examination, PFT or HRCT may not show any significant features but such abnormalities in CPX may give us a clue for determining small airway pathology.

Conclusion

HRCT is widely used as a standard test in the diagnosis and management of bronchiolitis obliterans as the main pathology in late pulmonary disorders due to mustard exposure. In the current study we have shown that no correlation exists between HRCT and CPX findings (as the gold standard test for evaluating pulmonary function).

Overall, HRCT seems not to be reliable in the management of mustard lung, and the presence or absence of air trapping in HRCT images of asymptomatic or symptomatic patients may be misleading. Therefore, HRCT is neither pathognomic of the disease nor a good predictor of the disease severity but it still may be used as a suggestive tool in the diagnosis of BO in mustard lung.

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