

High resolution computed tomography (HRCT) assessment of β_2 -agonist induced bronchodilation in chronic obstructive pulmonary disease patients

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Abstract. – The evaluation of airway obstruction reversibility in chronic obstructive pulmonary disease (COPD) patients is currently performed by means of an indirect assessment of drug inducing variations in pulmonary function tests. Imaging techniques, especially high resolution computed tomography (HRCT), usually provide a complete evaluation of lung parenchyma (bronchial and vascular structures), but so far they have never been applied to visualize the effects on the bronchopulmonary tree of some pharmacologic stimuli (β_2 adrenergic agonist), currently used in clinical practice to disclose the presence of airway reversibility.

In order to assess the possible role of HRCT in this setting, five COPD patients have been subjected to a double functional radiologic evaluation before and after salbutamol-induced broncho-dilation, with a rigorous assessment of bronchial diameter changes by means of "bronchus-vessel" ratio, currently used for diagnosing bronchiectasis in COPD patients.

The results of this experimental study enable us to visualize drug induced broncho-dilation, with a direct assessment of airway reversibility in these patients, and to show a good correlation between functional and HRCT findings, raising the possibility of evaluation COPD patients with abnormal spirometric results or with early signs of lung involvement.

Key Words:

Chronic obstructive pulmonary disease (COPD), Airway obstruction, High resolution computed tomography (HRCT).

Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by airflow obstruction

due to chronic bronchitis or emphysema; the airflow obstruction is generally progressive and may be accompanied by airway hyper-reactivity and may be partially reversible¹. In the past asthma was generally subsumed under COPD and an increased responsiveness of the tracheo-bronchial tree was the most prominent feature. Now the salient characteristic of asthma is considered to be inflammation. In many patients with COPD, obstruction may include a significant reversible component. A significant increase in FEV1 after inhalation of a beta-agonist has been observed in up to one third of COPD patients.

A few patients with asthma can develop irreversible airflow obstruction, which is indistinguishable from COPD. Asthma is by definition associated with reversible airflow obstruction and patients with asthma, whose airflow obstruction is completely reversible, are not considered to be COPD-affected. In many cases it is impossible to differentiate patients with asthma, whose airflow obstruction doesn't remit completely, from patients with chronic bronchitis and emphysema who have partially reversible airflow obstruction with airway hyper-reactivity. As a consequence, these patients are classified as COPD-patients. On the other hand, individuals with asthma exposed to chronic irritation, such as cigarette smoke, may develop chronic productive cough, a feature of chronic bronchitis².

As far as the pulmonary function tests are concerned, the response to a bronchodilator is commonly expressed by a per cent increase of

the FEV1 of at least 12-15% above the base value, that is an absolute change of 200 ml³.

The role of imaging techniques in the evaluation of patients with COPD is usually limited to chest X-ray examination. This is currently only used to define "morphologic" lung abnormalities due to chronic pulmonary disease (bronchial wall and pleural thickening, bronchiectasis, emphysema), or to acute processes (focal broncopneumonia, pneumothorax) without providing any "functional" information on airway obstruction^{4,5}.

Computed tomography (CT) and high resolution CT (HRCT) have been shown to allow a complete evaluation of the lung parenchyma; they may also provide useful information on the presence of allergic bronchopulmonary aspergillosis and/or bronchiectasis with the measurement of "bronchus-vessel" ratio, as validated by several studies on subjects with suspected bronchiectasis who underwent both CT and bronchography^{6,7}.

In order to assess the possible role of high resolution CT in the functional evaluation of airway obstruction in COPD patients, we have tested the value of HRCT in the detection of airway reversibility in these subjects. Furthermore, we tried to correlate morphologic data found at HRCT with pulmonary function results of spirometric evaluation before and after beta2-adrenergic agonistic inhalation⁸.

Methods

Five patients (4 males and one female, mean age 66 ± 7.5 years) with uncomplicated COPD were studied. None of the patients received treatment with oral steroids for four weeks, and inhaled bronchodilator agents were withheld for 12 hrs before the study. All patients stopped smoking at least one yr before the study and patients who had respiratory tract infection in 6 weeks preceding the study were excluded. We made a pulmonary function evaluation with equipment by Cosmed mod. Altair 1000 and (for FRC and RV measurement) with a HP nitrogen analyzer.

Parameters measured, according to ATS recommendations were FVC, FEV1, MEF50, FEF 25/75, RV, FRC, and TLC. After a basic spirometric test, all patients showed a reduction in flow/volume parameters, particularly, the FEV1 was less than 80% of theoretic value, and FRC and RV were increased. Twenty minutes after the inhalation of salbutamol (200 µg), we submitted the five patients to another pulmonary function test, in order to highlight a possible reversibility of airway obstruction (Table I).

HRCT: High resolution scanning was performed using a CT (Pace third generation) scanner without i.v. administration of contrast media. All images were obtained at

Table I. Physical characteristics and pulmonary function tests results of all five patients.

P ₂	Sex	Age	Height	Weight		FVC	FEV1	MEF50	FEF25/75
1	F	56	157	80	Pre	1.73	0.93	0.59	0.48
					Post	2.22	1.20	1.08	0.96
					% change	28	29	83	100
2	M	58	177	60	Pre	4.07	2.59	1.82	2.46
					Post	4.38	2.90	1.99	2.66
					% change	7	12	9	8
3	M	70	180	83	Pre	2.17	0.64	0.30	0.27
					Post	2.28	0.75	0.47	0.43
					% change	5	17	57	59
4	M	74	178	69	Pre	1.80	0.87	0.51	0.72
					Post	2.33	1.02	0.45	0.61
					% change	29	16	-11	-16
5	M	66	165	76	Pre	2.03	0.89	0.51	0.48
					Post	2.27	0.88	0.51	0.53
					% change	12	0	0	10

In the table we can see the physical features of the patients like sex, age, height and weight; next to them the base values of pulmonary function tests (Pre and post inhaled β2-agonist) are shown, together with relative percentual changes (% changes).

maximal inspiration at carina and subcarina levels by using 1 mm collimation at 120 kV and 130 mA, with a two seconds acquisition time and 2 mm scan interval.

Images were reconstructed by using a high spatial frequency (bone) algorithm, retargeted to the size of one lung and viewed at window levels from -700 to -800 HU and at widths included between 1400 and 1800 HU.

Each patients was subjected to a spirometric evaluation and to a HRCT examination. Then we administered 200 µg of salbutamol to all patients and after 20 minutes we repeated both examinations in order to highlight an obstruction airway reversibility. In order to obtain a real comparison between pre and post broncho-dilating HRCT studies, great accuracy was directed in the second one, to visualize the same bronchial segments, which had been taken into consideration before.

The radiologic evaluation was performed by means of the “bronchus-vessel” ratio: the diameter of the well visible bronchi was visually recorded and compared to that of the accompanying pulmonary artery. Bronchi in which the internal diameter is wider than that of their respective pulmonary arteries were not taken into account, as they probably had to be referred to bronchiectasis.

Results

The percentage variations obtained for each parameter after drug-induced bronchodilation are summarized in Table I: we can see that four patients obtained a FEV1 percentual increase of 12% above the basal value or even more; one patient did not show a significant increase in all parameters; and so we can observe a FEV1 average percentual increase of 14% in our patients, with a statistical significance of 0,044 (p: t test).

In four patients with a positive reversibility test, the “bronchus-vessel” ratio in the segments of the bronchopulmonary tree, selected for detailed HRCT analysis, showed a significant increase after salbutamol inhalation, especially at lobar and segmental levels, as visualized in Figures 1A-1B. In plural cases, it was possible to assess a good correlation between spirometric “functional” results and

“morphologic” evidence of drug-induced bronchodilation.

In the fifth subject (Table I) with only a slight response to salbutamol administration at the spirometric evaluation, no evidence of bronchus-vessel ratio increase was recorded by comparing pre and post bronchodilating HRCT studies.

Discussion

The evaluation of airway obstruction reversibility in COPD as in asthmatic patients is usually based on pulmonary function tests, pre-post pharmacologic inhalation.

Only recently, a few authors have tested the possible application of imaging techniques [pulmonary ventilation-perfusion (V/Q) scintigraphy] for the evaluation of drug induced V/Q mismatching in COPD patients⁹; on the other hand, the majority of HRCT studies in uncomplicated asthmatic patients have been addressed to verify the clinical suspicion of allergic bronchopulmonary aspergillosis or bronchiectasis^{6,7,9}. Nevertheless, nobody have ever suggested that CT scanning could be useful for the evaluation of bronchial airway obstruction reversibility, as pointed out in our study.

For an accurate HRCT assessment of drug induced bronchodilation, considering the double scanning protocol (possible bronchial misidentification), we only took into account well-visible bronchial segments which fulfilled the following three inclusion criteria:

- (1) presence of clear bronchial wall thickening;
- (2) “bronchus-vessel” ratio < 1 at baseline HRCT study;
- (3) absence of airway branching and/or oblique direction on scan plane.

The result of this double HRCT approach (before and immediately after β_2 -agonist administration) was the direct visualization of bronchial dilation, as shown by the drug induced increase of bronchus-vessel ratio and confirmed by spirometric results.

“Bronchus-vessel” ratio is commonly used in CT lung scanning for diagnosing allergic bronchopulmonary aspergillosis or bronchiectasis^{6,10,11}: when the bronchial luminal diame-

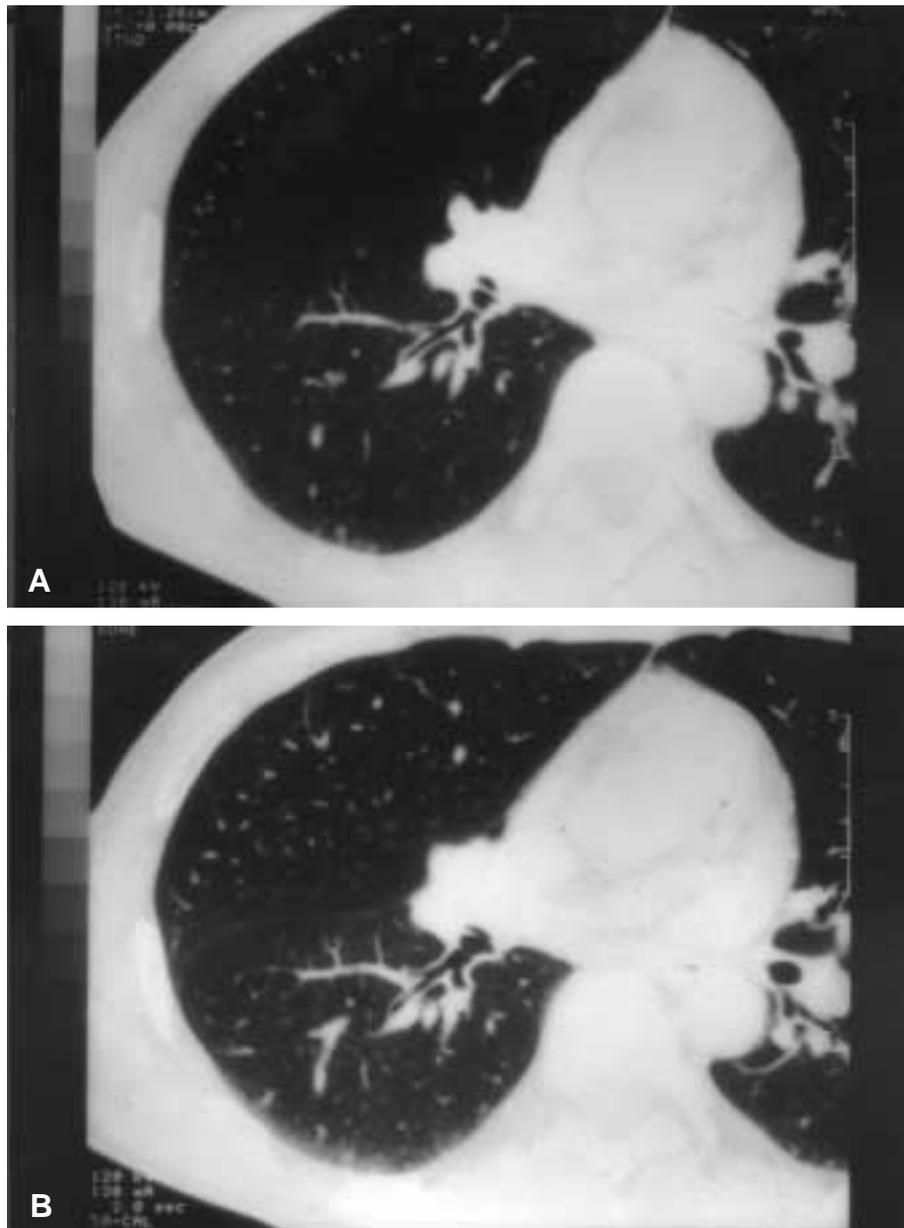


Figure 1A-B. HRCT visualization of drug induced broncho-dilation with a marked increase in “bronchus-vessel” ratio at lobar and segmental levels.

ter is wider than that of the accompanying pulmonary artery we can diagnose a bronchiectasis. This ratio has been shown to be useful for our purpose, enabling us to visualize the variations of luminal bronchial diameter induced by pharmacologic administration (β_2 -agonist inhalation).

In order to achieve these results, which allow us a very simple and clear evaluation of drug-induced effects on the broncho-pulmonary tree, we strictly selected bronchial seg-

ments to be examined and measured (see inclusion criteria), in order to avoid identification and/or interpretation problems. From this point of view, a clear bronchial wall thickening ensures the complete visibility of the structure (the visibility of bronchi or bronchioles on HRCT scans is determined by their wall thickness rather than their diameter), allowing the identification of the same structure on different scan planes and on different studies, as stated in our double HRCT protocol. On the

other hand, as the branching of bronchial structures at a given CT level always begins after that of the accompanying pulmonary arteries, an increase in the bronchus-vessel ratio may be recorded without any functional dilatation or organic (bronchiectasis) variation of bronchial luminal diameter.

In conclusion, the findings of our study raise the possibility of the evaluation of COPD patients with abnormal spirometric results (“non responders” or “paradoxical responders”) and helps disclosing early signs of lung involvement (bronchiectasis, focal fibrosis) in uncomplicated patients, which cannot influence the effectiveness of the therapeutic strategy, but also its suitability.

References

- 1) KONIECZNY B, ZIELINSKI Z. Can an aortic anomaly cause intense dyspnea in a patient with bronchial asthma? *Pneumonol Allergol Pol* 1998; 66: 216-220.
- 2) ATS STANDARDS FOR THE DIAGNOSIS AND CARE OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE. *Am J Respir Crit Care Med* 1995; 152: 77-120.
- 3) ATS LUNG FUNCTION TESTING: SELECTION OF REFERENCE VALUES AND INTERPRETATIVE STRATEGIES. *Am Rev Respir Dis* 1991; 144: 1202-1218.
- 4) WHITE CS, COLE RP, LUBETSKY HW. Acute asthma - admission chest radiography in hospitalized adult patients. *Chest* 1991; 100: 14-16.
- 5) PAGANIN F, TRUSSARD V, SENETERRE E et al. Chest radiography and high resolution computed tomography of the lungs in asthma. *Am Rev Respir Dis* 1992; 146: 1084-1087.
- 6) GRENIER P, MAURICE F, MUSSET D. Bronchiectasis: assessment by thin section CT. *Radiology* 1986; 161: 95-99.
- 7) SILVERMAN PM, GODWIN JD. CT/bronchographic correlations in bronchiectasis. *J Comput Assist Tomogr* 1987; 11: 52-56.
- 8) KEE ST, FAHY JV, CHEN DR, GANSU G. High resolution computed tomography of airway changes after induced bronchoconstriction and broncodilation in asthmatic volunteers. *Acad Radiol* 1996; 3: 389-394.
- 9) BARBERA JA, REYES A, ROCA J. Effect of intravenously administered aminophylline on ventilation/perfusion inequality during recovery from exacerbations of chronic obstructive pulmonary disease. *Am Rev Respir Dis* 1992; 145: 1328-1333.
- 10) NEELD DA, GOODMAN LR, GURNEY JW. Computerized tomography in the evaluation of allergic bronchopulmonary aspergillosis. *Am Rev Respir Dis* 1990; 142: 1200-1205.
- 11) PAGANIN F, TRUSSARD V, SENETERRE E. Chest radiography and high resolution computed tomography of the lungs in asthma. *Am Rev Respir Dis* 1992; 146: 1084-1087.