

# Smoking as a predictor for loosing control of treated bronchial asthma

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## REZUMAT

**Fumatul ca predictor al pierderii controlului astmului bronşic în tratament**

**Obiectiv.** Analiza factorilor implicați în astmul bronșic (AB) necontrolat.

**Materiale și metodă.** În perioada octombrie 2007- noiembrie 2008, am evaluat 584 de pacienți consecutivi, cunoscuți și tratați pentru AB, și am colectat date generale: istoric, debutul bolii, spirometrie, durata tratamentului, schema terapeutică, chestionarul de control al astmului (ACT). Asocierea variabilelor a fost analizată prin calcularea odds ratio (OR) împreună cu intervalele de confidență (CI) într-o analiză univariată. Variabilele independente semnificative au fost utilizate pentru a crea modele de analiză logistică multivariată pentru a identifica cei mai importanți factori de predicție.

**Rezultate.** 584 pacienți, 162 bărbați (27,74%), 422 femei (72,26%), vârstă medie  $45,38 \pm 17,48$  ani (4-85), 14% fumători, ACT <19 (36,2%), 20-24 (48,8%), 25 (15%), 43,1% exacerbări, 4 predictori pentru AB necontrolat: exacerbări OR 4,11, CI 3,30-7,48,  $p <0,001$ , expunere profesională OR 2,29, CI 1,23-4,26,  $p =0,009$ , disfuncție ventilatorie la spirometrie: OR =1,18, CI 1,02-1,36,  $p=0,021$  (sindrom obstractiv OR 3,78 CI 1,76-7,78,  $p =0,0001$ ), durata bolii (luni) OR=1,02, CI 1,00-1,03,  $p=0,021$ , fumat OR 0,57, CI 0,26-0,71,  $p=0,012$ .

**Concluzii.** Peste o treime (36, 2%) din pacienții astmatici tratați au astm necontrolat. Fumatul nu este un factor de predicție pentru lipsa controlului

**Cuvinte cheie:** astm, control, predictor, fumat

## ABSTRACT

**Aim.** Analysis of the factors involved in uncontrolled bronchial asthma (BA).

**Material and method.** Between October 2007 and November 2008 we evaluated 584 consecutive patients, known and treated for BA, and collected general data, medical history, disease onset, spiroometry, treatment duration, treatment, asthma control test (ACT). The association of variables was analyzed by calculating the odds ratio (OR) together with confidence intervals (CI) in a univariate analysis. The significant independent variables were utilized to create models of multivariate logistical analysis in order to identify the most important predictors.

**Results.** 584 patients, 162 males (27,74%), 422 females (72,26%), medium age  $45,38 \pm 17,48$  years (4-85), 14% smokers, ACT <19 (36,2%), 20-24 (48,8%), 25 (15%), 43,1% exacerbations, 4 predictors for uncontrolled BA: exacerbations OR 4,11, CI 3,30-7,48,  $p <0,001$ , professional exposure OR 2,29, CI 1,23-4,26,  $p =0,009$ , altered lung function on spirometry OR =1,18, CI 1,02-1,36,  $p=0,021$  (obstruction OR 3,78 CI 1,76-7,78,  $p =0,0001$ ), duration of disease (months) OR=1,02, CI 1,00-1,03,  $p=0,021$ , smoking OR 0,57, CI 0,26-0,71,  $p=0,012$ .

**Conclusions.** More than 1/3 (36, 2%) of treated asthmatic patients had uncontrolled asthma. Smoking is not among the predictors for lack of control.

**Key words:** asthma, control, predictor, smoking

## Introduction

In western countries, smoking is found at about 25% of adults with asthma. It is known that asthma and active cigarette smoking interact to cause more severe symptoms, accelerated decline in lung function, and impaired short-term therapeutic response to corticosteroids. The harmful influence of tobacco smoke on adults with asthma was increasingly recognized, with adverse effects being noted on the development of asthma and in aggravation of attacks<sup>1</sup>. There are important interactions between active cigarette smoking

and asthma, including effects on morbidity, therapeutic response to corticosteroids and mechanisms of the disease<sup>2</sup>. The World Health Organization has estimated that there are 1.25 billion smokers worldwide, with approximately two-thirds living in developing countries. In many developed countries, at least one in four adults smoke cigarettes<sup>3</sup>. Prevalence rates of smoking are higher in those countries with lower incomes and among young adults, particularly females, and are much higher in underdeveloped countries.

### Aim

Analysis of the factors involved in losing control at patients with treated bronchial asthma, focusing in smoking.

### Material and method

Between October 2007 and November 2008 we evaluated 584 consecutive patients, known and treated for asthma. We collected general data regarding age, gender, a detailed medical history, disease onset (duration in months), treatment duration, duration to achieve control. Type of treatment was registered and we noted any medication taken on regular basis by each patient. Asthma control test (ACT) and evaluation of control according to definition from GINA 2008 were performed. Uncontrolled asthma was defined as an ACT score less than 19.

### Study design

The present study is a post hoc analysis of an existing database that is continuously updated. The present analysis focuses on whether current smoking influences the control of asthma. ACT scores were recorded independently on one or more occasions for each patient. At each visit, asthma treatment was adjusted according to the Global Initiative for Asthma (GINA) guidelines recommendations<sup>4</sup>. The Asthma Control Test (ACT) is a five question health survey used to measure asthma control in individuals 12 years of age and older. The survey measures the elements of asthma control as defined by the *National Heart, Lung, and Blood Institute (NHLBI)*. ACT is an efficient, reliable, and valid method of measuring asthma control, with or without, lung functioning measures such as spirometry. ACT helps identify and detect asthma patients who are not well controlled<sup>5</sup>.

### Spirometry

Spirometry measurements (FEV<sub>1</sub>, FVC, FEV<sub>1</sub>/FVC) before and after a short-acting bronchodilator was taken at the visit in the clinic to determine whether there is airflow obstruction and whether it is reversible over the short term.

Spirometry measured the maximal volume of air forcibly exhaled from the point of maximal inhalation (forced vital

capacity, FVC) and the volume of air exhaled during the first second of the FVC (forced expiratory volume in 1 second, FEV<sub>1</sub>). Airflow obstruction is indicated by reduced FEV<sub>1</sub> and FEV<sub>1</sub>/FVC values relative to reference or predicted values. Significant reversibility is indicated by an increase of  $\geq 12$  percent and 200 mL in FEV<sub>1</sub> after inhaling a short-acting bronchodilator.

A reduced ratio of FEV<sub>1</sub>/FVC (i.e., <65 percent) indicated obstruction to the flow of air from the lungs, whereas a reduced FVC with a normal FEV<sub>1</sub>/FVC ratio suggests a restrictive pattern. The severity of abnormality of spirometric measurements was evaluated by comparison of the patient's results with reference values based on age, height, sex, and race. Although asthma is typically associated with an obstructive impairment that is reversible, neither this finding nor any other single test or measure is adequate to diagnose asthma. The patient's pattern of symptoms (along with other information from the patient's medical history) and exclusion of other possible diagnoses also are needed to establish a diagnosis of asthma.

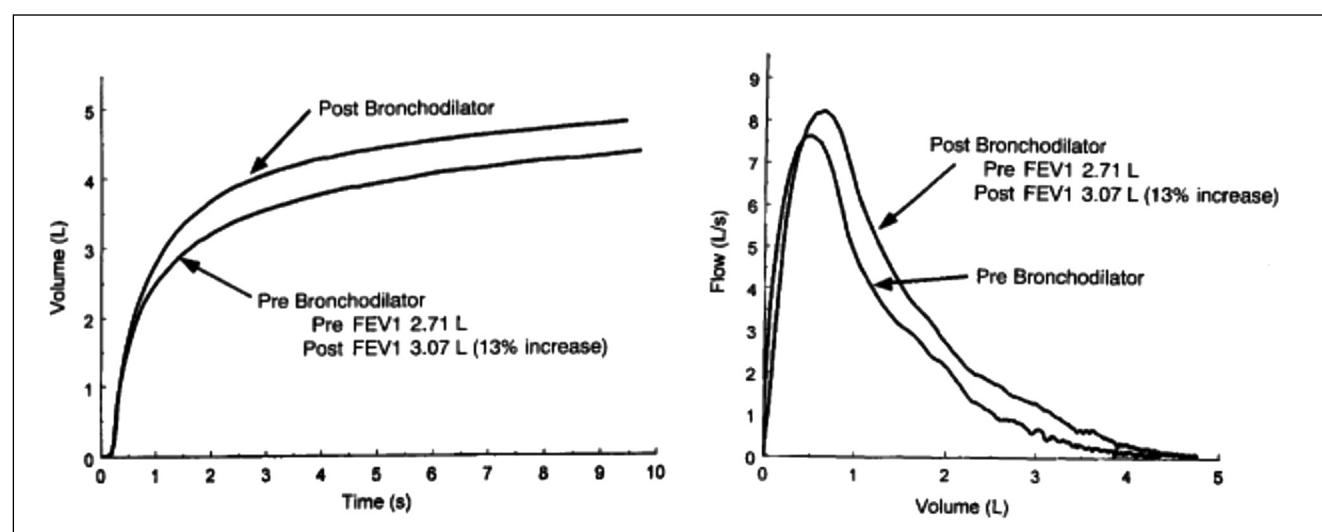
Spirometry is useful in both diagnosis and periodic monitoring. Spirometry was performed using equipment and techniques that meet standards developed by the American Thoracic Society<sup>6</sup>. Correct technique, calibration methods, and maintenance of equipment were assured to achieve consistently accurate test results. Maximal patient effort in performing the test was required to avoid important errors in diagnosis and management.

### Statistical analysis

STATA 9.1 and EpiInfo version 3.4 were used to perform statistical analysis. Evaluation of the strength of association between predisposing or causal factors and disease can be expressed as odds ratio in case-control studies. In order to interpret correctly a point estimation of odds ratio we need to look also to its confidence intervals quality.

The association of variables was analyzed by calculating the odds ratio (OR) together with confidence intervals (CI) in a univariate analysis. The significant independent variables were used to create models of multivariate logistical analysis in order to identify the most important predictors.

**Image 1.**  
**Sample Spirometry Volume Time and Flow Volume Curves**



## Results

584 consecutive patients from our clinic were evaluated. 162 (27.74%) were male, 422 (72.26%) were females. Medium age was  $45.38 \pm 17.48$  years (9-85). 14 % of all patients were smokers. ACT distribution: <19 (36.2%), 20-24 (48.8%), 25 (15%). Exacerbations were found at 43, 1%. 83% used different controller medication. We found 4 predictors for uncontrolled asthma: exacerbations OR 4.11 (CI 3.30-7.48, p <0.001), professional exposure OR 2.29 (CI 1.23-4.26, p =0.009), altered lung function on spirometry OR =1.18 (CI 1.02-1.36, p=0.021), with obstruction OR 3.78 (CI 1.76-7.78, p =0.0001), duration of disease (months) OR=1.02 (CI 1.00-1.03, p=0.021). Smoking had OR 0.57 (CI 0.26-0.71, p=0.012).

Many adult smokers with asthma do not believe that they are personally at risk from their smoking<sup>21</sup>. In the general population, smoking-cessation interventions using brief opportunistic advice, behavioral support, nicotine replacement therapy or bupropion are all effective, although only a minority of smokers successfully quit each year<sup>22</sup>. These interventions have not been studied specifically in an asthmatic population, although their efficacy is likely to be similar to the general population of current smokers.

Optimal asthma control appears more difficult to achieve in smoking patients<sup>23</sup>. In our group of selected consecutive patients from an asthma specialized clinic, the lower prevalence of smokers is related probable to a better approach of this

**Table I.**  
**Parameters regarding control of asthma**

| Parameters               | OR    | Confidence interval 95% | p         |
|--------------------------|-------|-------------------------|-----------|
| Exacerbations            | 4.15C | 2.309 – 7.489           | p < 0.001 |
| Professional exposure    | 2.29  | 1.233 – 4.262           | p = 0.009 |
| Spirometry – obstruction | 1.18  | 1.025 – 1.362           | p = 0.021 |
| Duration (in months)     | 1.02  | 1.002 – 1.035           | p = 0.021 |
| Smoking                  | 0.57  | 0.265 – 0.712           | P = 0.012 |

## Discussion

Active cigarette smoking has been associated with the development of asthma in some<sup>7</sup>, but not all studies<sup>8</sup>. Asthmatic smokers have more severe asthmatic symptoms<sup>9</sup>, greater need for rescue medication<sup>10</sup> and worse indices of health status when compared with never-smokers<sup>11</sup>. Emergency department visits as a result of exacerbations of asthma occur more frequently amongst heavy cigarette smokers with asthma following days with high levels of ambient ozone pollution<sup>12</sup>. Current smoking rates are similar in patients presenting with severe exacerbations of asthma to an emergency department, whether symptoms develop within 3 h or at a slower onset<sup>13</sup>. Admission rates to hospital for asthma and hospital-based care are increased in smokers<sup>14</sup>. There is conflicting evidence as to whether current smoking is a risk factor for near-fatal asthma or fatal asthma<sup>15</sup>.

Cigarette smoking and asthma accelerates the decline in lung function to a greater degree than either factor alone. The Copenhagen City Heart Study included longitudinal measurement of FEV<sub>1</sub> over a 15-yr period, and found that the average decline in FEV<sub>1</sub> was greater in asthmatic smokers than nonsmokers<sup>16</sup>. Recent guidelines of asthma management emphasize inhaled corticosteroids as the most effective anti-inflammatory therapy for chronic asthma<sup>17</sup>. Several studies have suggested that the efficacy of corticosteroids is reduced in asthmatics who are active cigarette smokers<sup>18</sup>, although this conclusion is not supported in another study<sup>19</sup>. Clinical studies suggest that smokers with asthma can be resistant to the beneficial therapeutic effects of corticosteroids. Current smokers are less likely to use appropriate methods to manage both acute and chronic asthma<sup>20</sup>.

association, an optimal intervention to help patients to quit smoking and a lower percentage of male population. Most of asthmatics were on controller medication, and this might explain the level on control.

## Conclusions

Most of our patients were female (72,26%). Only 14% of asthmatics were smokers. More than 1/3 (36,2%) of treated asthmatic patients had uncontrolled asthma. Smoking is not among the predictors for lack of control.

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