High-Resolution Computed Tomography Findings in Elderly Asthmatics

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SUMMARY
Objective: We hypothesized that if airway remodelling is related to duration of asthma, CT-scan in early onset asthmatics should show greater abnormalities than of late onset asthmatics. We evaluated the presence and frequency of airway and parenchymal abnormalities using high-resolution CT (HRCT) in elderly asthmatic patients.

Methods: The study group consisted of 68 stable elderly asthmatic patients (age > 60 year). None of the patients smoked. The patients were separated into two groups according to the duration of symptoms (late-onset asthma, < 5 year; early-onset asthma, ≥ 5 year). High resolution CT scanning and histamine inhalation test were performed on all patients. Asthma severity score was defined according to the National Asthma Education Program (NAEP) guidelines (ie, frequency of symptoms, degree of airflow obstruction, and frequency of use of oral glucocorticoids).

Results: In comparison with late-onset asthmatic patients, those with early-onset asthma had significantly greater frequency of emphysema (21.6% vs 0.0% respectively p=0.006), bronchiectasis (13.9% vs 0.0% respectively p=0.03), bronchial wall-thickening (41.7% vs 12.9% respectively p=0.01). Multiple logistic regression analysis identified that early-onset of disease was independent risk factor for presence of irreversible CT-scan abnormality in elderly asthmatics (odds ratio (OR) 9.4(2.7-32.7) p=0.00001).

Mean baseline FEV1% (77.5±21.05 versus 100.1±17.69, p=0.0001) and PD20 values (0.2±0.46 versus 1.55±2.24, p=0.001) of patients with early-onset asthma were significantly lower than those with late-onset asthma.

Conclusion: These data suggest that HRCT abnormalities in early-onset elderly asthmatics may reflect airway or parenchymal changes which may become irreversible ultimately.

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Key Words: Elderly, asthma, HRCT, emphysema

ÖZET
Yaşlı Astım国立arda Yüksek Rezolüsyon Bilgisayarı Tomografi Bulguları

Amaç: Bu çalışmada erişken hayat boyunun yeniden şekillenmesi astım süresi ile ilişkili ise erken başlayan astım国立arda BT bulgularının geç başlangıç astımı国立arda daha fazla anormallik gösterebileceğini düşündük. Bu yaşlı astım国立arda YRBT kullanarak hava yolu ve parankim anormalliklerinin varlığını ve sıkılığını değerlendirdik.


Sonuçlar: Erken başlangıç国立arda hastaların geç başlangıç国立arda hastalara göre önemli derecede daha sık amfizem (21.6% vs 0.0% sırayla% p=0.006), bronşektazi (13.9% vs 0.0% sıraya p=0.03) ve bronşial duvar kalınlamasına (41.7% vs 12.9% sıraya p=0.01) sahipti. Lojistik Regresyon Analizi yaşlı astım国立arda hastalının erken başlama-sonun geri dönüşımsüz BT anormalliklerinin varlığı için bağımsız risk faktörü olduğunu gösterdi (odds oranı (OR 9.4(2.7-32.7) p=0.00001). Ortalama temel FEV1% (77.5±21.05 ve 100.1±17.69, p=0.0001) ve PD20 (0.2±0.46 ve 1.55±2.24, p=0.001) değerleri geç başlayan hastalımlardan önemli derecede daha düşüktü.

Yorum: Bu veriler bize erken başlayan yaşlı astım国立arda YRBT anormalliklerinin zanıma geri dönüşımsüz ola-bilen hayavyolu veya parankimal değişiklikleri gösterebileceğini düşündürüür.

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Anahtar Kelimeler: Yaşlı, astım, YRBT, amfizem.
Introduction

The studies suggest that asthma is a more destructive disease than previously believed and that HRCT could be a useful examination even when chest film findings are normal (1-3). HRCT has recently been used to study overall parenchymal and bronchial damage in asthma (4). CT findings in asthmatic subjects may include bronchial dilatation, bronchial wall thickening, emphysema, diffuse or patchy areas of hyperlucency, and prominent centrilobular structures (5). Most of these abnormalities are likely to be related to bronchial destruction (6). It was reported that mucoid impaction, acinar pattern, and lobar collapse are reversible lesions, but bronchiectasis, bronchial wall thickening, and emphysema are irreversible abnormalities (7). The clinical significance of these findings is not yet classified (8). We are not aware of any previous study evaluating airway or parenchymal abnormalities on HRCT in elderly asthmatics.

The study is based on the hypothesis that if airways remodelling is related to duration of disease, the CT-scan abnormalities in early onset asthmatics should occur more frequent than of late onset asthmatics.

We examined the relation between the disease duration and the frequency of airway or parenchymal abnormalities on HRCT in elderly asthmatics patients.

Materials and Methods

The present study included 68 elderly asthmatic patients (age, > 60 year) who were followed in the Respiratory Disease Clinics of Kırıkkale University Hospital. Patients were consecutively recruited during a 2-year period. Asthma diagnosis was made according to the American Thoracic Society criteria with symptoms of episodic wheezing, cough and shortness of breath responding to bronchodilators, and reversible airflow obstruction documented in at least one previous pulmonary function study (9). Patients consisted of 54 women and 14 men and mean age was 66.09±4.83. None of patients were current or previous smokers. All patients gave their written informed consent at the start of the study.

Atopy was determined by skin-prick tests to common inhalant allergens (Center laboratories port Washington,N.Y.11050). The followings were taken as exclusion criteria; cardiac disorder, cognitive impairment, treatment with systemic corticosteroids, history of allergic bronchopulmonary aspergillosis, respiratory tract infection in the previous four weeks. All patients used inhaled beta agonist and inhaled steroid. Detailed physical examination and spirometric measurements were obtained from each patient. The patients were separated into two groups according to the duration of symptoms (late-onset asthma, < 5 year, early-onset asthma, ≥ 5 year). Asthma severity score was defined according to the National Asthma Education Program (NAEP) guidelines (ie, frequency of symptoms, degree of airflow obstruction, and frequency of use of oral glucocorticoids) (10). Histamine (H) inhalation test was performed on patients to determine the level of bronchial hyperreactivity. Prior to testing, inhaled and oral bronchodilators were withheld for at least 12 hours. Inhaled corticosteroids were not withheld. Histamine solution (Sigma®, Diesenhofen, Germany) was prepared in sterile isotonic saline. Histamine challenge test was performed according to standardized procedure (11). Pulmonary functions were measured by a flow-sensing spirometer connected to a computer for data analysis (Jeager®, Wuerzburg, Germany). Each subject inhaled doubling increasing concentrations of H (0.03 to 16 mg/ml), nebulized by a dosimeter with an output of 9 ± 0.3 ml/puff (Dosimeter APS Pro, Jeager®, Wuerzburg, Germany), until FEV1 was reduced by 20% from baseline values. Bronchial response to H was expressed as the provocative dose causing a 20% fall in FEV1 (PD20 in mg/ml), and was calculated by using the same computer program (LAB, version 4.3, Jeager®, Wuerzburg, Germany). CT scans of the chest performed on a Picker Sele CT (Haifa-Israel) in high-resolution mode according to the method of Mayo and colleagues (12). The matrix size was 512X512 and the scanning time 2.1s. The patients were examined in the supine position during full deep inspiration, with their arms held over their heads. Images were recorded at a window width of 1,600 HU and at a window level of -600 HU. No intravenous contrast medium was administered. Section cuts of 1.5 mm thickness at 10 mm increments were obtained throug-
hout the lungs. Two physicians who had no knowledge of clinical status of the subject’s diseases interpreted the scans independently. The first assessment was a subjective examination of the quality of each CT scan, followed by an evaluation of each lobe of the pulmonary parenchyma. The CT diagnosis of bronchiectasis, sequel linear shadows was based on the criteria of Naidich and colleagues (13). The CT diagnosis of emphysema was established according to adopted criteria: area of low attenuation in comparison with adjacent normal lung parenchyma, with vascular disruption lacking a well-defined wall or an area of low attenuation possessing a wall less than 1 to 2 mm in thickness (14). The presence of peribronchial thickening was accepted when the thickness of bronchial wall was equal to 50% of the diameter of the adjacent pulmonary artery or higher than that, by using a modification the Bhalla system (15).

Independent samples t test was used for comparing the clinical parameters (PD20, age, FEV1 as the % of predicted) on groups. Variables were used as dichotomous, emphysema, bronchiectasis, peribronchial thickening, and sequel linear shadows. Analysis of contingency tables was performed with the Chi Square or Fischer exact test when any table’s cell had expected values of less than five. Irreversible CT-scan abnormality were defined as any presence of emphysema, bronchiectasis, bronchial wall-thickening. Logistic regression was used to calculate odds ratios (OR) and 95% confidence intervals (CI) for the association between irreversible CT-scan abnormality with duration of asthma (late onset=0; early onset=1), disease severity score, PD20, age and gender. A p value < 0.05 was considered significant.

Results
The characteristics of the patients are presented in table I. Computed tomographic abnormalities in elderly asthmatics are presented in Table II. Multiple logistic regression analysis identified that early-onset of disease was independent risk factor for presence of irreversible CT-scan abnormality in elderly asthmatics (OR 9.4(2.7-32.7) p=0.00001), not with diseases severity score, PD20, age and gender in elderly asthmatics. Mean baseline FEV1% (77.52±21.05 versus 100.11±17.69 p=0.0001) and PD20 values (0.21±0.46 versus 1.55±2.24, p=0.001) of patients with early-onset asthma were significantly lower than those with late-onset asthma. Mean baseline FEV1 of patients with emphysema (57.00±16.92) was lower than in patients with early-onset asthma (83.19±18.57) (p=0.001) (Table III). Mean FEF25-75 of patients with emphysema (27.75±22.08) was lower than in patients with early-onset asthma (53.59±23.20) p=0.008).

Discussion
We showed that irreversible abnormalities such as, emphysema, bronchiectasis and bronchial wall-
thickening are more common in early onset than in late onset elderly asthmatic subjects. The duration of asthma was independent risk factor for the presence of irreversible CT-scan abnormality in elderly asthmatics. We have notified a higher rate of the remodelling patterns in patients with early onset asthma, therefore it may be suggested that with increased duration of asthma, there might be ongoing remodelling with an increase in airway tissue.

The evidence for the presence of emphysema in chronic asthma is controversial. Hruban et al reported that the diagnosis of emphysema assessed by pathologic examination was correlated with high resolution CT scans (16). Kuwano et al concluded that high resolution CT scan help to identify the presence and grading of mild emphysema (17). We are not aware of any previous study evaluating airway or parenchymal abnormalities on HRCT scans in elderly asthmatics. Similarly, Paganin and coworkers, using a visual scoring system for emphysema on CT, have reported the presence of emphysema in nonsmoking asthmatic patients (7,18). The other HRCT studies have indicated that emphysema in asthma may be related to smoking. Mochizuki et al and Kinsella et al. found CT evidence of emphysema, only in smoking asthmatics. (19,20). Linch et al and Kondoh et al showed the presence of emphysema in CT scan in some asthmatic subjects but again most were smokers (3,21). In the pathological investigation of asthmatic lungs, emphysema was observed in some cases, but smoking habits were not assessed in most of the patients studied. Interstitial emphysema was present in 10 of 53 clinical cases of fatal asthma, all of which had bronchial gland duct ectasia and a histological diagnosis of asthma. The authors concluded that bronchial gland duct ectasia is a common histological feature of severe asthma, and that interstitial emphysema may be a consequence of rupture of these dilated gland ducts (22). In a fatal case of a nonsmoking asthmatic with a toluene di-isocyanate sensitivity has been observed focal areas of alveolar destruction adjacent to areas of perfectly intact alveolar walls in lung parenchyma (23). Paganin et al. (24) conc-

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**Table II: Computed tomographic abnormalities in elderly asthmatic patients.**

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>Early-onset asthma n:37 (%)</th>
<th>Late-onset asthma n:31(%)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emphysema</td>
<td>8 (21.6)</td>
<td>0 (0.0)</td>
<td>0.006</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>5 (13.9)</td>
<td>0 (0.0)</td>
<td>0.039</td>
</tr>
<tr>
<td>Bronchial wall-thickening</td>
<td>15 (41.7)</td>
<td>4 (12.9)</td>
<td>0.014</td>
</tr>
<tr>
<td>Sequel line shadow</td>
<td>13 (36.1)</td>
<td>8 (25.8)</td>
<td>0.434</td>
</tr>
<tr>
<td>Pleural thickening</td>
<td>2 (5.6)</td>
<td>6 (19.4)</td>
<td>0.050</td>
</tr>
<tr>
<td>Bronchial mucoid impaction</td>
<td>9 (25.0)</td>
<td>8 (25.8)</td>
<td>0.940</td>
</tr>
<tr>
<td>Mosaic pattern</td>
<td>6 (16.7)</td>
<td>8 (25.8)</td>
<td>0.385</td>
</tr>
</tbody>
</table>

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**Table III: Clinical features of asthmatic patients with emphysema in HRCT.**

<table>
<thead>
<tr>
<th>No</th>
<th>Age</th>
<th>Gender</th>
<th>Duration (yr)</th>
<th>Atopy</th>
<th>FEV1 (%)</th>
<th>FEV1 (lt)</th>
<th>FEF25-75 (%)</th>
<th>PD20</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>67</td>
<td>F</td>
<td>32</td>
<td>-</td>
<td>62</td>
<td>1.02</td>
<td>24</td>
<td>0.13</td>
</tr>
<tr>
<td>2</td>
<td>60</td>
<td>F</td>
<td>16</td>
<td>-</td>
<td>90</td>
<td>1.89</td>
<td>81</td>
<td>0.59</td>
</tr>
<tr>
<td>3</td>
<td>79</td>
<td>F</td>
<td>18</td>
<td>-</td>
<td>56</td>
<td>0.97</td>
<td>21</td>
<td>0.15</td>
</tr>
<tr>
<td>4</td>
<td>62</td>
<td>M</td>
<td>12</td>
<td>-</td>
<td>43</td>
<td>1.06</td>
<td>15</td>
<td>0.001</td>
</tr>
<tr>
<td>5</td>
<td>68</td>
<td>M</td>
<td>10</td>
<td>-</td>
<td>60</td>
<td>1.70</td>
<td>23</td>
<td>0.02</td>
</tr>
<tr>
<td>6</td>
<td>68</td>
<td>M</td>
<td>48</td>
<td>-</td>
<td>31</td>
<td>0.86</td>
<td>13</td>
<td>0.01</td>
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<tr>
<td>7</td>
<td>62</td>
<td>F</td>
<td>15</td>
<td>-</td>
<td>59</td>
<td>1.22</td>
<td>17</td>
<td>0.06</td>
</tr>
<tr>
<td>8</td>
<td>65</td>
<td>M</td>
<td>12</td>
<td>-</td>
<td>55</td>
<td>1.70</td>
<td>28</td>
<td>0.07</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>66.38±5.93</td>
<td>20.13±13.29</td>
<td>57.00±16.92</td>
<td>1.30±0.39</td>
<td>27.75±22.08</td>
<td>0.13±0.19</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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luded emphysema is unlikely to be due to alveolar disruption but rather to an extensive peribronchial fibrosis or a rupture of dilated bronchial glands and may therefore, relate to cicatricial emphysema. Biernacki et al. confirmed that low lung computed tomography density, with values similar to those in patients with chronic bronchitis and emphysema, occurs in chronic asthma (25). These studies suggest that emphysema may be present in a subgroup of asthmatics.

Park et al. (8) reported that asthmatic patients might exhibit abnormal HRCT findings, such as bronchiectasis (17.5%), bronchial wall thickening (17.5%), and mosaic lung attenuation. These findings were common in bronchial asthma with moderate to severe airflow limitation and patients with these changes had a more prolonged history of asthma. Paganin et al. (7) showed that irreversible abnormalities observed in the lungs of nonsmoking asthmatic subjects on CT scans, such as bronchiectasis (25.7%), bronchial recruitment (23.1%), sequelae linear shadows (28.2%) are more extensive in severe forms than in milder forms of the disease, and in nonallergic than in allergic asthmatic subjects. As consistent to above studies, in present study, in comparison patients with late-onset asthma, those with early-onset asthma had more frequent CT-scan abnormalities and more severe disease. The prior studies showed that CT-scan abnormalities were found to be more frequent in more severe disease but its relationship with clinical parameters has not been investigated. Therefore, results of the above studies should be interpreted with caution. Also, we have performed this study interpreting the clinical parameters with CT scan abnormalities. Logistic regression analysis was performed with disease severity score, duration of disease, bronchial responsiveness degree, age and gender as independent factors, only early onset of disease was found to be an significant risk factor for the presence of irreversible CT-scan abnormalities. These results might imply that the duration of disease is an important factor rather than the severity of disease for the high frequency of irreversible CT-scan abnormalities in elderly asthmatics.

In conclusion, we observed that early onset elderly asthmatics had more frequent irreversible abnormalities than late onset elderly asthmatics, which may represent airway inflammation or remodeling. Long-standing chronic asthma may be associated with structural changes of both lung parenchyma and airways in elderly patients. Moreover, even asthma is well gotten under control, the long-term disease may be cause irreversible abnormalities.

References


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