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 FEV_1% (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.
Conclusion: These data suggest that HRCT abnormalities in early-onset elderly asthmatics may reflect airway or parenchymal changes may become irreversible ultimately.
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Key Words: Elderly, asthma, HRCT, emphysema

ÖZET
Yaşlı Astımlılarda Yüksek Rezolüsyonlu Bilgisayarlı Tomografi Bulguları
Amaç: Biz bu çalışmada eğer havayolunun yeniden şekillenmesi astım süresi ile ilişkili ise erken başlayan astımlı hastalarda BT bulgularının geç başlayan astımlı hastalarda daha fazla anormallik gösterebileceğini düşündük. Biz yaşlı astımlı hastalarda YRBT kullanarak hava yolu ve parankim anormalliklerinin varlığını ve sıklığını değerlendirdik.
Metotlar: Çalışma grubu 68 stabil yaşlı astımlı hastadan oluşmaktaydı (yaş>60). Hiçbiri sigara içmiyordu.Hastalar semptom sürelerine göre iki gruba ayrıldı (geç başlangıçlı astım<5 yıl, erken başlangıçlı astım≥5 yıl). Tüm hastalara YRBT ve Histamin inhalasyon testi yapıldı. Astım ciddiyet skoru National Asthma Education Program (NAEP) klavuzuna göre tanımlandı (semptomların sıklığı, hava yolu obstrüksiyon derecesi ve oral steroid kullanma sıklığı).
Sonuçlar: Erken başlangıçlı astımlı hastalar geç başlangıçlı astımlı hastalara göre önemli derecede daha sık amfizem (21.6% vs 0.0 sırayla% p=0.006), bronşektazi (13.9% vs 0.0% sırayla p=0.03) ve bronşial duvar kalınlaşmasına (41.7% vs 12.9% sırayla p=0.01) sahipti. Lojistik Regresyon Analizi yaşlı astımlı hastalarda hastalığın erken başlamasının geri dönüşümsüz BT anormalliklerinin varlığı için bağımsız risk faktörü olduğunu gösterdi (odds oranı (OR 9.4(2.7-32.7) p=0.00001). Ortalama temel FEV_1% (77.52±21.05 ve 100.11±17.69, p=0.0001) ve PD20 (0.21±0.46 ve 1.55±2.24, p=0.001) değerleri geç başlayan astımlılardan önemli derecede daha düşüktü.
Yorum: Bu veriler bize erken başlayan yaşlı astımlı hastalarda YRBT anormalliklerinin zamanla geri dönüşümsüz olabilen havayolu veya parankimal değişiklikleri gösterebileceğini düşündürür.
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Anahtar Kelimeler: Yaşlı, astım, YRBT, amfizem.

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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 centrilobuler 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 clasified (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 FEV_1 was reduced by 20% from baseline values. Bronchial response to H was expressed as the provocative dose causing a 20% fall in FEV_1 (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, FEV_1 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, PD_{20}, age and gender in elderly asthmatics.

Mean baseline FEV_1% (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 FEV_1 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 FEF_{25-75} 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-

Table I: Clinical features of the patients with asthma. Data is presented as mean ± standard deviation (SD).

	Early-onset asthma n: 37	Late-onset asthma n: 31	p Value
Age (yr)	64.86±4.82	67.55±4.49	0.02
Duration of asthma (yr)	19.65±10.12	3.26±1.26	0.0001
Atopy	4	3	
Gender (F / M)	29F, 8M	25F, 6M	
Severity score	1.43±1.32	0.74±0.93	0.01
Predicted FEV_1 (%)	77.52±21.05	100.11±17.69	0.0001
FEV_1 (lt)	1.63±0.48	2.02±0.40	0.001
FEF_{25-75} (%)	48.00±25.09	78.24±25.36	0.0001
PD20	0.21±0.46	1.55±2.24	0.001

thickenining 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 ashmatics. 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 scane 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-

Table II: Computed tomographic abnormities in elderly asthmatic patients.

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

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

No	Age	Gender	Duration (yr)	Atopy	FEV_1 (%)	FEV_1 (lt)	FEF_{25-75} (%)	PD20
1	67	F	32	-	62	1.02	24	0.13
2	60	F	16	-	90	1.89	81	0.59
3	79	F	18	-	56	0.97	21	0.15
4	62	M	12	-	43	1.06	15	0.001
5	68	M	10	-	60	1.70	23	0.02
6	68	M	48	-	31	0.86	13	0.01
7	62	F	15	-	59	1.22	17	0.06
8	65	M	12	-	55	1.70	28	0.07
Mean±SD	66.38±5.93		20.13±13.29		57.00±16.92	1.30±0.39	27.75±22.08	0.13±0.19

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%) and mosaic lung attenuation (17.5%). 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%), sequel 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 clinic 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 remodelling. 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

1. Rimondi MR, Zompatori M, Battaglia M, Barbara C, Fasano L, Canini R. Use of computed tomography in asthmatic patients. Radiol Med 1994; 88(6): 758-64.
2. Boulet LP, Belanger M, Carrıer G. Airway responsiveness and bronchial-wall thickness in asthma with or without fixed airflow obstruction. Am J Respir Crit Care Med 1995; 152:865-71.
3. Linch D, Newell J, Tschomper B, Cink T, Newman L, Bethel R. Uncomplicated asthma in adults: comparison of CT appearance of the lungs in asthmatic and healthy subjects. Radiology 1993; 188:829-33.
4. Ünal M, Özlü T, Yılmaz S, Bülbül Y, Dinç H, Serçe K. Bronşial astmada reverzibl bronşial dilatasyon: Yüksek rezolüsyonlu bilgisayarlı tomografiyle değerlendirilmesi. Tanısal ve Girişimsel Radyoloji1996;2:41-45.
5. Ünal M, Özlü T, Yılmaz S, Bülbül Y, Dinç H, Serçe K. Bronşial astmada reversibiliteye bağlı değişikliklerin bilgisayarlı tomografi ile kantitatif olarak tesbiti ve amfizzematöz değişimi ayırmadaki rolü. Bilgisayarlı Tomografi Bülteni 1996;4:42-7.
6. Lynch DA. Imaging of asthma and allergic bronchopulmonary mycosis. Radiol Clin North Am 1998; 36(1): 129-42.
7. Paganin F, Trussard V, Seneterre E, et al. Chest radiography and high resolution computed tomography of the lungs in asthma. Am Rev Respir Dıs 1992; 146:1084-7.
8. Park JW, Hong YK, Kim CW, Kim DK, Choe KO, Hong CS. High-resolution computed tomography in patients with bronchial asthma: correlation with clinical features, pulmonary functions and bronchial hyperresponsiveness. J İnvestig Allergol Clin İmmunol 1997; 7(3): 186-92.
9. American Thoracic Society. Standards for diagnosis and care of patients with chronic obstructive pulmonary diseases (COPD) and asthma. Am Rev Respir Dis 1987;136:225-44.
10. National Asthma Education Program. Guidelines for the diagnosis and management of asthma. Publication no. 91-3042. Bethesda, MD: National Institutes of Health, 1991.
11. Foresi A S, Mattoli G, Corbo M, Polidori G, and Ciappi G. Comparison of bronchial response to ultrasonically nebulized distilled water, exercise and methacholine in asthma. Chest 1986; 90:822–6.

12. Mayo JR, Webb WR, Gould R, et al. High-resolution CT of the lungs: an optimal approach. Radiology 1987; 163(2): 507-10
13. Naidich DP, McCauley DI, Khouri NF, Stitik FP, Siegelman SS. Computed tomography of bronchiectasis. J Comput Assist Tomogr 1982; 6(3): 437-44.
14. Bergin C, Muller NL, Nichols DM, et al. The diagnosis of emphysema: a computed tomographic-pathologic correlation. Am Rev Respir Dis 1986; 133:541-46.
15. Bhalla M, Turcios N, Aponte V, et al. Cystic fibrosis: scoring system with thin-section CT. Radiology 1991; 179(3): 783-8.
16. Hruban RH, Meziana MA, Zehrouni EA et al. High Resolution Computed Tomography of inflation-fixed lungs. Patologic-radiologic correlation of centrlobular emphysema. Am Rev Respir Dıs 1987; 136: 935-40.
17. Kuwano K, Matsuba K, Ikeda T, et al. The diagnosis of mild emphysema. Correlation of computed tomography and pathology scores. Am Rev Respir Dis 1990;141(1): 169-78.
18. Paganin F, Senetere E, Chanez P,et al. Computed tomography and of the lungs in asthma: Influence of disease severity and etiology. Am J Respir Crit Care Med 1996; 153: 110-4.
19. Mochizuki T, Nokajima H, Kokubu F, Kushiashi T, Adachi M. Evalution of emphysema in patients with reversible airway obstruction using High-Resolution CT. Chest 1997; 112:1522-26.
20. Kinsella M, Müller N.L., Staples C, Vedal S, Chan-Yeung M. Hyperinflation in asthma and emphysema. Assesment by pulmoner function testing and computed tomography. Chest 1988; 94(2): 286-9.
21. Kondoh Y, Taniguchi H, Yokoyama S, Taki F, Tagaki K, Satake T. Emphysematous change in chronic asthma in relation to cigarette smoking. Chest 1990; 97:845-49.
22. Cluroe A, Holloway L, Thomson K, Purdie G, Beasley R. Bronchial gland duct ectasia in fatal bronchial asthma: association with interstitial emphysema. J Clin Pathol 1989; 42(10): 1026-31.
23. Fabbri LM, Danieli D, Crescioli S, et al. Fatal asthma in a subject sensitized to toluene diisocyanate. Am Rev Respir Dis 1988; 137(6): 1494-8.
24. Paganin F,Jaffual D,Bouscuet J.Significance of emphysema observed on computed tomography scan in asthma. Eur Respir J 1997;10:2446-8.
25. Biernacki W, Redpath AT, Best JJK, MacNee W.Measurement of CT lung density in patients with chronic asthma. Eur Respir J 1997; 10:2455-9.