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Inflammatory profile in optimally treated patients with adult versus early-onset asthma

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ABSTRACT

Introduction: The age of asthma onset is often implicated in clinical manifestation, diagnosis, and management of the disease.

Aim: To define demographic, clinical and functional features and inflammatory characteristics in induced sputum in patients with adult-onset asthma.

Methods: Optimally treated patients from asthma clinics of two tertiary hospitals were included in the study. Patients underwent assessment of demographic characteristics, severity and treatment regimes, pulmonary function tests, and skin prick tests, as well as measurement of blood eosinophils and sputum induction for the assessment of sputum inflammatory cells, IL-8 and IL-13 levels in the supernatant.

Results: Of the 333 patients recruited, 234 (70.2%) had adult-onset asthma. Adult-onset asthmatics were older, had a higher BMI, a shorter disease duration, and were less often atopic, compared to patients with early onset asthma. Higher proportions of patients with severe asthma presented increased levels of FeNO and blood eosinophils, both in the early and the adult-onset patient groups. Finally, obese patients with early onset asthma were characterized by less atopy compared to non-obese patients in the same group.

Conclusion: Adult-onset asthma was characterized by less sputum eosinophilia, a nonatopic profile and a higher BMI compared to early-onset asthma. The presence of blood eosinophilia and increased FeNO in patients with severe asthma was comparable in the two groups.

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Introduction

Asthma is a heterogeneous disorder which includes several different phenotypes characterized by differences in age of onset, etiology, inflammatory profile, and response to treatment [1]. Although usually in asthmatic patients, asthma symptoms first appear early in life, some patients develop asthma for the first time in adulthood. In this case, asthma is characterized as late onset or adult onset and is recognized as one of the most severe and difficult to treat asthma subtypes [2].

Late-onset asthma is superimposed on a background of aging-related changes in respiratory and immune physiology, and often on multiple diseases and conditions such as occupational exposures, smoking and hormonal influences, common in older age [3,4]. Late-onset disease is generally less associated with allergy and usually involves different asthma inflammatory phenotypes and endotypes such as eosinophilic (often severe and present despite high ICS doses and often requiring systemic corticosteroids), exercise-induced, neutrophilic and smooth muscle-mediated (paucigranulocytic) asthma [2,5].

Severe asthma is defined as the form of asthma requiring treatment with high dose ICS and LABA or leukotriene modifier/theophylline for the previous year or systemic CS for over 50% of the previous year to prevent it from becoming 'uncontrolled' or which remains 'uncontrolled' despite this therapy [6]. Severe asthma [6–8] is associated with frequent exacerbations and/or rapid decline of lung function, despite avoidance of trigger factors, proper management of comorbidities and use of high-dose anti-inflammatory treatment. The choice of modern biologic treatments is based on clinical characteristics, and the presence of specific inflammatory biomarker profiles and such biomarkers may also predict treatment response.

The aim of the present study was to evaluate the differences in clinical, functional, and inflammatory characteristics between optimally treated patients with early and adult-onset asthma. We particularly focused on the identification of differences in patients with Severe Asthma of early or late onset, in order to provide information for the targeted therapeutic approach in such patients.

Methods

Study design

We included patients with previously diagnosed asthma, followed up in asthma clinics of two tertiary hospitals (first Respiratory Medicine Department, University of Athens, Sotiria Hospital, Athens, Greece, and second Respiratory Medicine Department, University of Athens, 'Attikon' Hospital, Chaidari, Greece). All patients provided a detailed medical history and their demographic data, smoking status, body mass index (BMI), and treatment were recorded. Diagnosis of asthma was based on the GINA guidelines [9] and adult-onset asthma was defined as the presence of asthma symptoms after the age of 18 years. Pulmonary Function values, Skin prick tests, measurement of blood eosinophils, as well as inflammatory biomarkers and cell counts in induced sputum were also measured and recorded. All measurements were performed with the patients in stable condition and optimally treated. Optimization of treatment was based on clinical and functional criteria and the results of the Asthma Control Test (ACT). High levels of ICS were defined according to the ATS/ERS guidelines [6]. Asthma severity was based on ATS/ERS guidelines [6]. Patients with a diagnosis of other respiratory diseases, concomitant malignancy or severe heart, liver, renal, or collagen disease were not included in the study. The study protocol was approved by the ethics committees of both hospitals and all subjects provided written informed consent.

Induced sputum analysis

Sputum induction was performed as previously described [10,11]. After selection, the sample was put into a polystyrene tube which has been preweighed empty. The next step was the weighing of the tube with the sample, followed by addition of a quantity of 0.1% Dithiothreitol (DTT) solution or its equivalent Dithioerythritol (DTE) $\times 4$ volumes of the weight of the sample, to break the disulfide bonds in the mucin molecules, allowing the release of cells. Subsequently, the sample was agitated on a vortex mixer for about 30 s and then placed for homogenization on a tube rocker (3D-Shaker) at 22°C for about 20 min. An equal volume of phosphate-buffer saline (PBS) solution was then added, to achieve a more efficient dilution of the sample and dispersion of the cells. The sample was agitated again on vortex for about 15 s and homogenized on the tube rocker for about 5 min. Sample filtration through a 48 μ m nylon mesh was performed for the removal of remaining mucus and debris. After centrifugation at 300–1500 $\times g$ for about 10 min, the emerging supernatant was stored at –70°C. Total cell count was evaluated with a hemocytometer using Trypan Blue stain. Slides were prepared by cytopsin (Shandon, Runcorn, UK) and were stained with May-Grunwald and Giemsa for differential cell counts. A blind observer counted a minimum of 500 inflammatory cells in each sample. Sputum samples were acceptable if they had a volume of at least 2 ml after final expectoration, and the percentage of squamous cells on the slides was <10%. Total cell count was expressed as the number of cells $\times 10^6$ /ml and sputum inflammatory cells as the percentage (%) of non-squamous cells. Sputum supernatants were kept at –70°C for

further measurement of Interleukin-13 (IL-13) and Interleukin-8 (IL-8). IL-13 and IL-8 were measured using enzyme-linked immunosorbent assay kits (ELISA, R&D systems, Minneapolis, Minnesota, USA with detection limits of 32 pg/ml and 3.5 ng/ml, respectively).

Assessment of lung function, atopy, and fraction of exhaled nitric oxide

Forced expiratory volume in 1 s (FEV₁) and Forced vital capacity (FVC) were measured using Master Screen Body (Viasys Healthcare, Jaeger, Hoechberg, Germany) according to the American Thoracic Society guidelines [12]. Atopy was defined as the presence of a positive skin prick test to at least 1 out of 20 common aeroallergens including trees (Olea Eur, Platanus, Betula, Cypress), grasses and cereals (Grass, Cereals, Secale er, Cynodon D, Lolium per), weeds (Taraxacum vulg, Plantago lan, Artemisia vul, Parietaria off, Chenopodium A), moulds (Atemaria, Aspergillus mix, Penicillium) and mites and epithelia (Cat Fur, Dog hair, Cockroach).

Patients were characterized as having severe asthma according to the ATS/ERS criteria [6]. The fraction of exhaled NO (FeNO) was measured using a portable NO analyzer (NIOX MINO, Aerocrine, Solna, Sweden) [13].

Statistical analysis

Categorical variables are presented as n (%), whereas numerical variables are presented as mean $\pm$ standard deviation (SD) or median (interquartile ranges) for normally distributed and skewed data, respectively. Normality of distributions was checked with the Kolmogorov–Smirnov test. Statistical comparisons between groups were performed with one-way analysis of variance (ANOVA) for normally distributed data and Kruskal–Wallis tests for skewed data, accompanied by appropriate post hoc tests for multiple comparisons (Bonferroni and Dunn's, respectively). Differences in numerical variables between two groups were evaluated with unpaired t-tests and Mann–Whitney U-tests for normally and skewed data, respectively, whereas comparisons of proportions were performed using chi-square tests. Correlations were performed using Spearman correlation coefficient. All p-values <0.05 were considered statistically significant. Data were analyzed using SPSS 17.0 for Windows (SPSS Inc., Chicago, IL, USA) and graphs have been created using GraphPad Prism 6 (GraphPad Software, Inc La Jolla, CA, USA).

Results

Demographic characteristics

Three hundred and thirty-three patients with asthma were included in our study. Ninety-nine (29.7%) were characterized as early-onset asthma patients and 234 (70.3%) as adult-onset asthma patients. Demographic characteristics of study participants are summarized in Table 1. Patients with late-onset asthma were older, had a higher BMI, a shorter disease duration, and were less often atopic, compared to patients with early-onset asthma.

Table 1. Demographic and functional characteristics of the study participants.

Variable	All N = 333	Early onset asthma N = 99	Adult onset asthma N = 234	p-Value
Age (years)	53.0 (42.0, 61.0)	42 (32.0, 57.0)	54.5 (47.0, 62.0)	<0.001
Gender (Female), N(%)	221 (66.4%)	66 (66.7)	155 (66.2)	0.940
BMI (kg/m ²)	27.0 (24.6, 30.0)	26.7 (24.3, 29.8)	27.0 (25.0, 30.3)	0.042
Current smokers, N (%)	129 (38.7)	41 (41.4)	88 (37.6)	0.514
Age at disease onset (y)	28.0 (15.0, 43.0)	9.0 (5.0, 14.0)	35.5 (27.0, 47.0)	<0.001
Disease duration (y)	21.0 (12.0, 31.0)	32.0 (23.0, 45.0)	15.0 (10.0, 23.0)	<0.001
FEV ₁ (%pred.)	77.0 (65.0, 91.0)	77.0 (62.0, 94.0)	77.0 (66.8, 91.0)	0.899
FVC (%pred.)	92.0 (80.0, 103.5)	93.0 (81.0, 106.0)	91.0 (80.0, 101.0)	0.562
FEV ₁ /FVC	70.0 (63.0, 77.0)	70.0 (61.0, 77.0)	70.0 (64.0, 76.0)	0.941
Atopy, N (%)	173 (52)	65 (65.7)	108 (46.2)	0.001
Criteria for severe asthma, N (%)	83(24.9)	25 (25.3)	58 (24.8)	0.928
Treatment				
LABA, N (%)	306 (91.9)	92 (92.9)	214 (91.5)	0.653
High dose ICS, N (%)	85 (25.5%)	26 (26.3)	59 (25.2)	0.841
LAMA, N (%)	25 (7.5)	12 (12.1)	13 (5.6)	0.038
LTRAs, N (%)	49 (14.7)	15 (15.2)	34 (14.5)	0.884
OCS, N (%)	42 (12.6)	16 (16.2)	26 (11.1)	0.204

Data are presented as median (IQR) unless otherwise indicated.

Abbreviations: FEV₁: Forced Expiratory Volume in 1 s, FVC: Forced exhaled Vital Capacity, LABA: Long-acting beta agonists, ICS: inhaled corticosteroids, OCS: oral corticosteroids, LAMA: Long-acting muscarinic antagonists, LTRAs: Leukotriene Receptor Antagonists.

Bold indicates statistically significant differences.

Inflammatory biomarkers

No difference was observed between the levels of blood eosinophils expressed either as an absolute number of cells or as a percentage of the total white blood cell count between patients with early and those with adult-onset asthma.

Patients with adult-onset asthma had significantly fewer sputum eosinophils (%) [2.0 (0.0, 5.0) vs 4.0 (1.0, 8.0), $p = 0.005$], although no difference was observed in the absolute number of sputum neutrophils [36.0 (22.0, 46.0) vs 38.0 (22.0, 52.0), $p = 0.610$] for patients with adult-onset and early-onset asthma, respectively. No difference was observed in the levels of FeNO, and the levels of IL-8 and IL-13 in the sputum supernatant between the two groups. (Table 2)

Patient classification according to eosinophilic inflammation and the presence of severe asthma

In order to identify patients with different levels of blood and airways eosinophilic inflammation, we classified our patients in groups according to widely used cut-points: FeNO <25, 25-50 and >50 ppb; blood eosinophils <150, 150-300 and >300 cells/ μ L; sputum eosinophils <3% and $\geq$ 3%.

Severe asthma was as frequent in early-onset as in adult-onset asthma (25.3% vs. 24.8%, respectively). Higher proportions of patients with severe asthma presented increased levels of

FeNO and blood eosinophils, both in the early and the adult-onset patient groups. No difference was observed in sputum eosinophilia between patients with severe asthma and mild to moderate asthma, although patients with early-onset severe asthma presented a trend for more prominent sputum eosinophilia that was not statistically significant (Table 3).

The effect of gender in patients with adult-onset asthma according to asthma severity

No difference was observed between genders and asthma severity in patients with early-onset asthma. In this group, males represented 35.1% of the patients with mild/moderate asthma and 28% of the patients with severe asthma ($p = 0.513$). However, this was not the case in the group of adult-onset asthma in which males represented 38% of the asthmatic patients with mild/moderate asthma but only 18.9% of the patients with severe asthma ($p = 0.004$).

The effect of obesity in early and adult-onset asthma

Obese patients with early onset asthma were characterized by less atopy compared to non-obese patients in the same group [45.4% vs 71.4% ($p = 0.024$) for obese and non-obese asthmatic patients with early onset asthma,

Table 2. Inflammatory biomarkers in patients with early and adult-onset asthma.

Variable	All N = 333	Early-onset asthma N = 99	Adult-onset asthma N = 234	p-Value
FeNO (ppb)	20.0 (12.0, 28.0)	18.0 (11.0, 27.0)	20.5 (12.0, 28.3)	0.376
Blood Eosinophils (cells/ μ L)	98.0 (1.5, 199)	120.0 (43.0, 210.0)	90.0 (0.0, 198.0)	0.255
Blood Eosinophils (%)	2.0 (0.0, 4.0)	2.0 (1.0, 4.0)	2.0 (0.0, 4.0)	0.279
Sputum Eosinophils (%)	2.0 (0.0, 6.0)	4.0 (1.0, 8.0)	2.0 (0.0, 5.0)	0.005
Sputum Neutrophils (%)	37.0 (22.0, 46.0)	38.0 (22.0, 52.0)	36.0 (22.0, 46.0)	0.610
Sputum IL-13 (ng/L)	0.87(0.66, 1.23)	0.89 (0.68, 1.37)	0.87 (0.65, 1.21)	0.205
Sputum IL-8 (ng/L)	15.0 (7.0, 29.0)	15.0 (7.0, 29.0)	15.0 (6.7, 29.0)	0.630

Data are presented as median (IQR) unless otherwise indicated.

Abbreviations: FeNO: fraction of exhaled nitric oxide, IL-13: Interleukin 13, IL-8: Interleukin 8.

Bold indicates statistically significant differences.

Table 3. Differences in inflammatory biomarkers in patients with mild/moderate asthma and severe asthma according to the age of disease onset.

	Early onset asthma		p-value	Late onset asthma		p-value
	Mild/moderate asthma N=74	Severe asthma N=25		Mild/moderate asthma N=176	Severe asthma N=78	
FeNO level						
<25ppb	79.8%	44.0%	0.002	75.0%	46.5	<0.001
25-50ppb	12.1%	24.0%		19.9%	20.8%	
>50ppb	8.1%	32.0%		5.1%	32.7%	
Blood eosinophils						
<150cells/ μ L	55.4%	52.0%	0.027	66.5%	51.8%	0.004
150-300cells/ μ L	36.5%	20.0%		25.6%	24.1%	
>300cells/ μ L	8.1%	28.0%		7.9%	24.1%	
Sputum eosinophils						
<3%	48.6%	28.0%	0.072	57.7%	50.9%	0.366
$\geq$ 3%	51.0%	72.0%		42.3%	49.1%	

Abbreviations: FeNO: Fraction of exhaled Nitric Oxide, ppb: parts per billion.

Bold indicates statistically significant differences.

respectively,]. There was no difference in the frequency of atopy between obese and non-obese patients in the adult-onset asthma group. Furthermore, obese patients with adult-onset asthma had worse lung function (expressed as FEV₁ and FVC %predicted) compared to non-obese-patients, [74.0 (63.0, 84.5) vs 78.0, 70.0, 94.0), $p = 0.046$ and 82.0 (76.0, 96.0) vs 94.0 (83.5, 104.0), $p < 0.001$ for FEV₁ and FVC, respectively,]. No difference was observed in this study group regarding the gender, smoking status, the levels of FeNO, blood eosinophils, percentage of sputum eosinophils and neutrophils and sputum levels of IL-8 and IL-13. Comparisons between obese and non-obese patients are shown in Table 4.

Discussion

In this cohort of patients managed in tertiary reference asthma clinics, we have shown that the patients with adult-onset asthma are characterized by greater BMI, less atopy and lower levels of sputum eosinophilia, but no other difference overall in inflammatory biomarkers, compared to patients with early onset asthma. In both groups of early and adult-onset asthma, patients with severe asthma were characterized by higher numbers of blood eosinophils and higher levels of FeNO compared to patients with mild/moderate asthma, although this was not the case with sputum eosinophils. Finally, obese patients with early onset asthma were

Table 4. Differences in the demographic and functional characteristics and inflammatory biomarkers in patients with early and adult-onset asthma according to the presence of obesity.

Variable	Early onset asthma N = 99		p-Value	Adult-onset asthma N = 234		p-Value
	Non-obese N = 77	Obese N = 22		Non-obese N = 165	Obese N = 69	
Age (years)	42.0 (31, 58.5)	44.0 (37.5, 54.8)	0.436	53.0 (43.0, 62.0)	57.0 (49.0, 64.0)	0.018
Gender (Female), N(%)	53 (68.8)	13 (59.1)	0.393	112 (67.9)	43 (62.3)	0.412
BMI (kg/m ²)	26.0 (23.6, 27.0)	31.2 (30.8, 32.3)	<0.001	26.0 (24.0, 27.5)	32.9 (31.2, 35.0)	<0.001
Current smokers, N (%)	34 (44.2)	7 (31.8)	0.300	68 (41.2)	20 (29.0)	0.078
Age at disease onset (y)	9.0 (5.5, 45)	8.5 (4.8, 12.5)	0.569	34.0 (26.0, 46.0)	42.0 (30.0, 48.0)	0.064
Disease duration (y)	31.0 (22.0, 45.0)	38.0 (31.0, 45.0)	0.305	14.0 (10.5, 23.0)	16.0 (9.5, 24.5)	0.520
FEV ₁ (%pred.)	78.0 (63.0, 97.0)	70.5 (55.2, 90.3)	0.185	78.0 (70.0, 94.0)	74.0 (63.0, 84.5)	0.046
FVC (%pred.)	94.0 (85.0, 106.0)	85.5 (75.5, 100.7)	0.135	94.0 (83.5, 104.0)	82.0 (76.0, 96.0)	<0.001
FEV ₁ /FVC	70.0 (61.0, 77.0)	70.0 (62.2, 78.0)	0.850	70.0 (62.0, 76.0)	71.0 (66.5, 77.0)	0.253
Atopy, N (%)	55 (71.4)	10 (45.5)	0.024	82 (24.2)	26 (37.7)	0.093
Criteria for severe asthma, N (%)	18 (23.4)	7 (31.8)	0.422	40 (24.2)	18 (26.1)	0.766
Treatment						
LABA, N (%)	71 (92.2)	212 (95.5)	0.600	153 (92.7)	61 (88.4)	0.281
High dose ICS, N (%)	18 (23.4)	8 (36.4)	0.222	41 (24.8)	18 (26.1)	0.870
LAMA, N (%)	8 (10.4)	4 (18.2)	0.323	8 (4.8)	5 (7.2)	0.465
LTRAs, N (%)	11 (14.3)	4 (18.2)	0.653	22 (13.3)	12 (17.4)	0.422
OCS, N (%)	12 (15.6)	4 (18.2)	0.770	19 (11.5)	7 (10.1)	0.761
FeNO (ppb)	18.0 (11.5, 28.0)	17.5 (10.0, 26.0)	0.514	20.0 (12.0, 29.0)	21.0 (14.0, 25.0)	0.913
Blood Eosinophils (cells/ μ L)	145.0 (49.0, 244.0)	93.0 (30.0, 181.5)	0.657	100.0 (45.0, 199.0)	70.0 (0.0, 188.5)	0.102
Blood Eosinophils (%)	2.0 (1.0, 4.0)	2.0 (0.8, 3.5)	0.698	2.0 (0.0, 4.0)	1.0 (0.0, 3.0)	0.161
Sputum Eosinophils (%)	4.0 (1.0, 7.5)	2.0 (0.0, 5.0)	0.875	2.0 (0.0, 5.0)	2.0 (0.0, 5.0)	0.722
Sputum Neutrophils (%)	38.0 (20.0, 45.5)	36.5 (25.0, 57.3)	0.533	35.0 (20.5, 46.0)	39.0 (26.0, 47.0)	0.233
Sputum IL-13 (ng/L)	0.87.0 (0.69, 1.50)	0.98 (0.67, 1.34)	0.950	0.87 (0.65, 1.27)	0.8 (0.65, 1.07)	0.247
Sputum IL-8 (ng/L)	15.0 (7.0, 28.0)	12.0 (6.0, 37.0)	0.956	13.0 (7.0, 29.0)	16.0 (8.0, 29.0)	0.457

Abbreviations: FEV₁: Forced Expiratory Volume in 1 s, FVC: Forced exhaled Vital Capacity, LABA: Long-acting beta agonists, ICS: inhaled corticosteroids, OCS: oral corticosteroids, LAMA: Long-acting muscarinic antagonists, LTRAs: Leukotriene Receptor Antagonists, FeNO: fraction of exhaled nitric oxide, IL-13: Interleukin 13, IL-8: Interleukin 8.**Bold** indicates statistically significant differences.

characterized by less atopy, while obese patients with adult-onset asthma had lower FEV₁ and FVC compared to patients with non-obese adult-onset asthma although no difference was observed in inflammatory characteristics.

Adult-onset asthma is usually related to obesity [2] and it seems to be associated to inherent abnormal lung mechanics, systemic inflammation, and direct effects of adipokines on airway hyperresponsiveness and inflammatory cells [14]. The association between adult-onset asthma and obesity also seems to be present in our study cohort since patients with adult-onset asthma had a greater BMI compared to patients with early onset disease. Furthermore, obesity-associated asthma of adult onset is also known to be characterized by lack of atopy [15] which was also confirmed in our study cohort. Finally, the fact that obese patients with adult-onset asthma were characterized by lower FEV₁ and FVC compared to non-obese patients in the same group leads to the hypothesis that especially in these patients, weight management might be an important therapeutic intervention.

In our study, we have found that in patients with disease of early onset, obesity was mainly related to non-atopic asthma. This finding is in accordance with the study of Gilliland et al. [16] which found a relationship between asthma and overweight in non-allergic but not in allergic children. On the contrary, in our study, patients with adult-onset asthma were mainly non-atopic regardless of the presence of obesity. This lack of atopy in patients with adult-onset asthma has been previously described [2] and leads to the conclusion that in patients with disease of late onset, asthma is probably related to factors beyond atopy.

Interestingly, although it has been reported that increased FeNO levels are associated to advancing age [17] in our study we did not find any difference in FeNO levels between patients with early and those with adult-onset asthma. This result is probably associated to the fact that FeNO levels are known to be affected by the use of inhaled corticosteroids, smoking status and the coexistence of allergic rhinitis in patients with asthma [18], and these factors may have influenced our results. Furthermore, it is interesting that no significant difference was observed in any of the studied biomarkers between the study groups, suggesting that both groups may be potential targets for newer biologic therapies. The aforementioned observation in combination with the lack of difference in FeNO levels is probably related to the higher BMI in these subjects and to the fact that obesity may lead to abnormal nitric oxide (NO) metabolism with the imbalance of L-arginine and one of its methylated products known as asymmetric dimethylarginine (ADMA) in obese subjects who acquire asthma after childhood [19,20].

In our study, we found that severe asthma occurred with the same frequency among early-onset and adult-onset asthma. Moreover, severe asthma was associated with higher blood eosinophilia and FeNO levels compared to mild/moderate asthma irrespective to the age of disease onset. This is in contrast with previous observations which have shown that adult-onset asthma is characterized by increased severity and increased eosinophilic inflammation [21]. Different definitions and study populations may account for this difference.

Finally, although both early and adult-onset asthma was mainly of female predominance, in our study we have found that in patients with early onset asthma the percentage of male patients was approximately the same regardless asthma severity whereas in patients with adult-onset asthma the majority of male patients had mild/moderate asthma. This is in accordance with previous studies showing that adult-onset severe asthma is mainly of female predominance [5].

Our study has some limitations. First, obesity was characterized according to the measurement of BMI and not the measurement of fat mass and fat-free mass; it is known that the best method to measure adiposity is the dual-energy X-ray absorptiometry (DEXA) [22]. Second, some patients were treated with high doses of ICS or received OCS which might affect the levels of some biomarkers such as FeNO, and blood and sputum eosinophils. However, our patients were optimally treated, and their asthma was stable during enrolment to the study. These facts strengthen our results and conclusions about the differences in the patients' characteristics according to disease onset. Furthermore, the differences in the decreased frequency of atopy in obese compared to non-obese patients with early-onset asthma, which is not present in patients with late-onset asthma, supports the fact that adult-onset asthma is mainly non-atopic regardless of the presence of obesity.

In this study in two tertiary asthma centers, patients with adult-onset asthma were characterized by less sputum eosinophilia, a nonatopic profile and a higher BMI compared to early-onset asthma. However, the presence of blood eosinophilia and increased FeNO in patients with severe asthma was comparable in the two groups, with the relevant implications for the selection of novel biologic treatments.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

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Declaration of interest

K Kostikas is a former Novartis employee. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties. Peer reviewers on this manuscript have no relevant financial relationships to disclose.

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