

Main contributory factors on asthma control and health-related quality of life (QoL) in elderly asthmatics

Running title: Asthma in the elderly

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Abstract

Objective: To assess the main contributory factors on asthma control and on health-related quality of life in elderly asthmatic subjects.

Methods: Retrospective case-control study nested in historical cohort that compared patients who had partly or uncontrolled asthma ($ACT \leq 19$) (cases) with patients who had well asthma control ($ACT \geq 20$) (controls). Data regarding clinical characteristics were collected from medical records. Outcomes included ACT (asthma control test), and health-related quality of life (AQLQ) (asthma-specific quality of life questionnaire). Pulmonary function was determined by spirometry.

Results: We evaluated 209 patients (151 women) ≥ 65 years old with asthma. Mean age was 73.55 years. Most patients had persistent moderate (47.60%) or severe (47.12%) asthma. A total ACT score ≤ 19 was obtained in 64 (30.62%) patients. Lack of adherence to treatment and presence of severe exacerbations behaved as a risk factor for partly controlled/uncontrolled asthma (OR 8.33 and OR 5.29, respectively). In addition, for each unit scored more in the AQLQ, the risk of poor control increased 1.51. Factors influencing AQLQ were asthma control (ACT) and presence of comorbidities such as depression, GERD and osteoporosis.

Conclusions: Despite receiving anti-asthmatic therapy, almost one-third of elderly patients had uncontrolled asthma. Factors related to treatment adherence, exacerbations and health-related quality of life should be considered. Non-respiratory comorbid conditions in older patients does not seem to be associated with worse asthma control of symptoms but their influence in health-related quality of life could indirectly affect asthma control.

Key words: Elderly asthma, Asthma control, ACT, Comorbidity, Health-related quality of life, AQLQ, Treatment adherence.

Resumen

Objetivo: Evaluar los principales factores que contribuyen al control del asma y la calidad de vida relacionada con la salud en personas asmáticas de edad avanzada.

Métodos: Estudio retrospectivo de casos y controles anidado en una cohorte histórica que comparó pacientes con asma mal o parcialmente controlada ($ACT \leq 19$) (casos) con pacientes que tenían buen control del asma ($ACT \geq 20$) (controles). Los datos relativos a las características clínicas se obtuvieron de las historias clínicas. Los resultados incluyeron los resultados del ACT (test de control de asma) y AQLQ (cuestionario de calidad de vida específica de asma). La función pulmonar se determinó mediante espirometría.

Resultados: Se evaluaron 209 pacientes (151 mujeres) ≥ 65 años con asma. La edad media fue de 73,55 años. La mayoría de los pacientes tenían asma persistente moderada (47,60%) o grave (47,12%). Se obtuvo una puntuación total de $ACT \leq 19$ en 64 pacientes (30,62%). La falta de adherencia al tratamiento y la presencia de exacerbaciones graves se comportaron como un factor de riesgo para el asma parcialmente o mal controlada (OR 8,33 y OR 5,29, respectivamente). Además, por cada unidad de mayor puntuación en el AQLQ, el riesgo de un control deficiente aumentó 1,51. Los factores que influyeron en el AQLQ fueron el control del asma (ACT) y la presencia de comorbilidades como depresión, ERGE y osteoporosis.

Conclusiones: A pesar de haber recibido tratamiento antiasmático, casi un tercio de los pacientes de edad avanzada tenía asma no controlada. Se debe tener en cuenta factores relacionados con la adherencia al tratamiento, las exacerbaciones y la calidad de vida relacionada con la salud. Las afecciones comórbidas no respiratorias en pacientes de edad avanzada no parecen estar asociadas con un peor control de los síntomas del asma, pero su influencia en la calidad de vida relacionada con la salud podría afectar indirectamente el control del asma.

Palabras clave: Asma en edad avanzada, Control de asma, ACT, Comorbilidad, Calidad de vida relacionada con la salud, AQLQ, Adherencia a tratamiento.

Background

Asthma is a complex chronic disease affecting patients of all ages. In the elderly, asthma frequently is underdiagnosed and undertreated, which can affect the rates of morbidity and mortality by asthma in this population [1-3]. Treatment is often suboptimal in elderly asthmatic patients due to underassessment of asthma control/severity by clinicians [1] and in addition, multiple patient factors may lead to suboptimal disease control, including misunderstanding of asthma as a disease and the treatment regimen, poor adherence, comorbidities, decrease of cognitive or physical capabilities, and socioeconomic challenges [3-6]. Although comorbidity and polypharmacy are considered to be major reasons for worse control of asthma in older adults, no conclusive evidence exists to support these assumptions [7] and little is known about the combination of multiple chronic diseases with asthma in the elderly.

Comorbidities have an impact on the course of asthma, but also affect quality of life of patients [8,9]. Quality of life is impaired in elderly people with a diagnosis of asthma [2,9,10]. The impairment may be influenced by age, asthma severity, duration of illness, socioeconomic conditions, somatic comorbidities and the presence of psychological factors such as anxiety and depression [2,9-15]. In recent years, there has been increased interest in the subjective quality of life (QoL) of patients with bronchial asthma. QoL is a significant indicator guiding the efforts of professionals caring for patients, especially chronically ill ones. The identification of factors affecting the QoL reported by patients, despite their existing condition, is important and useful to provide multidisciplinary care for these patients. However, the perspective of the patient about asthma and its treatment in specific populations such as the elderly are poorly developed [16].

The aim of our study was to assess the main contributory factors on asthma control and on health-related quality of life in elderly subjects.

Methods

Study subjects and collection of data

This was a retrospective case-control study nested in historical cohort data comparing patients who had partly controlled or uncontrolled asthma ($ACT \leq 19$) (cases) with patients who had controlled asthma ($ACT \geq 20$) (controls).

We included 209 consecutive patients aged ≥ 65 and diagnosed with asthma at Hospital Universitario 12 de Octubre supported by clinical history (dyspnea, chest tightness, coughing and wheezing) and the positive outcome of an objective diagnostic test (on enrolment or historical data in the medical record), either spirometry with reversibility, defined as at least 12% and 200 mL increase in FEV₁ from baseline, diagnostic methacholine challenge or historical data of reversibility of FEV₁ after oral steroid trial and/or diffusion test in patient with persistent FEV₁/FVC < 70 and/or FEV₁ < 80%. Current smokers were excluded. Patients unable to perform spirometry or without recent historical data of lung function were not included in the study.

The study protocol was reviewed and approved by the Ethics Committee of Hospital Universitario 12 de Octubre, Madrid (N^oCEIC 14/175).

Assessments

We collected self-reported information about age of asthma onset, disease duration, severe asthma exacerbations in the previous year (defined as asthma exacerbations requiring emergency department visit and/or hospitalization) and comorbidities. Height and weight data were collected from medical records and Body Mass Index (BMI) was defined as weight divided by height squared, considering obesity for BMI ≥ 30 .

Treatments received for longstanding asthma (short-acting β 2-agonists, inhaled corticoids, long acting β 2-agonists, combinations, and other treatments) were recorded. Daily dosage of inhaled corticosteroid was expressed as low, medium, or high doses according to GINA 2006 classification [17]. Medications adherence (self-reported compliance) and inhalation technique (evaluated by his/her doctor) were collected via their medical records. Atopic condition was assessed (at enrolment or historical data from medical records) by skin prick testing to a panel of common aeroallergens including pollens, moulds, house dust mite, and pets. A positive skin prick test was defined as a wheal at least 3 mm larger than the diameter of negative control. Asthma severity was classified following GINA 2006 determined by frequency of symptoms, night-time awakenings, short-acting β 2-agonists use, interference with normal activity and lung function for patients who were not taking long-term control medications at time on enrolment or determined by lowest level of treatment required to maintain control in those taking long-term control medication [17].

Pulmonary function was assessed with spirometry as a part of his/her routinely medical control according to the standardized technique [18]. Parameters of lung function such as forced vital

capacity (FVC), forced expiratory volume in 1s (FEV₁) and FEV₁/FVC at 2009 (basal spirometry on their treatment) were obtained using a Jaeger Pneumotach (Viasys HealthcareGmbH, Hoechberg, Germany). The clinical control status at 2009 was evaluated using the validated Spanish version [19] of ACT (asthma control test) [20] and health-related quality of life status was evaluated using a validated Spanish version [21] of Marks' Asthma-specific Quality of Life Questionnaire (AQLQ) [22].

Inhaled technique was checked by their doctor/nurses as a part of his/her routinely medical control.

Assessment scales

The ACT [20] is designed to measure asthma control without using pulmonary function values, with a cut-off point of ≥ 20 for the ACT score defining well controlled asthma, 16-19 for not well-controlled asthma and ≤ 15 for very poorly controlled asthma [17].

AQLQ [22] is a 20-item self-administered questionnaire which covers 4 dimensions (breathlessness, mood, social limitation and worrying) and gives a total score and subscales scores. Patients have to respond to a series of statements describing the way in which asthma (or its treatment) affects them and indicate which option closely applies to them over the past four weeks. A score of 10 corresponds to a maximum impairment of quality of life and a score of 0 corresponds to no impairment.

Statistical analysis

A descriptive, bivariate and multivariate analysis was conducted in order to identify factors associated with asthma control and asthma related quality of life.

The data is expressed as mean and standard deviation [SD], percentage (%) and 95% confidence interval where appropriate. The Chi-square test using cross table statistics, Mann–Whitney U tests or Student's t-test were used for comparison of two groups. The Kruskal–Wallis and ANOVA test were used for more than two independent groups with non-normal or normal distribution, respectively. Correlations between variables were calculated by Rho Spearman coefficient or R2 Pearson.

Multivariate analysis was performed using multiple linear regression for Asthma Quality of Life Questionnaire (total score and domains scores) as dependent variables and using logistic regression when poor control of asthma was analyzed as a dichotomous variable using as

independent variables all variables which were statistically significant in the bivariate analysis or clinical implication could be plausible. The results of the multivariable model were presented by coefficient, standard error (SE) and p-value. Values of $p < 0.05$ were considered statistically significant for all analysis.

The statistical tests were performed using Stata Data Analysis and Statistical Software (Version 10, StataCorp LP, College Station, TX, USA).

Results

Characteristics of population

We successfully evaluated 209 asthma patients (149 women and 60 men) aged 65 years and above. In the population studied, asthma was more common in women, mainly with intrinsic profile (non-allergic) and generally as a long-standing disease, with an onset in middle age of life. The mean age of participants was 73.55 years (SD: 5.44). 20.57% of patients ($n = 43$) were former smokers (for at least one year). The mean age of asthma onset was 46.76 (SD: 15.76). Mean age of asthma onset in men was 43.51 years (SD: 14.68) while in women was 48.08 (SD: 16.05) ($p = 0.048$). One hundred and eighty-three patients (87.98%) reported long-standing asthma with onset before 65 years of age and 25 patients (12.02%) had late-onset asthma (over 65 years of age). There were more women in the group of late-onset asthma ($p = 0.014$).

Most patients had persistent moderate asthma (99 patients; 47.37%) or severe (98 patients; 46.89%), according to GINA 2006 classification. During the preceding year, 23 patients (11%) had severe exacerbations requiring at least one emergency department visit and/or hospitalization. Regarding adherence to treatment, 92.34% reported performing the treatment prescribed by their doctors. Most patients suffered comorbidities with a median of 4 coexisting conditions. Acceptable spirometry was collected in all patients. Most patients 69.68% (146 patients) had a $FEV_1\% > 80$ predicted value, 25.84% (54 patients) had FEV_1 between 60-80% of predicted value and 4.31% (9 patients) had $FEV_1 < 60\%$ predicted. Patient with persistent $FEV_1/FVC < 70$ y/o $FEV_1 < 80\%$ in medical records ($n = 24$) had normal diffusion test ($n = 14$; ex-smokers $n = 6$) or an unequivocal history of longstanding asthma in patients who have never smoked (allergic asthma or Aspirin-exacerbated Respiratory Disease) with high reversibility and variability of FEV_1 but with persistent values within $FEV_1/FVC < 70$ y/o $FEV_1 < 80\%$. Demographic, clinical and functional data are summarized in Table 1.

Asthma control and factors affecting asthma control

An ACT (Asthma control test) total score ≥ 20 (well controlled) was obtained in 145 patients (69%), 35 patients (16%) had 19-16 score (partly controlled) and 29 patients (13%) had ≤ 15 score (uncontrolled). According to ACT punctuation, we classified patients into 2 groups (cases and controls), where cases were 64 patients (30.62%) with partly controlled/uncontrolled asthma (ACT ≤ 19) and controls were patients with well controlled asthma (ACT ≥ 20) 145 (69.38%). We have described main variables by level of asthma control (Table 2). Analysing comparisons between groups, we did not find any statistically significant differences as a function of age, atopy, disease duration, lung function, asthma severity, Aspirin-Exacerbated Respiratory Disease (AERD) or comorbid conditions. We did find, however, significantly poorer asthma control in women. The percentage of patients reporting severe exacerbations in the last year before the visit was lower in patients with controlled asthma compared to those with partly/uncontrolled asthma ($p < 0.001$). The number of comorbidities was not associated with asthma control status ($p 0.448$). Patients suffering from Aspirin-Exacerbated Respiratory Disease did not have more severity in their asthma according to GINA 2006 classification ($p 0.380$).

With regard to treatment, adherence was associated with asthma control ($p 0.021$), so correct adherence was more frequent in the well-controlled group. Anticholinergic treatment was more frequently prescribed in patients with partly/uncontrolled asthma ($p 0.006$). None patient was on specific immunotherapy at the moment of the study, but 42 (20.1%) had received in the past subcutaneous immunotherapy (when they were young or middle age), but it was not analyzed because of the great heterogeneity of the treatments. None patient was on biologic treatment.

In the score of AQLQ, both in the different domains and in the total score, partly/uncontrolled patients tend to have a higher score, which means greater impairment in quality of life.

In multivariate analysis of factors affecting asthma control measured by ACT (Table 3), lack of adherence to treatment and the presence of severe exacerbations behaved as a risk factor for partly controlled/uncontrolled asthma (OR 8.33 and OR 5.29, respectively). In addition, for each unit scored more in the AQLQ (total score or subscale dyspnea) the risk of poor control increased 1.51 and 1.88 times respectively.

Multiple linear regression was performed using the AQLQ total score and sub-scales as the dependent variable and selected variables (those with clinical implication or associated with AQLQ in the bivariate analysis) as independent variables, showing that worse quality of life (total

score) was predicted by depression, GERD, osteoporosis and asthma control (evaluated by ACT score) (Table 4).

Discussion

Suboptimal control of asthma has been reported in numerous studies [23,24,25]. In particular, in Spain the rate of uncontrolled asthma according to the ACT score could reach up to 57.6% of patients [26]. Recently, the LIAISON study, one of the largest observational studies on characteristics and management of asthmatics in Europe, based on patient reported outcomes and using the Asthma Control Questionnaire (ACQ), confirmed rates of suboptimal control in 56.5 % of patients [27].

Studies evaluating asthma control in the elderly are scarce but they coincided on one-third or more of elderly asthmatic patients having uncontrolled asthma. Milanese et al. performed a multi-center observational study analyzing a total of 350 patients more than 64 years old with documented physician-diagnosis of asthma in Italy, finding that the 39% had an Asthma Control Test score ≤ 19 [28]. Hwang et al. in Korea and Marincu et al. in Rumania found similar rates of uncontrolled asthma (35.2% and 30.15% respectively) [29,30]. Our findings indicate also that asthma control was suboptimal in one-third of older outpatients with asthma in a real-life study. This is a percentage lower than that observed in other age groups, but can be affected by being patient ongoing asthma treatment and followed-up at a tertiary care academic hospital for at least one year.

Comorbidities had been associated with poorly controlled asthma [4,30], and it is well known that older patients with asthma have an increased risk of comorbidities. Particularly some frequent comorbidities, such as chronic obstructive pulmonary disease, chronic sinusitis, obesity and depression are associated with uncontrolled asthma in elderly asthmatic patients [31]. Also, the number of comorbidities and polypharmacy have been linked with asthma control in the elderly [32,33]. Although, recent studies demonstrated that in elderly asthmatics under specialist care, non-respiratory comorbidities do not seem to have a direct negative effect on asthma control according to Global Initiative for Asthma criteria [34] or according to ACT score [28-30,33]. Our results are similar since none of the evaluated diseases *per se* or the number of comorbidities were associated with poor asthma control.

Milanese et al. found that the coexistence of COPD or Asthma-CPOD Overlap Syndrome (ACOS) due to the presence of chronic bronchitis and/or lung diffusion impairment had lower mean Asthma Control Test scores [28]. Persistent airway obstruction and/or mixed ventilator

dysfunction were also associated with poor asthma control in the elderly [30]. In general, there are important diagnostic challenges in asthma in the elderly, resulting from spirometric changes of ageing and similar clinical presentation of asthma, COPD and ACOS [1]. In our study, we exclude current smokers and those with persistent fixed airflow obstruction without normal diffusion test or an unequivocal asthma history at initial diagnosis in an attempt to exclude COPD patients, so we could not evaluate the influence of this comorbidity on asthma control score, but nevertheless, lung function did not modified asthma control score in our group of patients.

Previous findings showed that both a history of past asthma exacerbations and poor asthma control can increase the risk of future asthma exacerbations [35,36]. Also, poorly or partly controlled asthma in elderly patients has been characterized by higher exacerbation rates [28-30] and an ACT score < 19 may be a significant predictor of asthma exacerbation in the following six months [33]. Our results also observed an association between severe exacerbations in the last year and partly controlled/uncontrolled asthma in the past four week (OR 5.29) supporting that the ACT control test may be an important parameter for assessing risk of asthma exacerbations and healthcare resource consumption in elderly asthmatic patients.

Besides, good adherence is a predictor of asthma control [37], also in the elderly [15]. With regard with this topic, we detected that lack of adherence was a predictor for poor asthma control (OR 8.33). However, in the analysis we used patient self-reported data about adherence that become very high and probably imprecise. Nevertheless, other authors also reported high rates of asthma treatment adherence in the elderly using more precise measures of compliance [33].

In our work, asthma control and quality of life were directly related. Although comorbidities were not determinant for asthma control, the presence of some comorbidities like depression, GERD or osteoporosis were found to be associated to quality of life. The significant reduction in quality of life associated with comorbidity in asthma has been previously reported [8,15].

On the other hand, contrary to published by other authors [38], we do not detect relationship between quality of life and exacerbations. This can be due to the methodology used since exacerbations were collected during the last year, but the questionnaire of quality of life of Marks analyze a period fixed of the last four weeks.

Further, the quality of life perceived by patients directly affects the degree of control according to the ACT questionnaire, as has been previously observed [27]. In our opinion, the information contributed by both questionnaires is complementary, and in patients of this group of age they can help to take therapeutic decisions and to suspect the presence of depression. That is very important as depression is not only correlated to asthma control and quality of life but also is a predictor of

future exacerbation, highlighting the need for depression screening and evaluation in the elderly population [39].

To the best of the authors' knowledge, this is the first study in elderly subjects with asthma reporting main contributory factors on asthma control and health-related quality of life in Spanish population.

Some methodological limitations of the study should be mentioned. Patients were recruited from a tertiary hospital, which is likely to result in a group with a relatively severe asthma and frequent comorbidity. A complete psychological examination was not undergone and we did not use a specific geriatric assessment scale to determine depression and functional status; and adherence was not evaluated with an objective medication adherence measure or validated test.

In conclusion, most elderly asthmatic patients, even with severe or moderate persistent asthma, with comorbidities and long standing asthma, could achieve good control of asthma symptoms and normal lung function, but almost one-third had uncontrolled asthma despite receiving anti-asthmatic therapy. Determinants for uncontrolled asthma were severe exacerbations during the preceding year, lack of treatment adherence and health-related quality of life. The presence of non-respiratory comorbid conditions in older patients does not seem to be associated with worse asthma control of symptoms but their influence in health-related quality of life could indirectly affect asthma control.

Therefore, the management of elderly asthmatic patients should include further cares for clinical conditions including depression and treatment adherence among other measures. Moreover, ACT and AQLQ questionnaires are complementary and highly informative.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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Dr. FERNANDEZ CRESPO has nothing to disclose.

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Accepted Article

Table 1. Demographic, clinical and functional data.

n= 209	n(%) or means \pm SDs		n(%)
Male/Female	60/149 (28.7/71.3)	Degree of asthma severity	
Age (years)	73.55 (\pm 5.44)	Intermittent	3 (1.44)
Duration of disease	26.77 (\pm 15.38)	Mild Persistent	7 (3.35)
Atopy	70 (33.49)	Moderated Persistent	99 (47.37)
Comorbidity (%)		Severe Persistent	98 (46.89)
Obesity (BMI \geq 30)	84 (40.19)	Not known	2 (0.96)
Hypertension	124 (59.33)	Prescribed Treatment (%)	
Hypercholesterolemia	57 (27.27)	Inhaled corticosteroids-LABA	189(90.43)
Isquemic cardiomyopathy	21 (10.05)	Leukotriene Modifiers	80 (38.28)
Heart Arrythmias	22 (10.53)	Anticholinergics	36 (17.22)
Thyroid disease	28 (13.40)	Inhaled corticosteroids dose	
Other Cardiovascular disease*	30 (14.35)	Low	35 (17.16)
Glaucoma	21 (10.05)	Medium	71 (34.80)
Arthrosis	148 (70.81)	High	98 (48.04)
Osteoporosis	95 (45.45)	Pulmonary function	
Obstructive sleep apnea	7 (3.35)	FEV1/FVC (%)	
Other respiratory diseases**	35 (16.75)	\geq 70	135 (64.59)
Rhinitis	139 (66.51)	<70	74 (35.41)
Sinonasal polyposis	50 (23.92)	FEV1 (%)	
Gastroesophageal reflux	101 (48.33)	<60	9 (4.31)
Depression	61 (29.19)	60-80	54 (25.84)
AERD [#]	23 (11.00)	>80	146 (69.86)
		Severe exacerbations	23 (11.00)

*Heart failure, structural heart diseases.

**History of TBC infection, bronchiectasis, pulmonary embolism.

[#] Aspirin-Exacerbated Respiratory Disease

Table 2. Asthma control and factors affecting asthma control

	LEVEL OF ASTHMA CONTROL		p-value		LEVEL OF ASTHMA CONTROL		p-value
	ACT ≤19	ACT ≥20			ACT ≤19	ACT ≥20	
	(n=64)	(n=145)			(n=64)	(n=145)	
Gender			0.001	Atopy			0.648
Male	8 (12.50)	52 (35.86)		Atopic asthma	20 (31.25)	50 (34.48)	
Female	56 (87.50)	93 (64.14)		Non atopic asthma	44 (68.75)	95 (65.52)	
Age (years)			0.821	FEV1/FVC (%)			0.602
< 75	36 (56.25)	84 (57.93)		≥70	43 (67.19)	92 (63.45)	
≥ 75	28 (43.75)	61 (42.07)		<70	21 (32.81)	53 (36.55)	
Duration of disease*	27.51 (16.01)	26.45 (15.14)	0.572	FEV1 (%)			0.165
Degree of asthma severity			0.305	<60	3 (4.69)	6 (4.14)	
Intermittent	0 (0.00)	3 (2.07)		60-80	11 (17.19)	43 (29.66)	
Mild persistent	2 (3.13)	5 (3.45)		>80	52 (78.13)	96 (66.21)	
Moderate persistent	26 (40.63)	73 (50.34)		Treatment			
Severe persistent	36 (56.25)	62 (42.76)		Inhaled corticosteroids-LABA	60 (93.75)	129 (88.97)	0.278
Unknown	0 (0.00)	2 (1.38)		Leukotriene Modifiers	26 (40.63)	54 (37.24)	0.643
Comorbidity				Anticholinergics	18 (28.13)	18 (12.41)	0.006
Obesity	26 (40.63)	58 (40.00)	0.932	Inhaled corticosteroids dose			0.102
Hypertension	41 (64.06)	83 (57.24)	0.355	Low	10 (15.87)	25 (17.73)	
Hypercholesterolemia	13 (20.31)	44 (30.34)	0.133	Medium	16 (25.40)	55 (39.01)	
Isquemic cardiomyopathy	5 (7.81)	16 (11.03)	0.475	High	37 (58.73)	61 (43.26)	
Heart Arrhythmias	6 (9.38)	16 (11.03)	0.719	Severe exacerbations			0.000
Thyroid disease	11 (17.19)	17 (11.72)	0.285	No	49 (76.56)	137 (94.48)	
Other Cardiovascular disease*	14 (21.87)	16 (11,08)	0.411	Yes	15 (23.44)	8 (5.52)	
Glaucoma	8 (12.50)	13 (8.97)	0.433	Treatment adherence			0.021
Arthrosis	47 (73.44)	101 (69.66)	0.579	No	9 (14.06)	7 (4.83)	
Osteoporosis	32 (50.00)	63 (4.,45)	0.381	Yes	55 (85.94)	138 (95.17)	
Obstructive sleep apnea	2 (3.13)	5 (3.45)	0.905	Quality of life questionnaire score*			
Other respiratory diseases**	8 (12,12)	18 (12.41)	0.474	Mood	5.07 (2.49)	2.56 (2.37)	0.000
Rhinitis	46 (71.88)	93 (64.14)	0.275	Breathlessness	3.93 (2.18)	1.01 (1.32)	0.000

Sinonasal polyposis	12 (18.75)	38 (26.21)	0.244	Worrying	3.34 (2.13)	1.27 (1.59)	0.000
Gastroesophageal reflux	32 (50.00)	69 (47.59)	0.748	Social limitation	3.19 (2.60)	0.98 (1.69)	0.000
Depression	22 (34.88)	39 (26.90)	0.273	Total	3.87 (1.82)	1.44 (1.34)	0.000
AERD [#]	4 (6.25)	19 (13.10)	0.144				

* mean and standard deviation **History of TBC infection, bronchiectasis, pulmonary embolism [#] Aspirin-Exacerbated Respiratory Disease

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Table 3. Statistical analysis of the predictors for asthma control

	<i>Odds ratio</i>	<i>p-value</i>	<i>95% Conficende interval</i>
No treatment adherence	8.33	0.002	2.22-30.30
AQLQ Total score	1.58	0.024	1.06-2.23
Breathlessness subscale AQLQ score	1.82	0.001	1.28-2.59
Severe exacerbations	5.29	0.006	1.60-17.52

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Table 4. Multiple regression analysis of AQLQ total score in relation to selected variables.

Variable	AQLQ		p-value
	Total Score	SE	
Gender			
	Male	ref	0,351
	Female	0,24	0,26
Osteoporosis			
	No	ref	0,021
	Yes	0,52	0,22
GERD			
	No	ref	0,026
	Yes	0,47	0,21
Depression			
	No	ref	0,000
	Yes	0,99	0,22
ACT score			
	≤ 19	ref	0,000
	≥ 20	2,28	0,22
Severe exacerbations			
	No	ref	0,867
	Yes	-0,05	0,33