
Factors associated with severity and exacerbation of asthma: a baseline analysis of the COhort for Reality and Evolution of adult Asthma in Korea (COREA)

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Background: Asthma presents with heterogeneous features, and patients show various phenotypes of differing severities. Therefore, it is necessary to define reliable predictable clinical factors that influence severity. To date, few large-scale studies have gathered clinical data on adult asthma patients in Asia.

Objectives: To establish an adult asthma cohort in Korea and to define significant factors associated with asthma severity and exacerbation.

Methods: Researchers from 11 university hospitals have established an asthma cohort termed the COhort for Reality and Evolution of adult Asthma in Korea (COREA). We classified the severity of asthma into 3 groups: mild, moderate, and severe. In this article, the first analysis of our cohort, we evaluate various clinical factors associated with the severity and exacerbation of asthma using data from 1,260 asthma patients.

Results: Physician-evaluated severity of asthma was associated with a history of asthma exacerbation ($P < .001$), a history of smoking ($P < .001$), symptom duration ($P = .007$), and treatment duration ($P < .001$). It was also significantly correlated with predicted forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV₁) values and FEV₁/FVC ratio (all $P < .001$). Previous exacerbation was associated with smoking ($P = .02$), predicted FVC and FEV₁ values (both $P < .001$), FEV₁/FVC ratio ($P = .02$), airway hyperresponsiveness ($P = .002$), and duration of disease ($P < .001$).

Conclusions: Previous exacerbation, duration of disease, and decrease in lung function were important clinical indices associated with asthma severity in the COREA study patients. Our long-term follow-up study is expected to soon yield more accurate and detailed outcomes.

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INTRODUCTION

Asthma is a heterogeneous chronic obstructive airway disease, and patients present with various clinical phenotypes of differing severities. Therefore, long-term changes must be monitored in a large patient group. Although some long-term follow-up asthma observational studies have been performed on young children or on birth cohorts, few cohort studies have been performed on adult asthma patients of the whole spectrum of severity from mild to severe to date.^{1,2}

The representative adult asthma cohort work is the Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens (TENOR) study, which was a prospec-

tive, observational, multicenter, 3-year (2001–2004) study of US patients diagnosed as having severe or difficult-to-treat asthma.³ Although many outstanding publications resulted from the work, this cohort study did not completely cover the various phenotypes and severities of asthma because it was a relatively short-term follow-up study and included only patients with difficult-to-treat asthma. In view of the impact of severe asthma on health care resources and the need to understand the mechanisms involved in severe asthma, a European Network For Understanding Mechanisms of Severe Asthma was established by 12 clinical specialist centers in 9 European countries.⁴ However, this study was a cross-sectional comparison between patients with severe asthma and a group of patients with mild-to-moderate asthma.^{5,6} The National Heart, Lung, and Blood Institute (NHLBI) funded the Severe Asthma Research Program, a collaboration among 9 institutions in the United States and 1 in the United Kingdom^{7,8}; however, this study did not address the full spectrum of asthma phenotypes and natural courses. In addition, the NHLBI has funded the Asthma Clinical Research Network, a clinical grouping that tests the effectiveness and safety of interventions⁹; however, this work is not a long-term follow-up cohort study exploring the natural course of asthma.

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It is important to define reliable predictable clinical factors that influence the severity and define the various phenotypes of asthma. This can be achieved only when asthmatic patients are observed and analyzed in a long-term follow-up cohort study. Also, because risk factors for asthma severity may differ by race, country, and socioeconomic environment, it is necessary to define the clinical characteristics of asthma in Asian patients because they may not be identical to those of Western patients. Unfortunately, no observational, long-term cohort study on adult asthma patients in Asia has been reported.

The present study aims to publicize the establishment of such a cohort study, which will run for more than 9 years, and to define significant clinical factors associated with asthma severity and exacerbation by analyzing the baseline data of a cohort of adult asthmatic patients in Korea. These outcomes will permit a deeper understanding of asthma in Korea.

METHODS

Establishment and Design of the Cohort

The COhort for Reality and Evolution of adult Asthma in Korea (COREA) study is a prospective, observational, multicentered, 9-year (2005–2013), follow-up study of Korean patients diagnosed as having asthma. The patients are recruited by allergists or pulmonologists from 11 centers in diverse areas of Korea; the participating institutions are the Asan Medical Center at the University of Ulsan and hospitals of Seoul National University, Bundang Seoul National University, Yonsei University, Chungang University, Ewha Womans University, Hanyang University, Soonchunhyang University, Ajou University, Catholic University, and Chonbuk National University. When a patient has already been treated for or is newly diagnosed as having asthma, the physician introduces this cohort study to the patient, and if the patient agrees to participate in the study, a medical coordinator interviews the new recruit and registers the case on an Internet database (www.asthmacenter.co.kr). Written informed consent was obtained from the study participants. They are supposed to visit their hospitals regularly every 3 months (± 30 days) until the cohort is closed. The design and a protocol for this cohort study were approved by the institutional review board of each center.

Participants in the Cohort

The study participants are 14 years or older and have been diagnosed as having asthma by specialists in the fields of allergy or pulmonology. We studied patients with at least 1 of the chronic persistent respiratory symptoms of dyspnea, cough, sputum production, or wheezing for more than 3 months. To qualify, participants were selected in case they had a baseline forced expiratory volume in 1 second (FEV₁)/forced vital capacity (FVC) ratio of 80% or less and demonstrated either significant airway hyperresponsiveness (AHR) (provocation concentration that caused a decrease in FEV₁ of 20% [PC₂₀] methacholine, <16 mg/mL) or significant bronchodilator responsiveness (>12% improvement in FEV₁ per-

centage predicted after administration of 180 μ g of albuterol by means of a metered-dose inhaler) before asthma treatment.

A total of 1,520 patients have been registered by the 11 centers in the 2 years from 2005 to 2007. The severity of asthma was evaluated by physicians in 1,260 of these 1,520 patients. Table 1 gives the baseline characteristics of the patients who were able to be evaluated by severity. Omission of some data in each item was permitted because all items could not be investigated for all participants. For the sake of generalization, when we compared those 1,260 participants with the overall 1,520 ones, no significant differences were found for all items.

Analysis of Association Between Severity and Clinical Factors

We analyzed the associations between asthma severity and clinical factors, including lung functions, smoking, duration of disease, and exacerbation history. Severity was evaluated by specialists primarily based on the Global Initiative for Asthma (GINA) guidelines¹⁰ at the time of the registration in the cohort. Because the number of cases of mild intermittent severity is small, severity was classified into 3 basic categories: mild, moderate, and severe. Broadly speaking, mild asthma includes the patients who have nearly normal lung function and few daily symptoms. Moderate asthma is considered to be patients who have a moderate degree of FEV₁ reduction and/or daily symptoms. Severe asthma is considered to be patients who have very low FEV₁ and/or frequent exacerbations.

Table 1. Baseline Characteristics of Patients

Characteristic	Outcome
Age, mean (SD), y	49.25 (15.84)
M/F, No.	553/688
With/without atopy, No.	137/216
Log IgE, mean (SD)	2.20 (0.63)
Symptom duration, mean (SD), y	10.20 (10.71)
Diagnosis duration, mean (SD), y	8.29 (8.06)
Treatment duration, mean (SD), y	6.42 (6.15)
Peripheral blood eosinophil count, mean (SD), %	7.70 (5.66)
PC ₂₀ , mean (SD), mg/dL	5.20 (5.74)
Smoking, No. (%)	188 (15.4)
Ex-smoking, No. (%)	447 (36.8)
Nonsmoking, No. (%)	580 (47.8)
Duration of smoking, mean (SD), y	21.50 (13.39)
No. of cigarettes smoked per day, mean (SD)	17.46 (10.45)
Passive/nonpassive smoking, No.	350/791
With/without exacerbation visits, No.	431/810
With/without occupational relationships, No.	87/757
FVC, mean (SD), predicted %	88.82 (18.06)
FEV ₁ , mean (SD), predicted %	81.99 (21.68)
BDR increase, mean (SD), L	1.04 (8.98)
FEV ₁ /FVC, mean (SD), %	72.60 (15.61)

Abbreviations: BDR, bronchodilator responsiveness; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; PC₂₀, provocation concentration that caused a decrease in FEV₁ of 20%.

We selected the patients in stable condition who had been treated according to GINA guidelines at the time of registration. Patients with acute exacerbated asthma were enrolled after recovery. Current emergent visits to the hospital were excluded in this analysis. Because we differentiate between *emergency visit* and *regular visit*, we could register the patients who presented for either. Therefore, the patients registered in this analysis can be considered to be managed with appropriate treatment. Also, all physicians who treat the patients enrolled in this study are asthma specialists, so they keep the treatment guidelines in their minds. The previous history of hospital visits because of exacerbation of asthma was defined by the question, "Have you ever visited any hospital with suddenly exacerbated asthmatic symptoms such as cough, dyspnea, or wheezing so far?" In addition, a skin prick test to *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* (Allergopharma, Darmstadt, Germany), the most common inhalant allergens in Korea, for detection of atopy was performed as previously described.¹¹

Statistical Analyses

The relationships between severity and clinical factors were analyzed using the χ^2 test and Pearson correlation test. Also, comparisons of averages were performed with the independent *t* test and a 1-way analysis of variance test, with data presented as mean (SD). In addition, a generalized logit regression model was used to evaluate clinical factors that influence disease severity. Statistical analyses were performed using the SPSS statistical software package (version 12.0; SPSS Inc, Chicago, Illinois). *P* < .05 was considered statistically significant.

RESULTS

Demographic Data

Baseline demographic data and clinical characteristics of the study participants in this analysis are given in Table 1. The mean age of participants is 49 years, and there are approximately 1.24 times more women than men. The ratio of atopy to nonatopy is 0.63, as generally found. Our patients have experienced respiratory symptoms for a mean of 10.20 years, were diagnosed as having asthma an average of 8.29 years ago, and have been treated by physicians for a mean of 6.42 years. Most patients have never smoked (47.8%), whereas 36.8% have smoked but quit, and 15.4% currently smoke. The percentage of predicted prebronchodilator FEV₁ was 81.99% of the mean, and the prebronchodilator FEV₁/FVC ratio was 72.60% of average. When we analyzed the baseline data from the stratification by atopy, the mean age (37 years in atopic patients; 51 years in nonatopic patients), the duration of smoking (13.74 [11.05] years in atopic patients; 22.25 [11.59] in nonatopic patients), and log levels of serum total IgE (2.50 [0.53] in atopic patients; 2.20 [0.59] in nonatopic patients) showed statistically significant differences (*P* < .001). However, these results only show a small subset of patients from whom we had atopy data (137 atopic patients, 216 nonatopic patients). A similar situation is observed in some results given in Table 2 (eg, methacholine bronchial provocation test results, PC₂₀ values).

Table 2. Clinical Parameters and History of Exacerbation Visits

Parameter	Positive history of exacerbation visits	Negative history of exacerbation visits	<i>P</i> value
Age, mean (SD), y (n = 1,238)	48.21 (15.56)	49.39 (15.27)	.51 ^a
Log IgE, mean (SD) (n = 589)	2.28 (0.63)	2.17 (0.63)	.05 ^a
Atopy, No. (%) (n = 347)	50/68 (42.4)	86/143 (37.6)	.38 ^b
Peripheral eosinophil count, mean (SD), (%) (n = 914)	5.63 (14.79)	9.08 (71.58)	.38 ^b
Positive/negative MBPT result, No. (%) (n = 556)	118/8 (93.7)	354/76 (82.3)	.002 ^b
PC ₂₀ , mean (SD), mg/mL (n = 441)	4.53 (5.54)	5.46 (5.80)	.14 ^a
Positive/negative for rhinosinusitis, No. (%) (n = 1,154)	255/150 (63.0)	451/298 (60.2)	.36 ^b
Symptom duration, mean (SD), y (n = 1,021)	12.08 (11.01)	9.12 (10.45)	<.001 ^a
Diagnosis duration, mean (SD), y (n = 761)	10.14 (8.58)	6.67 (7.28)	<.001 ^a
Treatment duration, mean (SD), y (n = 638)	8.05 (6.98)	4.89 (4.84)	<.001 ^a
FVC, mean (SD), predicted % (n = 1,031)	85.9 (19.36)	90.5 (16.90)	<.001 ^a
FEV ₁ , mean (SD), predicted % (n = 1,031)	77.1 (22.15)	84.9 (20.77)	<.001 ^a
FEV ₁ /FVC, mean (SD), % (n = 908)	71.0 (22.15)	73.5 (15.03)	.02 ^a
Smoking, No. (%) (n = 1,203)	60 (14.4)	127 (16.2)	.02 ^b
Ex-smoking, No. (%)	174 (41.7)	266 (33.8)	
Nonsmoking, No. (%)	183 (43.9)	393 (50.0)	
Duration of smoking, mean (SD), y (n = 492)	21.72 (13.52)	21.18 (13.31)	.67 ^a
No. of cigarettes smoked per day, mean (SD) (n = 480)	16.84 (10.60)	17.88 (10.41)	.30 ^a
Passive smoking, No. (%) (n = 1,134)	144/253 (36.1)	205/529 (27.9)	.02 ^b

Abbreviation: FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; MBPT, methacholine bronchial provocation test; PC₂₀, provocation concentration that caused a decrease in FEV₁ of 20%.

^a Tested by independent *t* test analysis between groups.

^b Tested using the χ^2 test between groups.

Severity of Asthma and Clinical Indices

Severity is classified as mild, moderate, and severe in 511, 461, and 288 patients, respectively. The patients whose severity was not evaluated at the time of registration must be followed up in the future to complete their records. A significant difference in age was found among the groups ($P < .001$). We found no differences in sex, body mass index (BMI; calculated as weight in kilograms divided by height in meters squared), log levels of serum total IgE, atopy, or peripheral eosinophil counts among the groups. Interestingly, patients in the moderate severity group had the highest frequency of rhinosinusitis ($P = .009$). When we compared asthma severity with pulmonary function indices, we found significant differences among groups in FVC, FEV₁, and FEV₁/FVC ratios ($P < .001$) (Table 3).

Patients who had a history of smoking, despite cessation of smoking, showed more severe asthma than did nonsmokers, and duration of smoking affected the severity of asthma ($P = .007$), but the numbers of cigarettes smoked each day and pack-years showed no between-group differences (Table 4). Duration of disease was divided into 3 categories: symptom duration, duration of diagnosis by physicians, and drug treatment duration. Significant between-group differences were found in symptom duration ($P = .007$) and treatment duration ($P = .001$) (Table 5).

In terms of correlation analysis, as severity increased, age also tended to increase (Pearson correlation coefficient $r = 0.128$, $P < .001$). Furthermore, strong correlations were found between severity and lung function: FVC ($r = -0.392$, $P < .001$), FEV₁ ($r = -0.514$, $P < .001$), and FEV₁/FVC ratio ($r = -0.299$, $P < .001$). Positive correlations were also found between disease severity and the duration of symptoms, diagnosis, and treatment ($r = 0.071$, 0.076 , and 0.138 and $P = .02$, $.04$, and $<.001$, respectively).

We analyzed variables using a proportional odds model in a generalized logit regression analysis. We used age, sex, atopy, peripheral blood eosinophil counts, FVC, FEV₁, smoking history, previous history of exacerbation hospital visits, and the duration of symptoms, diagnosis, and treatment as dependent variables. The result was that previous asthma exacerbation, time from symptom onset to diagnosis, and FEV₁ were significant risk factors that influenced the severity of asthma (odds ratio [OR], 0.312; 95% confidence interval [CI], 0.182–0.535; OR, 1.036; 95% CI, 1.013–1.061; and OR, 1.063; 95% CI, 1.047–1.079, respectively; and $P < .001$, $.002$, and $<.001$, respectively) (data not shown).

Hospital Visits Because of Asthma Exacerbation and Severity

The history of hospital visits because of exacerbation of asthma showed significant differences among the 3 severity groups ($P < .001$) (Table 5) and a strong positive correlation with severity ($r = 0.207$, $P < .001$). Furthermore, patients with more severe asthma had more emergency department visits ($r = 0.148$, $P = .02$).

When we compared the patients with histories of exacerbation visits with the patients without such histories, no differences were found in age, log levels of serum total IgE, peripheral eosinophil count, atopy, rhinosinusitis, or PC₂₀ between the 2 groups. However, we found a significant between-group difference in AHR positivity as confirmed by a methacholine bronchial provocation test ($P = .002$). When we compared pulmonary function indices between the 2 groups, we found significant differences between groups in FVC ($P < .001$), FEV₁ ($P < .001$), and FEV₁/FVC ratio ($P = .02$). In addition, significant differences were found between 2 groups in time from symptom onset to diagnosis, diagnosis duration, and treatment duration (all $P < .001$). Passive

Table 3. Clinical Parameters and Severity of Asthma

Parameter	Mild asthma	Moderate asthma	Severe asthma	P value
No. (%) of patients (N = 1,260)	511 (39.8)	461 (35.9)	288 (22.4)	
Age, mean (SD), y (n = 1,257)	46.58 (15.11)	49.39 (15.24)	51.56 (15.19)	$<.001^a$
M/F, No. (n = 1,241)	204/296	207/247	142/145	.05 ^b
BMI, mean (SD) (n = 389)	23.42 (3.15)	23.67 (3.43)	23.30 (3.42)	.64
Log IgE, mean (SD) (n = 598)	2.16 (0.62)	2.24 (0.64)	2.20 (0.64)	.40 ^a
With/without atopy, No. (% positive) (n = 353)	49/64 (43)	56/81 (41)	32/71 (31)	.15 ^b
Blood eosinophil count, mean (SD), % (n = 949)	7.28 (51.48)	6.11 (15.16)	10.29 (88.13)	.82 ^a
With/without rhinosinusitis, No. (% positive) (n = 1,186)	260/200 (56.5)	290/154 (65.3)	162/105 (60.7)	.009 ^b
FVC, mean (SD), predicted %	96.37 (14.02)	88.86 (16.50)	78.06 (19.87)	$<.001^a$
FEV ₁ , mean (SD), % predicted (n = 1,070)	93.79 (16.31)	82.23 (17.60)	64.89 (22.53)	$<.001^a$
FEV ₁ /FVC, mean (SD), % (n = 942)	77.33 (12.55)	73.18 (15.68)	65.34 (16.65)	$<.001^a$

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity.

^a Tested by 1-way analysis of variance among groups.

^b Tested using the χ^2 test among groups.

Table 4. Smoking and Severity of Asthma

Smoking	Mild asthma	Moderate asthma	Severe asthma	P value
Smoking, No. (%) (n = 1,215)	72 (14.9)	74 (16.5)	42 (14.8)	<.001 ^a
Ex-smoking, No. (%)	135 (28.0)	175 (39.1)	137 (48.2)	
Nonsmoking, No. (%)	276 (57.1)	199 (44.4)	105 (37.0)	
Duration of smoking, mean (SD), y (n = 498)	19.86 (12.65)	20.89 (13.19)	24.58 (14.20)	.007 ^b
No. of cigarettes smoked per day, mean (SD) (n = 486)	17.77 (10.08)	16.41 (10.82)	18.58 (10.33)	0.174 ^b
Pack-years, mean (SD) (n = 422)	19.40 (17.99)	21.35 (24.20)	25.13 (17.65)	0.108 ^b
Passive smoking, No. (n = 1,144)	140/307	133/293	77/191	0.493 ^a

^a Tested using the χ^2 test among groups.^b Tested by 1-way analysis of variance among groups.

Table 5. Duration of Disease, Previous History of Exacerbation Hospital Visits, and Severity of Asthma

Variable	Mild asthma	Moderate asthma	Severe asthma	P value
Symptom duration, mean (SD), y (n = 1,034)	8.91 (10.53)	11.29 (11.36)	10.41 (9.71)	.007 ^a
Diagnosis duration, mean (SD), y (n = 771)	7.41 (8.47)	8.45 (8.06)	9.02 (7.52)	.10 ^b
Treatment duration, mean (SD), y (n = 647)	5.02 (4.93)	6.94 (6.57)	7.13 (6.43)	.001 ^a
With/without exacerbation visits, No. (%) (n = 1,242)	118/386 (23.4)	176/277 (38.8)	137/147 (48.2)	<.001 ^b
No. of emergency department visits, mean (SD) (n = 251)	1.92 (1.50)	2.73 (3.63)	6.88 (23.14)	.04 ^a

^a Tested by 1-way analysis of variance among groups.^b Tested using the χ^2 among groups.

smokers and ever-smokers presented higher percentages compared with never-smokers in the group of patients with histories of exacerbation visits (Table 2). Also, smokers who had more pack-years also had more frequencies of admission due to exacerbation ($r = 0.482$, $P = .03$).

DISCUSSION

The new guidelines prepared by GINA in 2006 introduced the concept of asthma control.¹² Although the concept of control provides convenient standards that can be easily applied to clinical situations, control has a dynamic aspect; hence, focus on control only may neglect the intrinsic asthmatic condition, compared with classification of severity primarily based on lung function tests. Therefore, the present study evaluated the severity of asthma by physician primarily based on the earlier GINA severity classification. Basically, we classified severity into 3 types: mild, moderate, and severe. Severity was also categorized as mild and moderate to severe, but this did not greatly affect the results. Indeed, there is currently no gold standard for assessing asthma severity. There is a clear lack of agreement among asthma severity evaluation modalities used in the National Asthma Education and Prevention Program,¹³ the GINA guidelines, and physician assessments. The TENOR study revealed that patient medication use and consumption of health care should be considered in assessing the severity of asthma.¹⁴ Considering that current asthma treatment recommendations are based primarily on asthma severity, trials searching for clinical factors associated with severity are essential for proper management. Furthermore, a major role for the physician is to try to prevent progression to severe asthma by identifying important factors that affect the severity of disease.

Considering classification of the severity of asthma mainly according to lung function, the physician-evaluated severity of asthma would predictably be strongly correlated with lung function in our study. This means that many physicians pay greater attention to lung function data rather than symptoms and medication when classifying severity for themselves. This is eminently reasonable because asthma is an obstructive lung disease and lung function test results can best reflect the degree of obstruction. In addition, old age is also an important risk factor associated with severity; this probably reflects age-related declines in lung function, implying that elderly asthma patients need careful clinical attention.

In our study, BMI was not associated with asthma severity. A previous study suggested that obesity is associated with worse asthma outcomes, especially an increased risk of asthma-related hospitalizations.¹⁵ However, despite this association between BMI and asthma control, it was reported that there was no relationship between BMI and asthma severity.¹⁶ Durations of symptoms, diagnosis, and treatment were well correlated with asthma severity, probably because airway remodeling occurs during these timeframes.¹⁷ One study revealed that the duration of symptoms before diagnosis was significantly longer in the moderate-to-severe group in occupational asthma.¹⁸ These results differed from those of a previous study that showed no relationship between disease severity and asthma duration among those with adult-onset asthma,¹⁹ but the work explored only cases of severe asthma. Duration of asthma is associated with the degree of airflow limitation and hyperinflation.²⁰ Accordingly, this implies that physicians should diagnose and treat asthma particularly to prevent progression to more severe disease, even when patients have trivial respiratory symptoms in early stages of

adult asthma. Although asthma is a common chronic disorder with an overall population prevalence of 5% to 10%, physicians often neglect major or minor respiratory symptoms of patients or fail to detect such symptoms in time, thereby making inappropriate diagnoses and neglecting to initiate timely treatment. Whether timely diagnosis and treatment can make a difference to the severity of later asthma may require further study, but it is time that physicians, patients, and local communities changed their attitudes toward asthma.

Asthmatic patients with a history of smoking have more severe asthma and poorer lung function despite treatment. The harmful impact of smoking on asthma is well known. An increased rate of lung function decline during adult life, because of smoking, contributes to progressive irreversible airway obstruction in asthmatic patients.²¹ Asthmatic patients who smoke are at an increased risk of death, experience more severe asthma symptoms,²² show accelerated decline in lung function, need more hospital-based care, and have increased mortality rates after hospital admission for episodes of near-fatal asthma than do nonsmoking asthmatic patients.^{23–26}

Another important discovery from our analysis is that previous asthma exacerbation is strongly associated with severity. The TENOR study showed that recent severe asthma exacerbations are a strong independent factor predicting future exacerbations and, as such, should be considered as part of the clinical evaluation of patients with severe or difficult-to-treat asthma.²⁷ The same study showed evidence of an association between poor asthma control and future severe asthma-related health care events.²⁸

Asthma exacerbation has been used as 1 of the most important clinical indicators reflecting the degree of control of asthma and as a key factor determining patient quality of life in many clinical trials. Patients with more severe asthma show higher frequencies of previous exacerbation than do those with milder asthma, although this might be expected. Conversely, this result implies that patients who have poor lung function despite appropriate treatment have a higher chance of acute exacerbation, considering that most enrolled patients have been carefully treated with regular medications. Indeed, children with persistent asthma with previous exacerbations are more likely to have a repeat exacerbation despite controller treatment.²⁹ Miller et al³⁰ also revealed that previous severe disease was an important risk factor to identify patients at risk for future asthma morbidity in children. In our study, most patients with incidents of acute asthma exacerbation had persistent AHR, poor lung function during treatment, a history of smoking, and a long duration of asthma. These characteristics are ultimately similar to those of severe asthma patients, and physicians should therefore treat and monitor such patients more intensively.

In conclusion, we found through an initial analysis of COREA study data that previous asthma exacerbation, duration of disease, and decrease in lung function may be important clinical indices associated with severity of asthma. In the future, we hope that our long-term follow-up cohort study of

adults with asthma in Korea will contribute to a more systematic and precise understanding of asthma.

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