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Obstructive sleep apnea is associated with reduced quality of life in adult patients with asthma

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ARTICLE INFO

Article history:

Received for publication August 13, 2012.

Received in revised form January 7, 2013.

Accepted for publication January 7, 2013.

ABSTRACT

Background: Recent data suggest that obstructive sleep apnea (OSA) is an important contributor to severe uncontrolled asthma.

Objective: To investigate the clinical characteristics, asthma control, and asthma-related quality of life in adult patients with asthma at a high risk for OSA.

Methods: A total of 217 patients with asthma who visited our tertiary-care clinic were randomly recruited. They completed the Berlin questionnaire, which screens for OSA risk, a quality-of-life questionnaire for adult Korean patients with asthma (QLQAKA), and underwent an asthma control test (ACT). Fraction of exhaled nitric oxide (FeNO), lung function, blood lipid profiles, and body composition were evaluated.

Results: The mean age was 58.4 ± 15.4 , and 91 (41.9%) were male. Eighty-nine subjects (41.0%) were classified as high risk for OSA from the Berlin questionnaire. Patients with a high OSA risk were significantly older, had a higher prevalence of hypertension, higher BMI, non-atopic predisposition, and longer asthma treatment duration in the baseline clinical characteristics. The high OSA risk group had a lower ACT score than the low OSA risk group, but it was not statistically significant (20.9 ± 3.6 vs 21.5 ± 3.3 , $P = .091$). The QLQAKA score was significantly lower in the high OSA risk group compared with the low OSA risk group (64.4 ± 10.9 vs 68.1 ± 11.1 , $P = .026$), especially in the activity-domain ($P = .005$). The FeNO was not significantly different between the 2 groups.

Conclusion: Quality of life is significantly decreased in adult patients with asthma with a high risk of OSA. Special consideration is needed for the care and treatment of patients with asthma who have a high risk of OSA.

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Introduction

Obstructive sleep apnea (OSA) is a potentially disabling condition characterized by excessive daytime sleepiness, disruptive snoring, repeated episodes of upper airway obstruction during sleep, and nocturnal hypoxemia.¹ The prevalence of OSA is estimated at 3% to 7% in males and 2% to 5% in females in the United States.² In Korea, the prevalence was reported as 4.5% in males and 3.2% in females of middle age.³

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Disclosures: Authors have nothing to disclose.

Funding Sources: This study was supported by a grant of the Korea Healthcare technology R&D Project, Ministry of Health and Welfare, Republic of Korea (A102065).

A subgroup of patients with severe refractory asthma depend on corticosteroids, have persistent symptoms, require frequent hospitalizations, and have fixed airway obstruction.^{4,5} OSA is more prevalent in difficult-to-treat and severe asthma.^{6,7} Much evidence supports the hypothesis that OSA contributes to poor asthma control and increased airway hyperresponsiveness and inflammation.^{5,7} The mechanism of the association between OSA and asthma is not yet clarified, but several possible explanations have been suggested. OSA can cause oxidative stress and systemic inflammation, which can possibly influence asthma and airway inflammation.⁸ OSA is closely linked with obesity, and proinflammatory cytokines such as tumor necrosis factor alpha and interleukin-6 (IL-6) are increased in patients with OSA.⁸ Some studies have suggested that mechanical events during apneas lead to vagal activation or other neural pathways, resulting in increased bronchoconstriction.⁹ Central respiratory control

mechanisms that mediate sleep-related bronchomotor tone could be influenced by neural changes related to OSA.^{10,11} In another study, the acid-pepsin reflux was frequent in patients with OSA and may worsen asthma.¹²

The prevalence and clinical features of OSA and its comorbid conditions such as obesity, metabolic syndrome, and gastroesophageal reflux can differ geographically according to variances in lifestyle and culture, and to genetic and ethnic differences.² However, the effects of OSA on asthma and its importance for asthma care in Asians have been underexplored. We evaluated the clinical characteristics, asthma control, and asthma-related quality of life in Korean adult patients with asthma with a high risk of OSA, using the validated screening tool for OSA risk, the Berlin questionnaire.

Materials and Methods

Study Subjects

We randomly recruited adult patients with asthma who routinely visited the tertiary-care clinic of Seoul National University Bundang Hospital from January to October 2011. Patients who met the following asthma diagnosis criteria were enrolled: (1) airway reversibility documented by an increase of forced expiratory volume in 1 second (FEV₁) of 12% and 200 mL after inhalation of 200 µg salbutamol or airway hyperresponsiveness documented by a methacholine provocation concentration causing a 20% fall in FEV₁ of 16 mg/mL or less, in the past or at the time of enrollment; (2) the presence of persistent asthma symptoms; (3) physician's diagnosis of asthma. Patients who could not perform the study because of conditions such as illiteracy, impaired vision, lack of cognitive function, serious psychiatric mental problems, and so forth, or who did not wish to be enrolled were excluded.

Enrolled patients completed the questionnaire for OSA risk screening, asthma control, and asthma-related quality of life.^{13–15} Also, we checked and assessed the baseline characteristics of the patients, including age, sex, height (cm), weight (kg), history of smoking, presence of atopy and allergic rhinitis, duration of asthma symptoms and treatment, asthma medications, and comorbid diseases. Spirometry, fraction of exhaled nitric oxide (FeNO), and analysis of body composition were performed at enrollment. Blood tests were performed in those patients who were willing to have their lipid profiles checked. All subjects provided written informed consent, and the study protocol was approved by the institutional review board.

Questionnaires

All patients completed the Berlin questionnaire, asthma control test (ACT), and the quality of life questionnaire for adult Korean patients with asthma (QLQAKA) (eTable 1). The Berlin questionnaire was validated for screening of OSA by Netzer et al in 1999¹³; it consists of 3 categories and a total of 10 questions. Category 1 includes presence of weight change, severity of snoring, snoring frequency, bothering other people, and awareness of own breathing pauses; category 2, tiredness after sleeping or during wake time and falling asleep while driving; category 3, high blood pressure. It is regarded as positive if the total score is 2 or more points in categories 1 and 2. Category 3 was positive if a patient had hypertension or a body mass index (BMI) greater than 30 kg/m². If 2 or more categories have a positive score, the patient is classified into the high-risk OSA group. The sensitivity and specificity of the Berlin questionnaire were 86% and 77%, respectively.¹³

Asthma control status was evaluated using the Korean version of the ACT, which consisted of 5 items: use of rescue medication, self-evaluation of control status, presence of dyspnea, sleep disturbances caused by asthma symptoms, and limited ability to exercise. Each item was scored from 1 to 5 points, and a score of 25 points

corresponded to completely controlled status.¹⁵ Asthma severity was determined based on the intensity of treatment required to achieve each patient's best level of asthma control, as proposed in a recent classification of asthma severity.¹⁶ Briefly, asthma that could be well-controlled with low-intensity global initiative for asthma (GINA) guideline step 2 treatment, such as low-dose inhaled corticosteroids or leukotriene modifiers, was classified as mild. Well-controlled asthma with GINA step 3 treatment was classified as moderate. Severe asthma was defined as asthma requiring high-intensity treatment such as GINA steps 4 or 5 to maintain good control or where good control was not achieved despite high-intensity treatment.

QLQAKA is a Korean modification of the asthma quality-of-life questionnaire and consists of 4 domains (activity limitations, emotions, symptoms, and exposure to environmental stimuli) and 17 items regarding the asthma-related quality of life. The QLQAKA has been validated for assessment of the quality of life of Korean adult patients with asthma.^{14,15} Answers to each question were scored on a 5-point scale, with a score of 1 representing greatest impairment and a score of 5 representing no impairment. Items were weighted equally, and patients' total QLQAKA scores were reported.

FeNO measurements were performed according to the American Thoracic Society and European Respiratory Society guidelines using NIOX MINO (Aerocrine, Solna, Sweden), which was in clinically acceptable agreement with measurements provided by a stationary analyzer (NIOX; Aerocrine).¹⁷ Patients had not consumed food or beverages and had not smoked for 2 hours before the measurement was taken. A dynamic flow restrictor yielded a constant flow rate of 50 mL/second. Acceptable patient compliance is mandatory for the measurement to be considered accurate.

Body Impedance Test

Body Composition Bioelectrical impedance analysis was performed using the direct segmental measurement bioelectrical impedance analysis method (InBody 720; Biospace Company Ltd, Seoul, Korea), which has been found to be reliable for the calculation of body composition.¹⁸ It automatically displays measurements of waist-hip ratio, body fat mass, percent body fat (PBF), visceral fat area (VFA), soft lean mass, and skeletal muscle mass (SMM).

Statistical Analysis

To compare the baseline demographic and clinical characteristics of the 2 groups (high risk vs low risk of OSA), categorical data were compared using a χ^2 or Fisher exact test, and numerical data were compared using Student's *t* test. Multiple linear regression analyses were applied to adjust for the effects of age and sex to compare asthma-related parameters such as ACT, QLQAKA score, and FeNO, according to the OSA risk. Spearman's correlation test was used to evaluate the associations between QLQAKA scores and parameters related to BMI, body composition, and lipid profile. All statistical analyses were performed using SPSS, ver. 18.0 (SPSS, Inc., Chicago, Illinois), and a *P*-value < .05 was considered to indicate statistical significance.

Results

Baseline Clinical Characteristics of Study Subjects

A total of 217 patients were enrolled in this study. Eighty-nine patients (41.0%) were classified as high risk, and 128 patients were classified as low risk. Their baseline characteristics are shown in Table 1. The mean age of study subjects was 58.4 ± 15.4, and 91 (41.9%) were male. No significant differences were seen between the groups in sex, history of smoking, presence of allergic rhinitis, methacholine provocation concentration causing a 20% fall in FEV₁

Table 1
Baseline characteristics of study population

Characteristics	Total, N (%) (n = 217)	High risk, N (%) (n = 89)	Low risk, N (%) (n = 128)	P value
Age (years)	58.4 ± 15.4	62.9 ± 12.4	55.3 ± 16.6	<.001
Gender (male)	91 (41.9)	39 (43.8)	52 (40.6)	.639
BMI (kg/m ²)	24.7 ± 3.2	25.7 ± 3.2	23.9 ± 3.8	.001
Smoking				
Current smoker	17 (7.8)	4 (4.5)	13 (10.2)	.195
Former smoker	77 (35.5)	36 (40.4)	41 (32.0)	
Nonsmoker	123 (56.7)	49 (55.1)	74 (57.8)	
Presence of allergic rhinitis	63 (29.0)	23 (25.8)	40 (31.3)	.368
Intermittent/persistent	32/31	11/12	21/19	.721
Mild/mod-severe	45/18	16/7	29/11	.804
Comorbidity				
Hypertension	81 (37.3)	57 (64.0)	24 (18.8)	<.001
Diabetes	22 (10.1)	12 (13.5)	10 (7.8)	.173
GERD	9 (4.1)	5 (5.6)	4 (3.1)	.494
Other ENT disease	7 (3.2)	2 (2.2)	5 (3.9)	.703
Atopy (N = 138; 46/92)	89 (64.5)	23 (50.0)	66 (71.7)	.012
Methacholine PC20 (N = 73)	7.2 ± 7.1	7.6 ± 6.1	7.1 ± 7.5	.750
Prebronchodilator FEV ₁ (% of predicted value)	86.8 ± 22.5	86.2 ± 22.9	87.3 ± 22.4	.720
Asthma duration (months)				
Symptom	149.2 ± 154.4	161.4 ± 155.0	140.9 ± 154.0	.340
Diagnosis	109.8 ± 117.9	125.8 ± 129.2	98.8 ± 108.6	.097
Treatment	103.5 ± 113.0	123.9 ± 130.0	89.3 ± 97.6	.035
Asthma severity (mild/moderate/severe)	35/134/48	11/57/21	24/77/27	.448
Asthma medication				
ICS	22 (10.1)	5 (5.6)	17 (13.3)	.066
ICS/LABA	173 (79.7)	77 (86.5)	96 (75.0)	.038
LTRA	127 (58.5)	58 (65.2)	69 (54.0)	.098
Theophylline	16 (7.4)	9 (10.1)	7 (5.5)	.198

Abbreviations: ICS, inhaled corticosteroid; ENT, ear, nose and throat; GERD, gastroesophageal reflux disease; LABA, long-acting beta agonist; LTRA, leukotriene receptor antagonist.

Data presented as mean ± standard deviation or N (%).

(high-risk group vs low-risk group; 7.6 ± 6.1 vs 7.1 ± 7.5 , $P = .750$), prebronchodilator FEV₁% of predicted value (86.2 ± 22.9 vs 87.3 ± 22.4 , $P = .720$), or duration of asthma symptoms and time since diagnosis.

The mean age was significantly higher in the high-risk group than in the low-risk group (62.9 ± 12.4 vs 55.3 ± 16.6 , $P < .001$). BMI was significantly higher in the high-risk group than in the low-risk group (25.7 ± 3.2 vs 23.9 ± 3.8 ; $P = .001$). Hypertension was more frequent in the high-risk group than in the low-risk group (64.0% vs 18.8% ; $P < .001$). Atopy was less likely in the high-risk group (50.0% vs 71.7% ; $P = .012$), and the duration of asthma treatment was significantly longer in the high-risk group than in the low-risk group (123.9 ± 130.0 days vs 89.3 ± 97.6 days; $P = .035$). The number of patients who used the combination of inhaled corticosteroid and a long-acting β agonist was higher in the high-risk group (86.5% vs 75.0% ; $P = .038$), but asthma severity was not significantly different between the groups.

Differences in Asthma-Related Parameters According to the Obstructive Sleep Apnea Risk Group

To examine differences between the OSA risk groups, their characteristics were analyzed by linear regression and adjusted for age and sex. The difference in ACT, QLQAKA scores, and FeNO values according to OSA risk group are presented in Figure 1.

The mean QLQAKA score was significantly lower in the high-risk group than in the low-risk group (64.4 ± 10.9 vs 68.1 ± 11.1 ; $P = .026$). To evaluate which domains of QLQAKA made the difference between the OSA high-risk group and low-risk group, each QLQAKA domain's mean values were analyzed (Table 2). A QLQAKA domain mean value was calculated as sum of QLQAKA scores in the domain divided by the number of questions of the domain. The mean values were used because the number of questions was different according to the domain. The average of activity-domain means was significantly lower in the high-risk group than in the low-risk group (3.8 ± 0.72 vs 4.1 ± 0.67 ; $P = .005$).

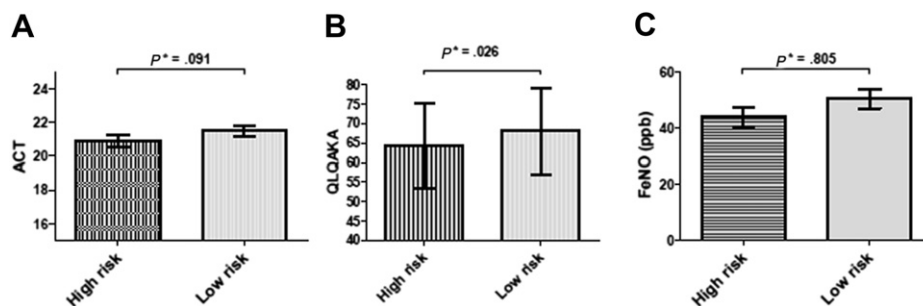


Figure 1. ACT, QLQAKA scores, and FeNO values according to the risk group of OSA. A, ACT scores (high risk vs low risk, 20.9 ± 3.6 vs 21.5 ± 3.3 as mean ± standard deviations, $P = .091$); B, QLQAKA scores (64.4 ± 10.9 vs 68.1 ± 11.1 , $P = .026$); C, FeNo (ppb) (40.8 ± 42.3 vs 43.8 ± 37.3 , $P = .805$, total $n = 192$). Error bars represent means ± standard errors of the mean; *age, sex-adjusted P -value.

Table 2

Comparisons of each QLQAKA domain mean values between high-risk group and low-risk group

Domains of QLQAKA	High-risk group (n = 89)	Low-risk group (n = 128)	P value
Symptoms	3.7 ± 0.75	3.9 ± 0.70	.054
Activities	3.8 ± 0.72	4.1 ± 0.67	.005
Emotions	3.8 ± 0.97	4.0 ± 1.0	.144
Environmental effects	4.0 ± 0.97	4.0 ± 0.84	.782

Data were described as mean ± standard deviation. Age, sex were adjusted.

A QLQAKA domain mean value = sum of QLQAKA scores in the domain/number of questions of the domain; Mean scores were used because the number of questions was different, depending on the domain.

The high-risk OSA group had a lower ACT score than the low-risk OSA group, although the difference was not statistically significant (20.9 ± 3.6 vs 21.5 ± 3.3 ; $P = .091$). The mean FeNO value was not significantly different between the 2 groups (40.8 ± 42.3 vs 43.8 ± 37.3 ; $P = .805$).

Correlation Between QLQAKA and Factors That Were Significantly Correlated with the OSA Risk

Body composition profiles and blood lipid profiles according to OSA risk group are shown in Table 3. PBF, SMM, and especially VFA were significantly higher in the high-risk group than in the low-risk group (PBF, 32.0 ± 7.7 vs 26.6 ± 16.1 ; $P = .008$; SMM, 28.0 ± 25.0 vs 24.2 ± 7.5 ; $P = .001$; VFA, 119.6 ± 27.8 vs 94.2 ± 43.9 ; $P = .001$). Blood lipid profiles, including serum cholesterol, high-density lipoprotein, and low-density lipoprotein cholesterol, were not significantly different between the groups. The triglyceride (TG) level was significantly higher in the high-risk group than in the low-risk group (154.8 ± 102.9 vs 101.8 ± 47.9 ; $P = .002$).

A correlation was found between the values of VFA and QLQAKA, although the correlation was weak (ρ [rho] = -0.154 ; $P = .04$). The QLQAKA was not correlated with other factors, including BMI ($\rho = -0.106$; $P = .158$), PBF ($\rho = -0.090$; $P = .230$), SMM ($\rho = 0.090$; $P = .227$), and TG ($\rho = 0.069$; $P = .523$).

Discussion

Patients with OSA have difficulties with asthma control and severe asthma symptoms.^{5,8,19} OSA is more prevalent among patients with severe asthma.⁶ A high OSA risk was significantly

Table 3

Body mass index (BMI), body composition profiles, and blood lipid profiles according to the risk group of obstructive sleep apnea (N = 180)

Characteristics	High risk (N = 69)	Low risk (N = 111)	P value	Adjusted P value ^a
Body composition profiles				
WHR	1.1 ± 1.3	1.3 ± 0.13	.868	.806
PBF (%)	32.0 ± 7.7	26.3 ± 16.1	.002	.008
BFM (kg)	39.9 ± 12.0	38.7 ± 16.1	.564	.825
VFA (cm ²)	119.6 ± 27.8	94.2 ± 43.9	<.001	.001
SLM (kg)	42.5 ± 8.4	43.0 ± 8.8	.718	.790
SMM (kg)	28.0 ± 25.0	24.2 ± 7.5	.137	.027
Lipid profiles ^b				
Cholesterol	191.4 ± 33.2	190.1 ± 36.5	.865	.331
Triglyceride	154.8 ± 102.9	101.8 ± 47.9	.004	.002
HDL-cholesterol	56.0 ± 22.4	63.3 ± 26.2	.175	.311
LDL-cholesterol	109.5 ± 40.5	105.2 ± 33.7	.591	.739

Abbreviations: BFM, body fat mass; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PBF, percent body fat; SLM, soft lean mass; SMM, skeletal muscle mass; VFA, visceral fat area; WHR, waist-hip ratio.

Data presented as means ± standard deviations.

^aAge, sex-adjusted P value.

^bLipid profiles were measured in 89 patients (40 in high-risk group and 49 in low-risk group).

associated with poorly controlled asthma independent of other asthma aggravators.¹⁹ Asthma patients with OSA experience frequent hypoxemia, which may induce enhanced bronchial hyperresponsiveness.^{8,20} Both snoring and OSA are associated with increased airway inflammation assessed by FeNO levels and induced sputum cellularity in both adults and children.^{21–23} In addition, many reports have demonstrated that treatment for OSA, including continuous positive airway pressure or adenotonsillectomy, improves asthma outcomes.^{24,25}

In the present study, patients with asthma with a high risk of OSA had a poorer quality of life compared with those with a low OSA risk. However, no significant difference between asthma control score and exhaled NO concentration was found, unlike previous reports.^{19,21} Most subjects of our study had been taking asthma medication, such as inhaled corticosteroids, long-acting β -2 agonists, and leukotriene antagonists, and their medications had been adjusted according to their control status. Moreover, patients with high risk for OSA were taking higher levels of asthma controller treatment. Exhaled NO concentrations can be affected by such controller medications, which may lead to the lack of difference according to OSA risk. Asthma control status can change dynamically. A single evaluation of the asthma control score includes symptoms, activity limitation, self-evaluation, and use of relievers, but it may fail to reflect overall control status and the difference between the groups. Conversely, the quality-of-life assessment involves emotional factors such as psychological stress, anxiety, and concern as well as more detailed questions on symptoms and activity limitations. Given these characteristics, the quality-of-life questionnaire seems a more appropriate tool for evaluating various aspects of patients' asthma status. Furthermore, our data suggested that high risk of OSA affects asthma-related limitation of activities more than other domains of quality of life. QLQAKA deals with detailed aspects of activity limitations, whereas ACT includes only 1 question of activity limitation. This difference in the questionnaires may influence the significant reduction in the quality of life rather than the asthma control score.

OSA can affect the quality of life of patients with asthma in many ways, such as lower-quality sleep.^{26,27} Patients with OSA have increased vagal tone during sleep apnea, which may increase bronchoconstriction and trigger nocturnal asthma symptoms.⁸ Intermittent obstruction of the upper airway leads to airway turbulence and local mucosal stress and inflammation.^{8,28} Increases in polymorphonuclear leukocytes and inflammatory mediators were found in the nasal mucosa of patients with OSA.²⁹ Chronic inflammation of the soft palate with increased mucosal edema was also noted. OSA can cause lower airway inflammation and oxidative stress as well as upper airway mucosal inflammation. Previous reports revealed increased levels of IL-6, 8-isoprostane, leukotriene B₄, and exhaled NO in exhaled condensate or induced sputum.^{30,31} Local tissue damage and inflammation caused by snoring can induce systemic inflammation, and these changes may affect coexistent airway inflammation. C-reactive protein was significantly increased in patients with obstructive sleep apnea compared with healthy individuals.²⁸ Proinflammatory cytokines, such as IL-6 and tumor necrosis factor alpha, were also elevated in patients with OSA, and the levels of these cytokines were correlated with the severity of sleep apnea.^{32,33}

Patients with asthma or obstructive sleep apnea share many risk factors.³⁴ Obesity, gastrointestinal reflux disorder, and upper airway inflammatory conditions such as allergic rhinitis are closely related to both OSA and asthma.⁸ In particular, obesity increases sleep apnea risk through various mechanisms, including altered upper airway configuration, increased collapsibility, and reduction in the functional residual capacity. Also, obesity contributes to airway hyperresponsiveness and is characterized by systemic inflammation, which may increase airway inflammation.³⁵ Obese patients with

asthma tend to have poorly controlled asthma, a high hospitalization rate, and reduced response to asthma medication, especially compared with non-obese patients with asthma.³⁶ In our data, BMI, VFA, and blood TG levels were significantly higher in the high-risk OSA group than in the low-risk OSA group. VFA was significantly correlated with the QLQAKA score, although neither a significant correlation between BMI and QLQAKA score nor an association between the waist–hip ratio and OSA risk were found. These data suggest that the amount of visceral fat—which represents central abdominal obesity—is involved in the mechanism of the association between OSA and asthma. Particularly, central obesity associated with metabolic abnormalities is known to be strongly associated with OSA.³⁷ Furthermore, several reports have suggested that central obesity is a more relevant factor for assessing the risk of asthma.³⁸ Systemic inflammation caused by the production of proinflammatory cytokines and chemokines, generation of oxidative stress, and changes in hormones such as leptin and adiponectin were noted in patients with central obesity.²⁸ Although these factors were not evaluated in this study, these phenomena could aggravate the asthma control status and quality of life related to OSA.

Our study has several limitations. First, polysomnography as a diagnostic tool for OSA was not performed, and therefore our results are applicable to patients with asthma who are at high risk for OSA rather than those diagnosed with OSA. The Berlin questionnaire is a validated OSA screening tool with high sensitivity and specificity and seems appropriate for assessing the risk of OSA. Second, as mentioned previously, asthma control status and quality of life were evaluated at a single instance, and most patients had taken asthma medication at the time. This cross-sectional assessment may have failed to adequately represent overall control status and quality of life. Finally, factors mediating the association between OSA and asthma, such as cytokines and chemokines, were not investigated sufficiently. Further studies of the precise causal relationship among OSA, central obesity, and asthma, and its pathogenic mechanisms, are warranted.

Nevertheless, our data provide clinical evidence that OSA is an important contributing factor for poor quality of life in adult patients with asthma and that central abdominal obesity may be involved in this association. Special consideration is needed for the care and treatment of patients with asthma at high risk for OSA, particularly elderly or centrally obese patients.

Supplementary Data

Supplementary data related to this article can be found online at <http://dx.doi.org/10.1016/j.anai.2013.01.005>

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eTable 1

Items of the Berlin questionnaire, asthma control test (ACT), and the quality of life questionnaire for adult Korean patients with asthma (QLQAKA)

The Berlin questionnaire (3 categories consist of 10 questions)

Category 1

- Has your weight changed?
- Do you snore?
- Snoring loudness
- Snoring frequency
- Does your snoring bother other people?
- How often have your breathing pauses been noticed?

Category 2

- Are you tired after sleeping?
- Are you tired during waketime?
- Have you ever fallen asleep while driving?

Category 3

- Do you have high blood pressure?

ACT

- The effect of asthma on daily functioning
- Daytime asthma symptoms (shortness of breath)
- Nocturnal symptoms
- Use of rescue medications
- Self-assessment of asthma control

QLQAKA

Domain of symptoms

- Chest tightness
- Dyspnea-related asthma
- Wheezing
- Cough
- Awake during nighttime because of cough or dyspnea
- Expectoration or feeling of stuck sputum at throat

Domain of activities

- Asthma-related limitation of tough daily activities
- Asthma-related limitation of light daily activities
- Asthma-related limitation of social activities
- Asthma-related limitation of activities at school or workplace
- Asthma-related limitation of total daily activities

Domain of emotions

- Worry about asthma attack
- Asthma-related mental stress
- Worry about difficulties in treating asthma

Domain of environmental effects

- Asthma exacerbation by cigarette smoke or irritating odor or being bothered by these exposures
- Asthma exacerbation by weather, temperature changes and pollution or limitations of outdoor activities
- Asthma exacerbation by indoor dust or unclear air