

A Computerized Asthma-Specific Quality of Life: A Novel Tool for Reflecting Asthma Control and Predicting Exacerbation

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Key Words

Health-related quality of life · Asthma control status ·
Asthma exacerbation

Abstract

Background: Proper assessment of health-related quality of life is essential to achieve and maintain a controlled status in asthmatic patients. We developed our own computerized asthma-specific quality-of-life (cA-QOL) questionnaire based on in-depth interviews with adult asthmatic patients. In this study, we evaluated this cA-QOL in terms of the Asthma Control Test (ACT) score and Global Initiative for Asthma (GINA) guidelines as well as asthma exacerbation, and compared it with the asthma-related quality-of-life questionnaire (AQLQ). **Methods:** We conducted a multicenter, prospective, observational study in 133 adult asthmatic patients recruited from 5 university hospitals in South Korea, who were randomized into 2 groups according to the operating order of the cA-QOL and AQLQ. At every visit (3-month interval), physicians evalu-

ated asthma control status with monitoring spirometry. The self-administered cA-QOL, AQLQ(S) and ACT were completed. **Results:** The cA-QOL scores correlated significantly with ACT and AQLQ(S) scores ($r = 0.814$, $p < 0.001$; $r = 0.900$, $p < 0.001$). The cA-QOL score was significantly lower where the ACT score was < 19 , in the patients with an uncontrolled asthma status according to the GINA guidelines and in those with asthma exacerbation ($p < 0.001$, respectively). A multivariate analysis showed that this cA-QOL was a significant parameter associated with an uncontrolled asthma status and asthma exacerbation ($p < 0.001$, $p = 0.045$, $p = 0.019$, respectively). **Conclusion:** The cA-QOL is a valid tool for reflecting current asthma control status and for assessment to predict the future risk of asthma exacerbation in adult asthmatics.

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Introduction

In 2006, when the Global Strategy for Asthma Management and Prevention proposed the management of asthma based on clinical control status rather than on a classification by severity, a goal for the treatment of asthma was to achieve and maintain a control status and to determine the steps involved in treatment [1]. To determine asthma control status, several questionnaires were developed [2]. If a patient's symptoms are under control, then their health-related quality of life (HRQOL) is also improved [3–6]. To assess HRQOL is important, not only for aspects of disease control but also the perception patients have of their whole life. In 2010, the Global Allergy and Asthma European Network (GA²LEN) consensus report was released to reflect the importance of consideration of patient-reported outcomes and HRQOL as evaluating tools in clinical trials for asthma and allergic diseases [7]. So assessment of both asthma control status and the HRQOL is considered important.

The asthma-related quality-of-life questionnaire (AQLQ) was proposed in 1992 by Juniper et al. [2], was validated in 1999 and is now used widely for the evaluation of HRQOL impairment in asthma [8, 9]. The AQLQ(S) is an extended version of this, replacing individualized activities with general activities. The Asthma Control Test (ACT) correlates well with the AQLQ scores in our cohort and is considered a reliable and valid tool for measuring asthma control [10]. However, expression of QOL is closely linked to language, culture and social consensus [11], and so there was a need to develop our own QOL questionnaire.

In 2009, we developed our own asthma-specific quality-of-life (A-QOL) questionnaire based on in-depth interviews with adult asthma patients [12]. A-QOL is produced by our language and so reflects our patients' perceptions of real life. A-QOL takes into account six elements, which make it more diverse and detailed, especially with regard to monitoring symptoms and emotions, than other asthma-specific HRQOLs [8, 13].

We also developed a computerized A-QOL (cA-QOL), which is a digital version of A-QOL that uses a touchscreen. The cA-QOL is expected to be more useful in clinical practice and clinical trials because it is easier and more rapid, and there is less room for error than when using paper versions [14]. In this study, we evaluated this cA-QOL in adult asthmatic patients at multicenters in terms of the ACT score and the Global Initiative for Asthma

(GINA) guidelines, as well as asthma exacerbation. The data were compared with what was collected by AQLQ from adult asthma patients.

Methods

Study Subjects

Adult asthma patients with an uncontrolled asthma state (ACT score ≤ 19) were recruited from asthma and allergy clinics in 5 university hospitals (Ajou University, Yonsei University, Dong-A University, Inha University and Hallym University) in South Korea, between August 2010 and April 2012. Criteria for inclusion in the study were as follows: age 20–70 years, a 6-month asthma diagnosis, airway reversibility or airway hyperresponsiveness or airflow variability, $\geq 55\%$ of FEV₁ (% of predicted value), inhaled corticosteroid (ICS) or a combination therapy of ICS and long-acting β -agonist (LABA) during the last 4 weeks and being literate in Korean. Patients were excluded from the study if they were current smokers, had a history of smoking of >15 pack-years, had other chronic diseases that would influence the HRQOL (including heart and renal failure, cerebral infarction, malignancy and tuberculosis or other chronic lung diseases), had had a respiratory infection within the previous 2 weeks or had recently changed their asthma medication.

Study Design

A prospective observational study was conducted to validate the cA-QOL. Patients were divided randomly into 2 groups. Group A conducted the test starting with the cA-QOL and then the AQLQ(S) and Group B started with the AQLQ(S) and then took the cA-QOL. After an initial screening visit, patients from both groups were monitored 3 times during a 6-month period (at 1, 12 and 24 weeks). At each visit, a spirometry test was conducted followed by the self-administered ACT, cA-QOL and AQLQ(S). Patients were questioned about adherence to asthma medication, asthma control status according to the GINA guidelines and asthma exacerbation. Laboratory tests, including sputum eosinophils, neutrophils and fractional exhaled nitric oxide (FeNO) were performed where possible (sputum eosinophils and neutrophils in all institutes and FeNO at Ajou University). The study protocol was reviewed and approved by the institutional review boards of all participating university hospitals.

Health-Related Quality of Life

We evaluated the HRQOL using two different measurements: cA-QOL and the Korean version of the AQLQ(S). The cA-QOL contains 30 questions with a 5-response scale answer, scoring from 0 to 4. The items are grouped into 6 categories: physical and social activity (8 items), difficulties related to cough (5 items), emotional status (6 items), symptoms related to breathing (4 items), uncertain future (4 items) and environmental distress (3 items) [12]. AQLQ(S) contains 32 items in 4 categories: activity limitations (11 items), symptoms (12 items), emotional function (5 items) and exposure to environmental stimuli (4 items) [8, 10].

Asthma Control Test, Asthma Control Status and Asthma Exacerbation

We evaluated the Korean version of ACT (K-ACT; a trademark of QualityMetric Incorporated, Richmond, Va., USA) with a score

Table 1. Patient characteristics

Characteristics	Group A ^a (n = 69)	Group B ^b (n = 64)	p value
Age, years	48.3±12.5	48.6±10.0	0.907
Sex, male	28 (40.6)	27 (42.2)	0.851
Smoking history, never-smoker	53 (76.8)	45 (70.3)	0.453
Rhinitis comorbidity	45 (68.2)	44 (74.6)	0.431
Duration of asthma, months	86.7±77.5	97.5±95.0	0.480
Inhaler prescribed (ICS + LABA)	44 (63.8)	42 (65.6)	0.643
FEV ₁ (% pred)	84.5±11.2	84.0±13.8	0.802
ACT score at screening	16.9±2.7	16.5±3.3	0.369
ACT score at visit 1	16.9±2.8	16.9±3.7	0.994
ACT score at visit 2	18.9±4.5	18.7±4.0	0.810
ACT score at visit 3	18.8±3.9	19.6±4.5	0.259
ACT score (≤19) at visit 1	67 (97.1)	54 (84.4)	0.010
ACT score (≤19) at visit 2	25 (52.1)	25 (52.1)	1.000
ACT score (≤19) at visit 3	33 (49.3)	23 (39.7)	0.282
Asthma control status at visit 1 ^c	10/36/17 (16/57/27)	9/29/22 (15/48/37)	0.503
Asthma control status at visit 2 ^c	13/17/18 (27/35/38)	11/18/19 (23/37/40)	0.895
Asthma control status at visit 3 ^c	14/28/15 (25/49/26)	16/25/15 (28/45/27)	0.863
cA-QOL score at visit 1	82.4±25.8	80.7±28.2	0.727
cA-QOL score at visit 2	7.4±30.8	86.0±28.4	0.823
cA-QOL score at visit 3	89.3±28.2	90.6±28.8	0.797
AQLQ(S) score at visit 1	149.0±43.8	149.1±43.3	0.989
AQLQ(S) score at visit 2	159.9±46.7	156.5±40.9	0.705
AQLQ(S) score at visit 3	161.8±43.6	164.6±42.9	0.714

All values are denoted as mean ± standard deviation or as a number with percentage in parentheses.

^a Group A started with cA-QOL and then took AQLQ(S). ^b Group B started with AQLQ(S) and then took cA-QOL. ^c Well-controlled/partly controlled/uncontrolled status according to GINA guidelines.

Table 2. Associations with uncontrolled asthma status (ACT score ≤19)

Parameters	Adjusted OR	95% CI	p value
Age	1.010	0.984–1.036	0.443
Rhinitis comorbidity	0.651	0.322–1.313	0.230
Asthma control status according to GINA guidelines			
Controlled	reference		
Partly controlled	1.025	0.491–2.138	0.948
Uncontrolled	0.854	0.307–2.379	0.763
FEV ₁ (% pred)	0.972	0.950–0.994	0.013
cA-QOL score	0.946	0.918–0.975	<0.001
AQLQ(S) score	0.984	0.969–0.999	0.035

CI = Confidence interval; OR = odds ratio.

from 1 to 5, where a higher score represents well-controlled asthma [10]. The asthma control status was evaluated at every visit, based on the ACT score and the GINA guidelines [1]. Asthma exacerbation was defined as: a use of systemic steroids, an unscheduled visit to an outpatient department, a visit to the emergency room or hospitalization.

Table 3. Parameters predictive of asthma exacerbations

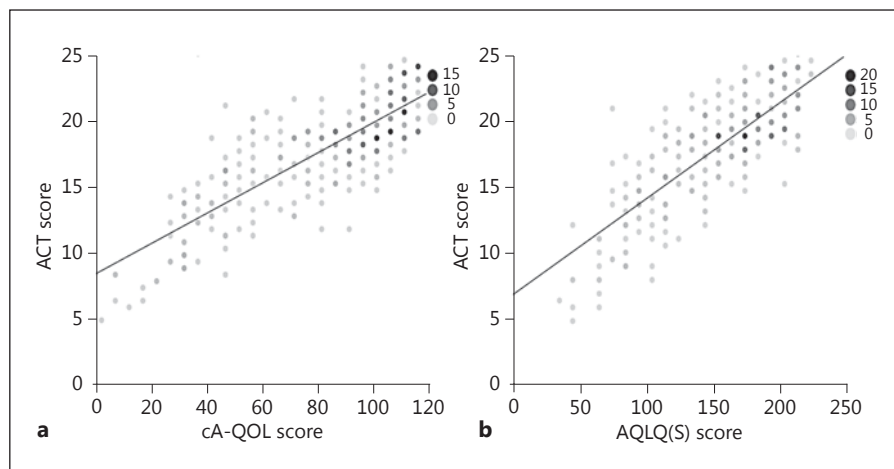
Parameters	Adjusted OR	95% CI	p value
Duration of asthma (months)	1.003	0.999–1.008	0.182
Rhinitis comorbidity	6.615	1.434–30.511	0.015
cA-QOL score	0.960	0.927–0.993	0.019
AQLQ(S) score	1.011	0.989–1.035	0.330
Sputum neutrophil count	0.991	0.979–1.002	0.114

CI = Confidence interval; OR = Odds ratio.

Statistical Analysis

SPSS version 19 (Statistical Package for Social Scientists Inc., Chicago, Ill., USA) was used to analyze the data, including Pearson's correlation, paired Student's t test, one-way ANOVA and logistic regression analyses. Univariate logistic regression analysis was conducted using the parameters, age, sex, smoking history (never-smoker or exsmoker), rhinitis comorbidity, duration of asthma, adherence to asthma medication, asthma control status according to the GINA guidelines, FEV₁ (% pred), ACT score, cA-QOL score, AQLQ(S) score, FeNO, sputum eosinophil count and

Fig. 1. Score correlation between cA-QOL and ACT (**a**), AQLQ(S) and ACT (**b**). A Pearson's correlation analysis of the cA-QOL versus ACT scores and the AQLQ(S) versus ACT scores was conducted. A statistically significant correlation was found between the cA-QOL and ACT ($r = 0.814$, $p < 0.001$) scores and between the AQLQ(S) and ACT ($r = 0.797$, $p < 0.001$) scores.



sputum neutrophil count to determine the predictability of an uncontrolled status (according to the ACT score ≤ 19 or the GINA guidelines) or asthma exacerbation. A multivariate analysis was performed using the parameters found to be statistically significant in each univariate analysis.

Results

Study Subjects

A total of 133 patients were enrolled in this study, and 354 visits took place. Characteristics of the study subjects are summarized in table 1. There were no significant differences in ACT, cA-QOL and AQLQ(S) scores between groups A and B at each visit, except for the ACT scores at visit 1. cA-QOL and AQLQ(S) scores at each visit are summarized in figure 1.

Score Correlation between cA-QOL and ACT

Statistically significant correlations were observed between cA-QOL and ACT ($r = 0.814$, $p < 0.001$) scores and between AQLQ(S) and ACT ($r = 0.797$, $p < 0.001$) scores, as shown in figure 1. We found that cA-QOL correlated significantly with AQLQ(S) ($r = 0.900$, $p < 0.001$, as shown in fig. 2).

Comparison of cA-QOL and AQLQ(S) Scores Grouped by Asthma Control Status, Asthma Exacerbation and Asthma Severity

Both the cA-QOL and AQLQ(S) scores were well within the asthma control status according to the ACT score or GINA guidelines (fig. 2). The cA-QOL score was also significantly lower in the group showing asthma exacerbation. However, the cA-QOL and AQLQ(S) scores did

not correlate with asthma severity according to FEV₁ (% pred) (fig. 3).

Association with an Uncontrolled Asthma Status

Clinical parameters associated with an uncontrolled asthma status were analyzed (ACT score ≤ 19), as summarized in table 2, in which statistically significant parameters were the FEV₁ (% pred) value and cA-QOL and AQLQ(S) scores. The clinical parameters associated with an uncontrolled asthma status according to the GINA guidelines were cA-QOL and AQLQ(S) scores ($p = 0.045$, $p = 0.015$, respectively, data not shown). A ROC curve was drawn to estimate the cut-off value of cA-QOL for predicting an uncontrolled asthma status (according to ACT score ≤ 19 : AUC 0.851, $p < 0.001$ or GINA guidelines: AUC 0.846, $p < 0.001$; fig. 3). The cut-off value of cA-QOL was 97.5 with 72.7% sensitivity and 82.7% specificity for predicting ACT score ≤ 19 and 91.5 for uncontrolled status by GINA with 82% sensitivity and 71.6% specificity.

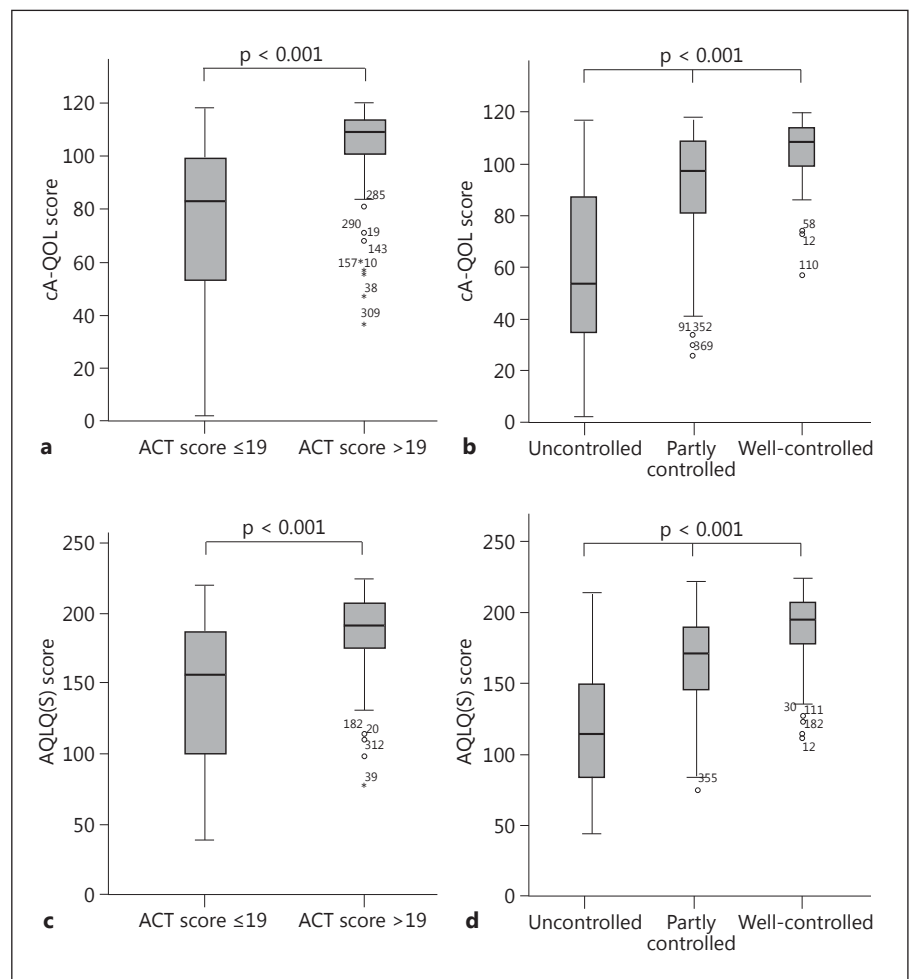
Predictability of an Asthma Exacerbation

The clinical parameters predictive of an asthma exacerbation are shown in table 3. After a multivariate analysis, the cA-QOL score and rhinitis comorbidity remained statistically significant.

Domain Analysis of cA-QOL and AQLQ(S)

Univariate and multivariate logistic regression analyses of the questionnaire areas [6 areas in cA-QOL and 4 in AQLQ(S)] were conducted to estimate the predictability of an uncontrolled asthma status or asthma exacerbation. The univariate analysis revealed that all 10 questionnaire areas were statistically significant in terms of

Fig. 2. Comparison of cA-QOL and AQLQ(S) scores grouped by asthma control status according to the ACT scores (**a**, **c**) and the GINA guidelines (**b**, **d**). A paired Student t test and one-way ANOVA were conducted to compare cA-QOL or AQLQ(S) scores grouped by asthma control status. Asthma control status was defined according to the ACT score or GINA guidelines. The cA-QOL score was significantly higher in an uncontrolled asthma status, defined as an ACT score ≤ 19 (**a**) or according to the GINA guidelines (**b**).



predicting an uncontrolled asthma status or asthma exacerbation. According to the multivariate analysis, however, the difficulties related to the cough area in the cA-QOL remained statistically significant in predicting an uncontrolled asthma status and asthma exacerbation (data not shown).

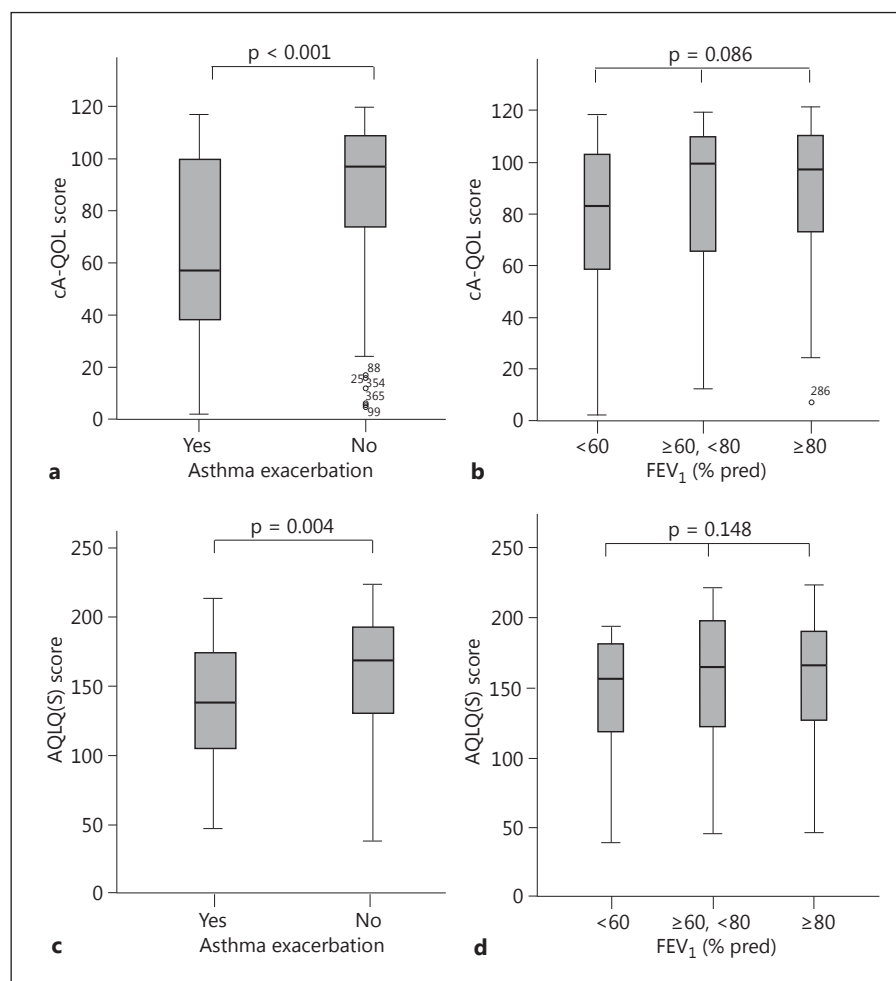
Discussion

As people with chronic respiratory disease, such as asthma and COPD, can suffer a poor QOL, accurate measurement of the QOL of asthma patients is vital [15]. Because QOL differs among cultures and languages, having the means to accurately measure Korean-specific QOL is important. However, no common HRQOL for Korean asthmatics is in use. With this in mind, we developed our own specific A-QOL. Validation of the A-QOL was achieved by

testing in 422 patients from 5 university hospitals in South Korea [12]. We compared the conventional paper-and-pencil version of A-QOL (pA-QOL) and a touch-screen version of the cA-QOL questionnaire, using a randomized prospective study. cA-QOL compared reliably with pA-QOL, and was preferred by the asthma patients as well as being useful in busy practices for the assessment, collection and evaluation of asthma-specific HRQOL [14]. The cA-QOL was evaluated and compared the responsiveness with the AQLQ devised by Juniper et al [2], by means of a multicenter study over a 6-month period and was then correlated with the AQLQ(S) and ACT scores.

The GINA guidelines emphasize the control status of asthma rather than the severity, with patients' QOL reflecting this status [15]. In this study, as an aspect of asthma control status (defined as ACT score ≤ 19 or according to the GINA guidelines), the cA-QOL score was effective in distinguishing the asthma control status, i.e. well-con-

Fig. 3. Comparison of cA-QOL and AQLQ(S) scores grouped by asthma exacerbation (**a, c**) and asthma severity grouped by FEV₁ (% pred) (**b, d**). A paired t test and one-way ANOVA were conducted to compare the cA-QOL or AQLQ(S) scores grouped by asthma exacerbation and asthma severity grouped by FEV₁ (% pred). The cA-QOL score was significantly lower in the acute asthma exacerbation group (**a**). However, the cA-QOL and AQLQ(S) did not correlate with asthma severity according to FEV₁ (% pred).



trolled, partly controlled or uncontrolled. Moreover, the cA-QOL, together with AQLQ(S), constituted a valid parameter for identifying an uncontrolled asthma status (defined as ACT score ≤ 19 or according to the GINA guidelines). These findings suggest that the cA-QOL may be used to draw a distinction between uncontrolled and well-controlled/partly controlled status of asthma in adult asthmatics.

As well as distinction regarding the current level of asthma control, there is a need to develop future methods of risk reduction and prevention of asthma exacerbation [16]. Asthma exacerbation results in an impaired QOL, presents a significant risk to patients and is a drain on healthcare budgets. In this study, the cA-QOL score was able to not only highlight asthma control but also predict exacerbation. Moreover, the cA-QOL score was the only parameter that could predict asthma exacerbation when adjusted by the ACT and AQLQ(S) scores. This finding

suggested the cA-QOL to be very useful for predicting asthma exacerbation in adult asthmatic patients. Consequently, the cA-QOL will likely prove useful in our clinical practices and in clinical trials, as it is a convenient and accurate method of assessing the HRQOL in adult asthmatics.

This study was conducted only in the Korean language and in a homogenous population. The questionnaire was validated only for Koreans; the result indicated the importance of the instrument for measuring QOL using the patients' own language, and patient recognition was stronger than objective tools, such as FEV₁, FeNO, sputum cell count and the blood test. This instrument may be valuable in other Asian countries that share emotional similarities and social atmosphere. Further studies are necessary to facilitate translation into other Asian languages.

To date, no other reports have been published regarding the predictive asthma exacerbation of asthma-specific HRQOLs, likely because diverse areas and symptoms were taken into account in creating the cA-QOL [3, 5, 17, 18]. Univariate and multivariate logistic regression analyses of the questionnaire areas revealed that the area relating to coughing is a decisive subclass in terms of predicting an uncontrolled asthma status according to the GINA guidelines, and that asthma exacerbation resulting from the coughing is a major contributor to poor asthma control [19]. We also confirmed that rhinitis comorbidity was an important factor in predicting asthma exacerbation, as reported previously [20].

In conclusion, the cA-QOL is a valid tool for reflecting current asthma control status and predicting the future risk of asthma exacerbation in adult asthmatics. The cA-QOL is expected to be widely adopted in clinical practices, clinical trials and initial investigations. Future work should focus on the development of tools that take into account cultural characteristics for the purpose of assessing the HRQOL of asthmatics.

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