



Association between asthma control and health-related quality of life in severe asthma: a cross-sectional study from KoSAR

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Uncontrolled severe asthma impairs HRQoL, especially daily functioning. ACT correlates with HRQoL, supporting its clinical use. Improving asthma control through optimised management can reduce disease burden and enhance HRQoL. <https://bit.ly/3GLkBXl>

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Abstract

Background Severe asthma (SA) imposes a significant burden on patients' health-related quality of life (HRQoL). This study aimed to quantify HRQoL burden and identify clinical determinants associated with HRQoL impairment in patients with SA.

Methods Cross-sectional data were collected from 701 patients (592 with SA, 109 with non-severe asthma (NSA)) in the Korean Severe Asthma Registry (KoSAR). HRQoL was measured using the EuroQoL 5-dimension 5-level (EQ-5D-5L) and Severe Asthma Questionnaire (SAQ). Asthma control status was assessed with the Asthma Control Test (ACT) scores. Multivariable and ordinal logistic regression analyses were conducted to identify factors associated with HRQoL.

Results Patients with SA had lower EQ-5D-5L scores than those with NSA (SA: 0.83 versus NSA: 0.87, $p < 0.001$). Among patients with SA, recent rescue medication use, reduced lung function and uncontrolled symptoms were associated with impaired HRQoL. Uncontrolled SA was associated with greater impairments than controlled SA (uncontrolled: 0.75 versus controlled: 0.85, $p < 0.001$). Uncontrolled SA was associated with higher odds of worse health states across all five domains, with greatest impairments in the usual activities domain. The EQ-5D-5L scores decreased in proportion to the level of asthma control. ACT scores strongly correlated with both EQ-5D-5L ($r = 0.608$, $p < 0.001$) and SAQ ($r = 0.680$, $p < 0.001$). Amongst ACT items, "daily functioning" was the strongest determinant of HRQoL.

Conclusion Uncontrolled asthma, particularly its impact on daily functioning, was associated with HRQoL impairment in patients with SA. Enhancing asthma control may significantly reduce the disease burden and improve HRQoL in SA.

Introduction

Asthma is a prevalent respiratory disease affecting an estimated 260 million people worldwide [1]. Severe asthma (SA) is characterised by persistent symptoms, frequent exacerbations and a high reliance on oral corticosteroids [2, 3]. SA affects ~5–10% of patients with asthma but contributes disproportionately to



healthcare utilisation and costs. Direct and indirect costs are markedly higher in patients on Global Initiative for Asthma (GINA) step 4/5 therapy, and exacerbation-related costs significantly increase the economic burden among those with moderate-to-severe asthma [4–6]. SA is also associated with an increased risk of various comorbidities, which further aggravates future health outcomes [7].

Health-related quality of life (HRQoL) encompasses physical, psychological and social dimensions which are crucial to understand the overall impact of SA [8]. These assessments provide critical insights into the effectiveness of current management strategies and support health-economic evaluations through metrics such as quality-adjusted life-years (QALYs) [9]. Demographic, socioeconomic and treatment-related factors have been identified as the predictors of HRQoL in patients with asthma [10, 11]. Of these, poor asthma control is associated with increased symptom burden, activity limitations and emotional distress [12, 13]. However, the role of asthma control in shaping HRQoL outcomes, particularly in SA, remains insufficiently studied.

We hypothesised that poorer asthma control would be associated with lower HRQoL in patients with SA. To test this, we used the EuroQoL 5-dimension questionnaire (EQ-5D), a generic HRQoL instrument that facilitates cross-disease comparisons [14, 15]. Although asthma-specific tools such as the Severe Asthma Questionnaire (SAQ) provide disease-focused insights [16, 17], their complexity often limits its use in routine care. Moreover, the validity of using generic tools to capture asthma severity and control status remains less understood. Therefore, this study aims to evaluate the disease burden of HRQoL in SA using EQ-5D and to explore the determinants of HRQoL impairments, focusing on asthma severity and control status.

Methods

Study design and study participants

Cross-sectional data were collected from the Korean Severe Asthma Registry (KoSAR) between April 2022 and November 2023. KoSAR is an ongoing, nationwide prospective cohort study established in 2011 to assess the clinical characteristics and long-term outcomes of Korean patients with SA. This database has been described in detail in previous publications [18, 19]. Briefly, patients aged ≥ 18 years diagnosed with SA who satisfied any of the following criteria were included: 1) patients who did not consistently reach a well-controlled status despite the use of medium- to high-dose inhaled corticosteroids (ICSs); or 2) those who had well-controlled asthma after medium- to high-dose ICS use but who either had a history of more than one unscheduled urgent visit, ≥ 3 administrations of systemic corticosteroids in the previous year, or a near-fatal asthma attack or worsening symptoms when oral corticosteroids or ICS were reduced to 25% at any point. Patients with major medical conditions including severe bronchiectasis, tuberculosis-destroyed lungs, interstitial lung disease or severe congestive heart failure were excluded.

Data for patients with non-severe asthma (NSA), those who are on as-needed or low-dose ICS/long-acting β_2 -agonists (LABA), were also collected as a control group. This study was approved by the Institutional Review Board (IRB) of all participating centres, and written informed consent was obtained from all study participants (IRB number: HYUH 2022-03-038).

Data collection

Patient information – age, sex, smoking history, body mass index (BMI), comorbidities defined based on medical records and emergency room (ER) visit due to exacerbation(s) during the previous year – was collected *via* structured interviews and self-report questionnaires using an electronic case report form.

Laboratory test results were collected for blood and sputum eosinophil counts and fractional exhaled nitric oxide (F_{ENO}). Pulmonary function tests were performed using standard equipment in accordance with current guidelines [20]. The predicted percentages were calculated using an equation validated for the Korean population [21]. Bronchodilator response positivity was defined as elevated forced expiratory volume in 1 s (FEV_1) $>12\%$ and >200 mL from baseline FEV_1 after the inhalation of 200 μ g of salbutamol.

Drug prescription records related to asthma were collected for ICS, LABA and oral corticosteroids (OCS) over the prior 6 months. Adherence to ICS was defined as patient-reported daily use within the past month and was asked at each visit, and responses were confirmed through face-to-face interviews conducted by trained study personnel. NSA patients may have received ICS on an as-needed basis rather than for daily use.

HRQoL measurements and ACT scores

Generic HRQoL was assessed using the EQ-5D-5L index score [22]. The EQ-5D-5L includes the domains of mobility, self-care, activities, pain/discomfort and anxiety/depression. Each domain is rated by patients using a 5-point scale (no/slight/moderate/severe/extreme problems). The EQ-5D-5L also contains one

visual analog scale (EQ-VAS) for patients to self-assess their overall health status from 0 (worst imaginable health) to 100 (best possible health).

For asthma-specific HRQoL assessments, SAQ scores were measured [16]. The SAQ is a 16-item questionnaire which was administered to patients with SA only and includes three domains: daily activity, emotion and extrapulmonary symptoms/medication side-effects. The linguistic validation of the Korean SAQ has been published previously [23].

The Asthma Control Test (ACT) is a validated, five-item questionnaire that provides a numerical score to assess asthma control over the past 4 weeks, focusing on frequency of shortness of breath, night-time/early awakenings, activity limitations, rescue medication use and overall self-assessment. Each question is answered on a 5-point scale, with a total score ranging from 5 to 25; higher scores indicate improved asthma control [24]. To examine the association between asthma control and HRQoL, patients were classified based on total ACT score: 5–14, 15–17, 18–19, 20–21 and 22–25 [25]. An ACT score of 19 or less was considered as uncontrolled asthma.

Statistical analysis

Categorical variables were summarised as frequencies and percentages, and continuous variables as medians with interquartile ranges (IQR). The Shapiro–Wilk test was used to assess the normality of continuous variables. For non-normally distributed variables, group comparisons were performed using the Mann–Whitney U-test. Categorical variables were compared using Fisher’s exact test, regardless of expected cell sizes, to ensure robust p-value estimation in cases of small cell counts.

Model assumptions were evaluated using the Shapiro–Wilk test and quantile–quantile (Q–Q) plots of residuals. Although the residuals showed deviation from normality based on the Shapiro–Wilk test ($p < 0.001$), visual inspection indicated approximate symmetry (supplementary figure S1). Robust standard errors were applied to account for potential heteroscedasticity, and results remained consistent.

To identify clinical determinants of EQ-5D index scores in patients with SA, a structured four-step modeling strategy was employed. First, univariable linear regression analyses were conducted. Second, a base model adjusting for potential confounders (age, sex and BMI) was constructed. Third, each candidate determinant was evaluated in separate models adjusted for the base confounders. Finally, a full multivariable model including all covariates was built. Variables included in the full model were age, sex, BMI, chronic rhinosinusitis, recent rescue medication use, ER visits, blood eosinophil count, pre-bronchodilator FEV₁ (L) and asthma control status. For Model 3, the Benjamini–Hochberg procedure was used to adjust for multiple comparisons *via* false discovery rate (FDR) correction.

To further explore the association between asthma control and each individual EQ-5D-5L domain, ordinal logistic regression was performed, adjusting for age, sex and BMI. Correlations among the five EQ-5D-5L domains were assessed using Spearman’s rank correlation, as these ordinal variables were not normally distributed.

For item-level analysis of the ACT, only patients with SA were included to maintain consistency with the main regression analyses. The distribution of responses for each ACT item was examined and found to be well balanced across all five response categories (supplementary table S1).

All tests were two-sided, and a value of $p < 0.05$ was considered statistically significant. All statistical analyses were performed using Stata (version 16.0; Stata Corporation).

Results

Baseline demographic and clinical characteristics

The demographic and clinical characteristics of study patients are summarised in table 1. Among the 592 patients with SA, 21.8% were classified as having uncontrolled asthma. In contrast, only five patients (4.6%) in the NSA group ($n = 109$) met the criteria for uncontrolled asthma. Due to the very small sample size of this subgroup, further comparative analyses were not performed.

Patients with SA were older (SA: 58 (IQR 49–66) *versus* NSA: 52 (IQR 39–64) years, $p = 0.002$), had a higher prevalence of comorbidities and received higher daily ICS doses (SA: 400 (IQR 400–640) *versus* NSA: 320 (IQR 200–400) μg , $p < 0.001$), compared to the patients with NSA. ICS use in the past month was more frequent in the SA group (81% *versus* 44%, $p < 0.001$). Rescue medication use (51% *versus* 7%, $p < 0.001$) and ER visits within the past year (10% *versus* 3%, $p = 0.007$) were also more common in the SA

TABLE 1 Characteristics of the study participants (n=701)

	NSA (n=109)	SA (n=592)	p-value
Age years	52 (39–64)	58 (49–66)	0.002
Female sex	62 (57)	352 (59)	0.627
Body mass index kg·m ⁻²	24.1 (21.9–26.8)	24.4 (22.3–27.4)	0.158
Never smoked	48 (44)	361 (61)	<0.001
Comorbidities (n=694)			
Allergic rhinitis	68 (62)	380 (64)	0.745
Chronic rhinosinusitis	23 (21)	197 (33)	0.013
Hypertension	18 (17)	181 (31)	0.003
GERD	14 (13)	148 (25)	0.004
Diabetes mellitus	6 (6)	89 (15)	0.006
Depression/anxiety	4 (4)	47 (8)	0.158
Atopic dermatitis	6 (6)	43 (7)	0.682
Malignancy	5 (5)	41 (7)	0.526
MI/angina	4 (4)	35 (6)	0.495
Daily ICS use within 1 month	48 (44)	478 (81)	<0.001
Daily ICS dose within 1 month µg [#]	320 (200–400)	400 (400–640)	<0.001
Rescue medication use within 1 month	8 (7)	300 (51)	<0.001
Systemic steroid	2/8	181/300	
MART	4/8	71/300	
Ventolin	4/8	135/300	
OCS use within 6 months	5 (7)	321 (55)	<0.001
ER visits within 1 year	3 (3)	62 (10)	0.007
Laboratory test results			
Blood eosinophil count/µL (n=521)	261 (138–395)	240 (60–589)	0.731
F _{ENO} ppb (n=438)	33 (19–63)	47 (26–82)	0.011
Sputum eosinophils % (n=131)	23 (12–42)	25 (3–53)	0.928
Atopic status	6 (6)	77 (13)	0.024
Pulmonary function test (n=687)			
FVC L	3.30 (2.89–4.01)	2.90 (2.34–3.52)	<0.001
FVC % pred	96.2 (92.2–100.3)	78.8 (68.2–88.6)	0.010
FEV ₁ L	2.54 (2.22–2.89)	1.89 (1.45–2.48)	<0.001
FEV ₁ % pred	92.5 (84.8–100.4)	68.2 (54.6–78.7)	0.006
FEV ₁ /FVC %	77.0 (70.8–81.1)	69.0 (59.0–76.2)	<0.001
FEF _{25–75} L·s ⁻¹	2.05 (1.42–2.79)	1.32 (0.76–2.13)	<0.001
Controlled asthma (ACT >19)	104 (95)	463 (78)	<0.001

Categorical variables are presented as n (%) and were compared using Fisher's exact test. Continuous variables are presented as median (IQR) and were compared using the Mann–Whitney U-test due to non-normal distribution confirmed by the Shapiro–Wilk test. NSA: non-severe asthma; SA: severe asthma; GERD: gastro-oesophageal reflux disease; MI: myocardial infarction; ICS: inhaled corticosteroid; MART: maintenance and reliever therapy; OCS: oral corticosteroid; ER: emergency room; F_{ENO}: fractional exhaled nitric oxide; FVC: forced vital capacity; FEV₁: forced expiratory volume in 1 s; FEF_{25–75}: forced expiratory flow between 25% and 75% of vital capacity; ACT: asthma control test. #: budesonide equivalent dose.

group. Patients with SA had higher F_{ENO} levels (SA: 47 (IQR 26–82) *versus* NSA: 33 (IQR 19–63) ppb, p=0.011) but lower pulmonary function parameters (*e.g.*, FEV₁, FVC, forced expiratory flow between 25% and 75% of vital capacity (FEF_{25–75}); all p<0.050). Blood eosinophil counts and sputum eosinophil percentages did not differ between groups.

Impact of asthma severity and control on HRQoL

The EQ-5D index score of total patients was 0.84 (IQR 0.76–1.00) and was significantly lower in the SA group compared to NSA group (SA: 0.83 (IQR 0.76–1.00) *versus* NSA: 0.87 (IQR 0.83–1.00), p<0.001) (figure 1). Patients with uncontrolled SA had a lower EQ-5D index score than that of patients with controlled symptoms (uncontrolled SA: 0.75 (IQR 0.59–0.83) *versus* controlled SA: 0.85 (IQR 0.78–1.00), p<0.001) (figure 1). EQ-VAS was also lower in patients with SA with uncontrolled symptoms (uncontrolled SA: 50 (IQR 30–65) *versus* controlled SA: 70 (IQR 50–80), p<0.001) (supplementary figure S2).

Determinants of EQ-5D index score in severe asthma

A multivariable model was initially conducted on the total population to assess the impact of asthma severity on EQ-5D index scores. SA remained significantly associated with lower EQ-5D scores

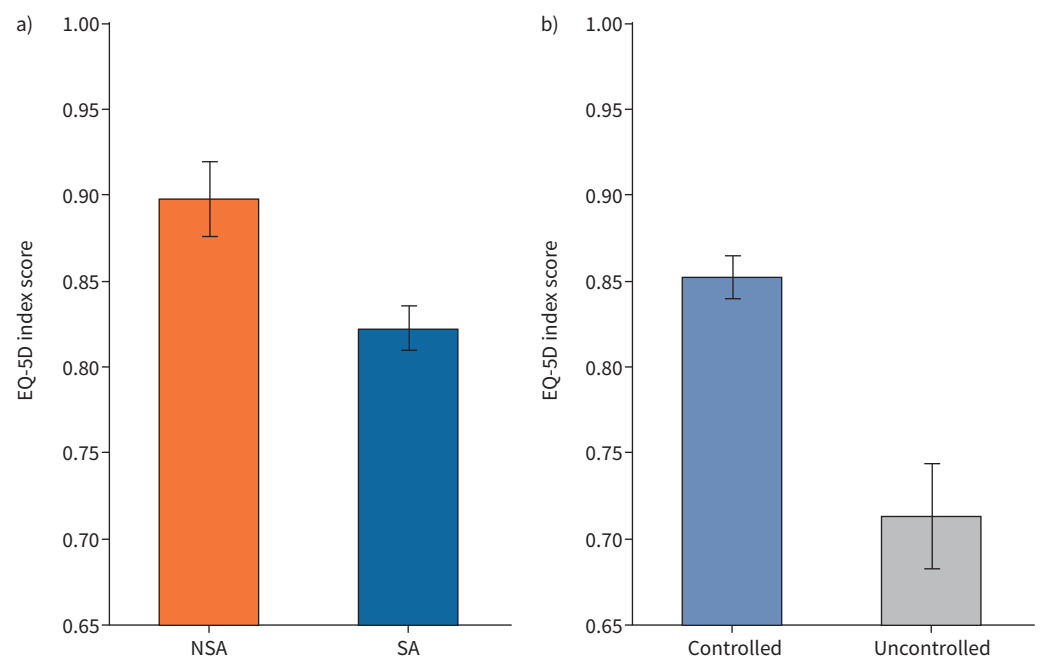


FIGURE 1 EQ-5D index scores across a) asthma severity (NSA versus SA) and b) asthma control status (controlled SA versus uncontrolled SA). Boxplots show the distribution of EQ-5D index scores and whiskers indicate the 95% confidence interval of the EQ-5D index in each group. EQ-5D: EuroQoL 5-dimension; NSA: non-severe asthma; SA: severe asthma.

($\beta = -0.106$; 95% CI: -0.173 to -0.039 ; $p = 0.002$) (supplementary table S2). In the patients with SA, lower EQ-5D index scores were independently associated with higher BMI ($\beta = -0.003$; 95% CI: -0.006 to -0.000 ; $p = 0.050$), recent use of rescue medication within the past month ($\beta = -0.040$; 95% CI: -0.069 to -0.010 ; $p = 0.009$), lower pre-bronchodilator FEV₁ ($\beta = 0.001$; 95% CI: 0.000 to 0.001 ; $p = 0.001$) and uncontrolled asthma symptoms ($\beta = 0.095$; 95% CI: 0.062 to 0.129 ; $p < 0.001$), after adjusting for potential confounders including age, sex, BMI, treatment history and lung function (table 2). Cumulative OCS dose over the past 6 months was not significantly associated with EQ-5D index scores ($\beta = 0.000$; 95% CI: -0.000 to 0.000 ; $p = 0.800$) (table 2).

Table 3 presents the stepwise adjusted models for key determinants of EQ-5D index scores. In the confounder-adjusted base model (Model 2), older age, female sex and higher BMI were associated with

TABLE 2 Univariable and multivariable linear regression analysis of factors associated with EQ-5D index scores in patients with SA (n=592)				
	Univariable coefficient (95% CI)	p-value	Multivariable coefficient (95% CI)	p-value
Age	-0.001 (-0.002 – -0.000)	0.041		
Female sex	-0.040 (-0.066 – -0.015)	0.002		
BMI	-0.003 (-0.006–0.001)	0.056	-0.003 (-0.006 – -0.000)	0.050
Chronic rhinosinusitis (versus none)	0.001 (-0.025–0.028)	0.919		
Use of systemic steroid in past 6 months (versus none)	-0.044 (-0.069 – -0.019)	<0.001		
Cumulative OCS dose over the past 6 months	0.000 (-0.000–0.000)	0.800		
Recent (<1 month) use of rescue medication (versus none)	-0.074 (-0.098 – -0.050)	<0.001	-0.040 (-0.069 – -0.010)	0.009
Recent (<1 year) ER visit due to asthma exacerbation	-0.057 (-0.098 – -0.016)	0.006		
Blood eosinophil count	0.002 (-0.000–0.004)	0.073		
Pre-bronchodilator FEV ₁ % pred	0.002 (0.001–0.002)	<0.001	0.001 (0.000–0.001)	0.006
Symptom control (versus uncontrolled)	0.139 (0.111–0.167)	<0.001	0.095 (0.062–0.129)	<0.001
EQ-5D: EuroQoL 5-dimension; SA: severe asthma; BMI: body mass index; OCS: oral corticosteroid; ER: emergency room; FEV ₁ : forced expiratory volume in 1 s.				

TABLE 3 Adjusted regression models for determinants of EQ-5D index score in patients with SA (n=592)

	Model 1 (univariable)	Model 2 (adjusted for age, sex, BMI)	Model 3 (each determinant + age, sex, BMI)	Model 4 (all variables)	FDR-adjusted p-value
Recent (<1 month) use of rescue medication (<i>versus</i> none)	$\beta = -0.074$; 95% CI: -0.098 to -0.050 $p < 0.001$	-	$\beta = -0.073$; 95% CI: -0.097 to -0.049 $p < 0.001$	$\beta = -0.040$; 95% CI: -0.069 to -0.010 $p = 0.009$	0.009
Pre-bronchodilator FEV ₁ % pred	$\beta = 0.053$; 95% CI: 0.036 to 0.071 $p < 0.001$	-	$\beta = 0.002$; 95% CI: 0.001 to 0.003 $p < 0.001$	$\beta = 0.001$; 95% CI: 0.000 to 0.001 $p = 0.006$	0.009
Symptom control (<i>versus</i> uncontrolled)	$\beta = 0.139$; 95% CI: 0.111 to 0.167 $p < 0.001$	-	$\beta = 0.136$; 95% CI: 0.108 to 0.164 $p < 0.001$	$\beta = 0.095$; 95% CI: 0.062 to 0.129 $p < 0.001$	<0.001

Model 1: univariable linear regression. Model 2: multivariable regression including age, sex and BMI only (confounder adjustment model). Model 3: separate models for each determinant adjusted for age, sex and BMI. Model 4: full model including all determinants and confounders simultaneously. FDR-adjusted p-values were calculated for Model 3 to account for multiple comparisons using the Benjamini–Hochberg procedure. EQ-5D: EuroQoL 5-dimension; SA: severe asthma; BMI: body mass index; FDR: false discovery rate; FEV₁: forced expiratory volume in 1 s.

lower EQ-5D scores. In determinant-specific models (Model 3), recent use of rescue medication, lower pre-bronchodilator FEV₁ and uncontrolled symptoms were significantly associated with poorer HRQoL, even after adjusting for age, sex and BMI. All three variables remained statistically significant after FDR correction. In the full multivariable model (Model 4), these determinants remained independently associated with EQ-5D scores.

Domain-specific impairments by asthma severity and control

Patients with SA exhibited greater impairment in all EQ-5D-5L domains compared to NSA (mobility, $p < 0.001$; self-care, $p = 0.011$; usual activities, $p < 0.001$; pain/discomfort, $p = 0.003$; and anxiety/depression, $p = 0.082$) (figure 2a). Severity was greater for patients with uncontrolled SA reported than for patients with controlled SA in each of the five domains (mobility, $p < 0.001$; self-care, $p < 0.001$; usual activities, $p < 0.001$; pain/discomfort, $p < 0.001$; and anxiety/depression, $p < 0.001$) (figure 2b). Ordinal logistic regression models were used to evaluate the association between asthma control status and the level of reported problems in each EQ-5D-5L domain, with adjustments for age, sex and BMI. Uncontrolled asthma was significantly associated with higher odds of reporting worse health states across all five domains (all $p < 0.001$), especially with greater impairments in usual activities (OR 5.08, 95% CI 3.42–7.55, $p < 0.001$) (supplementary table S3).

Association between ACT score and HRQoL

The mean EQ-5D index scores according to the asthma control level are presented in figure 3. Amongst each composition of ACT questionnaires, “impact of asthma on daily functioning” was identified as the most significant predictor of HRQoL impairment, with coefficients of 0.039 (95% CI 0.027–0.051, $p < 0.001$) (table 4). The items “overall self-assessment of asthma control”, “frequency of shortness of breath” and “use of rescue medications” also showed statistical significance; however, “nocturnal symptoms” showed no statistical significance. A visual representation of the association between each ACT item and EQ-5D is shown in supplementary figure S3.

Comparison of ACT, SAQ and EQ-5D index score for HRQoL assessment

ACT, SAQ and EQ-5D index scores were compared to evaluate the association between asthma control, disease-specific HRQoL and generic HRQoL. Overall, the EQ-5D index score was strongly correlated with the ACT score ($r = 0.608$, $p < 0.001$) (supplementary figure S4). There was a strong correlation between the EQ-5D index score and ACT score in SA ($r = 0.618$, $p < 0.001$), while only a weak correlation was observed in NSA ($r = 0.211$, $p = 0.028$). The EQ-5D index score also showed a strong correlation with the SAQ scores ($r = 0.709$, $p < 0.001$) (supplementary figure S4) and for both severely uncontrolled ($r = 0.363$, $p < 0.001$) and severely controlled asthma ($r = 0.669$, $p < 0.001$). The ACT score and the SAQ score showed a strong correlation ($r = 0.680$, $p < 0.001$) (supplementary figure S4).

Discussion

This nationwide multicentre study found that patients with SA had significantly lower HRQoL compared to those with NSA. Among patients with SA, recent rescue medication use, reduced lung function and

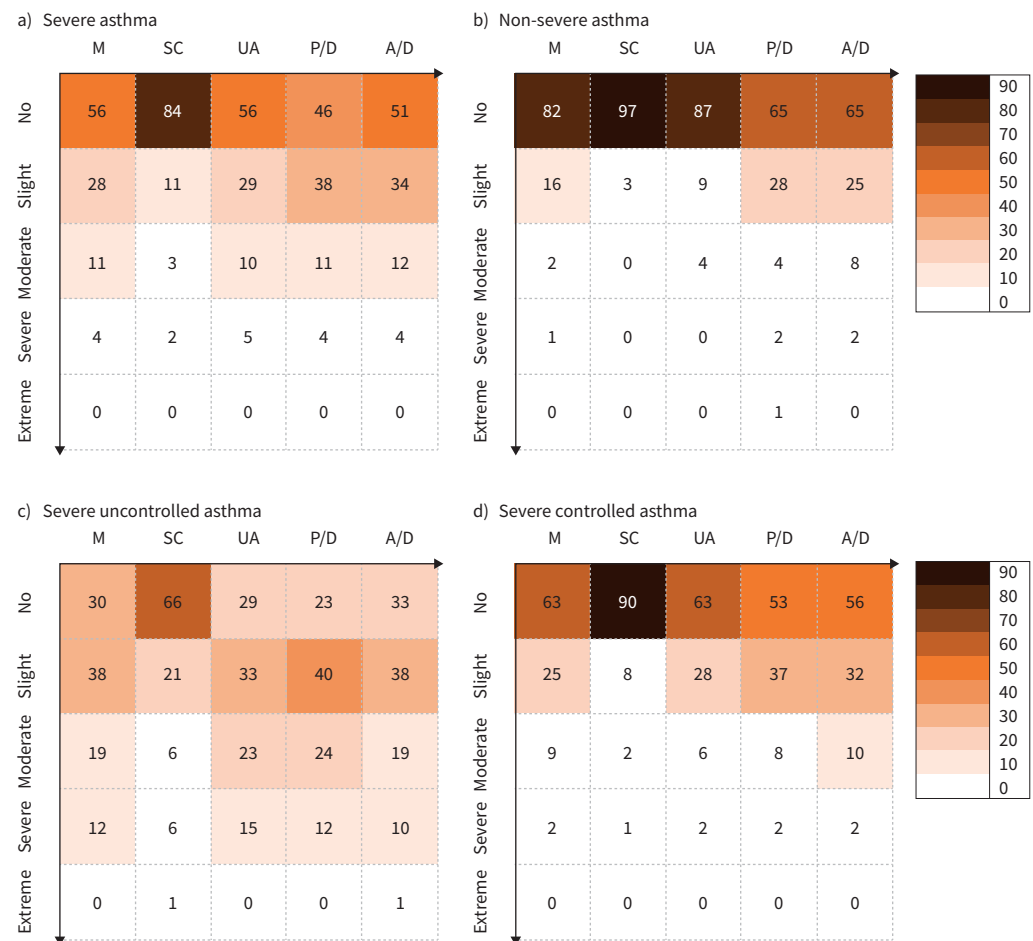


FIGURE 2 Proportional distribution of problems reported for each of the five domains of the EQ-5D questionnaire in **a)** SA and **b)** NSA and **c)** uncontrolled and **d)** controlled SA within the SA group. A/D: anxiety and depression; EQ-5D: EuroQoL 5-dimension; M: mobility; NSA: non-severe asthma; P/D: pain and discomfort; SA: severe asthma; SC: self-care; UA: usual activities.

uncontrolled symptoms were associated with impaired HRQoL. After adjusting for age, sex and BMI, uncontrolled asthma was also significantly associated with greater perceived problems across all five domains of the EQ-5D-5L, especially in usual activities domain. The asthma control status correlated with both disease-specific and generic HRQoL measurements, and “effect of asthma on daily functioning” in the ACT questionnaire was a critical factor contributing to HRQoL impairment.

Generic instruments such as EQ-5D were designed to assess the overall health status over specific diseases. EQ-5D provide a practical approach for routine HRQoL monitoring and can support health-economic evaluations to optimise treatment strategies [9]. However, utilising EQ-5D for evaluating patients with asthma is often criticised in that it may lack sensitivity in capturing disease-specific aspects. To address this limitation, we used the five-level version of the EQ-5D-5L, which has improved sensitivity and reduced ceiling effects compared with those of the earlier three-level version (EQ-5D-3L). Although the difference in EQ-5D index scores between the SA and NSA groups was relatively smaller than anticipated, a more pronounced disparity was observed within the SA group when stratified by asthma control status. The magnitude of this difference exceeded the minimal clinically important difference threshold reported in previous studies [26–28]. These findings suggest that, while SA is associated with impaired quality of life, the asthma control may play an even more critical role in determining HRQoL among patients with SA.

The findings from this study differ from previous studies in several key aspects. Both asthma-specific and generic instruments were used to establish the correlation asthma control status and HRQoL. The current study contributes to a more comprehensive understanding of the disease burden of SA by emphasising the

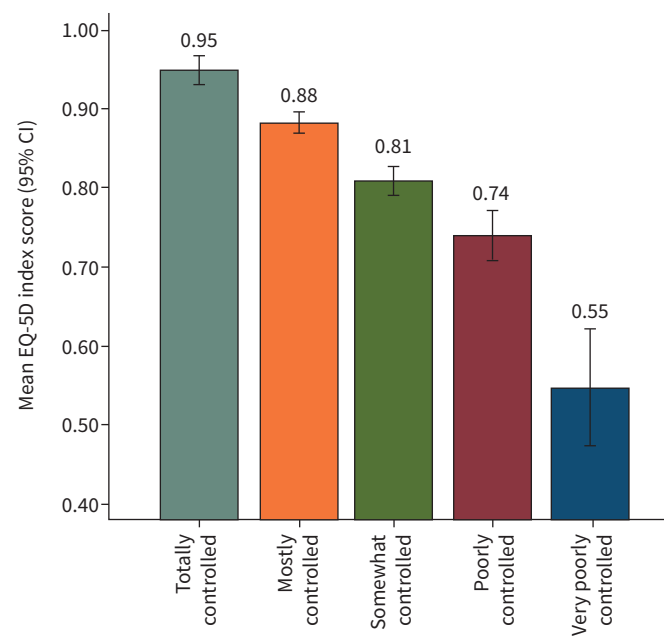


FIGURE 3 Mean EQ-5D index score according to ACT categories in patients with severe asthma. ACT scores were stratified into five categories based on methods used in previous studies: very poorly controlled (5–9), poorly controlled (10–14), partially controlled (15–19), well controlled (20–22) and fully controlled (23–25). ACT: Asthma Control Test; EQ-5D: EuroQoL 5-dimension.

impact of asthma control on generic HRQoL. Besides from utilising EQ-5D to assess its broader application, the specific item of ACT “impact of asthma on daily functioning” was identified as the most significant predictor of HRQoL impairment in SA. The ability to perform daily activities is central to a patient’s experience of asthma [29, 30]. It also suggests that interventions aiming to improve daily functioning by reducing symptom burden could have a meaningful effect on improving patients’ overall HRQoL. Other ACT items, such as “overall self-assessment of asthma control”, “frequency of shortness of breath” and “use of rescue medications”, also had significant associations with HRQoL, and were significant contributors to HRQoL impairment, which further highlights the importance of addressing these aspects in asthma management. Additionally, the strong correlation of ACT scores and the EQ-5D index score suggests that the ACT could serve as an indirect but more practical clinical tool for assessing HRQoL of patients with SA.

In this study, several other factors such as the recent use of rescue medications and lower pre-bronchodilator FEV₁ values were also associated with lower EQ-5D-5L index in patients with SA. Whilst HYLAND *et al.* [16] observed a weak correlation between the EQ-5D-5L and lung function, our multivariate analysis showed that a low FEV₁ was significantly associated with lower EQ-5D-5L scores. Although the EQ-5D-5L may not be correlated directly with FEV₁, a lower FEV₁ may still contribute to lower EQ-5D-5L index scores [16]. Given that patients with low FEV₁ are likely undergoing higher treatment steps, the early introduction of alternative treatments, such as biologics or macrolides, should be considered to optimise lung function.

TABLE 4 Multivariable linear regression analysis of ACT items on EQ-5D index score		
	Coefficient (95% CI)	p-value
Impact of asthma on daily functioning	0.039 (0.027–0.051)	<0.001
Frequency of shortness of breath	0.013 (0.003–0.023)	0.011
Nocturnal symptoms	0.007 (–0.002–0.016)	0.113
Use of rescue medications	0.013 (0.005–0.021)	0.001
Overall self-assessment of asthma control	0.028 (0.024–0.041)	<0.001
ACT: asthma control test; EQ-5D: EuroQoL 5-dimension.		

The presence of comorbidities or type 2 (T2) biomarkers did not play a significant role in determining HRQoL in this study. T2 biomarkers may influence underlying disease activity without directly translating into daily life quality, which the HRQoL scales tend to capture. The overall symptom burden and limitations may be dominated by asthma-related impairments rather than by coexisting conditions in SA. The presence of comorbidities may contribute to longitudinal changes in QoL in patients with SA [31]. However, previous studies have shown that asthma control remains a significant predictor of long-term HRQoL, even after adjusting for baseline asthma severity and the presence of comorbidities [32].

It is also worth noting that the cumulative OCS dose was not associated with EQ-5D index scores. While this finding may appear counterintuitive given the well-documented adverse effects of long-term corticosteroid use [33], several explanations are possible. First, patients with SA may initially experience symptomatic relief and improved asthma control after OCS treatment, potentially leading to a transient improvement in perceived QoL despite the long-term risks [34]. Second, the EQ-5D-5L may not sufficiently capture treatment burdens specific to chronic OCS use, such as fatigue, mood changes or alterations in physical appearance, that are highly relevant to patients. The impact of OCS on quality of life likely depends on both treatment duration and cumulative dose over a longer period. Therefore, longitudinal studies are warranted to investigate potential dose–response relationships between OCS exposure and HRQoL, preferably using asthma-specific instruments that can better capture treatment burden.

Patients with SA showed greater impairment in all five domains of the EQ-5D-5L, compared to those with NSA, and patients with uncontrolled SA showed greater impairment compared to those with controlled SA. In several previous studies, some domains of EQ-5D are pointed out to be partially or completely irrelevant and do not account for asthma-specific features. WHALLEY *et al.* [35] noted that only the “usual activity” domain in EQ-5D was relevant to the experiences of patients with asthma. However, their study focused on patients with mild-to-moderate asthma, whereas our study involved patients with SA. SZENDE *et al.* [36] suggested that disease severity should be considered when selecting instruments to measure health status in patients with asthma, with the EQ-5D being more appropriate for patients with severe disease or poor disease control. In a study using SF-8, another generic HRQoL instrument, patients with SA have worse physical and mental HRQoL than those of patients without asthma, and the anxiety and depression scores were higher than those of patients without asthma [37].

Despite the valuable insights provided by this study, several limitations should be noted. First, the cross-sectional design of this study limits the ability to establish causal relationships between asthma control and HRQoL. Unlike longitudinal studies, which can track changes over time, our design cannot assess the direct impact of improving asthma control on HRQoL outcomes. Future longitudinal studies are warranted to clarify whether targeted interventions such as early intervention with biologics in patients showing low HRQoL could lead to sustained improvements in HRQoL. Additionally, although the EQ-5D-5L provides a broad measure of health status, it may not fully capture the specific challenges faced by patients with SA, such as the long-term side-effects of systemic steroid use. Lastly, although our analysis included a large patient population, it was based on a Korean cohort, which might have limited the generalisability of our findings to other populations.

In conclusion, better asthma control may be associated with improved HRQoL and should be considered an important target in the management of patients with SA. ACT may serve as a simple and practical tool to monitor how asthma affects daily life, potentially reducing the need for more complex HRQoL instruments in clinical practice.

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