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Chronic rhinosinusitis in asthma is a negative predictor of quality of life: results from the Swedish GA^{2}LEN survey

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Abstract

Background: Asthma and chronic rhinosinusitis (CRS) both impair quality of life, but the quality-of-life impact of comorbid asthma and CRS is poorly known. The aim of this study was to evaluate the impact of CRS and other relevant factors on quality of life in asthmatic subjects.

Methods: This Swedish cohort (age 17–76 years) consists of 605 well-characterized asthmatics with and without CRS, 110 individuals with CRS only, and 226 controls and is part of the Global Allergy and Asthma European Network (GA^{2}LEN) survey. The Mini Asthma Quality of Life Questionnaire (mAQLQ), the Euro Quality of Life (EQ-5D) health questionnaire, spirometry, skin prick test (SPT), exhaled nitric oxide (FeNO), smell test, and peak nasal inspiratory flow were used.

Results: Subjects having both asthma and CRS have lower mAQLQ scores in all domains ($P < 0.001$) and a lower EQ-5D index value and EQ-5D VAS value ($P < 0.001$) compared to those with asthma only. Asthmatics with CRS have significantly lower FEV1%pred and FVC%pred (88.4 [85.1–91.7] and 99.9 [96.7–103.0], respectively) compared with asthma only (91.9 [90.3–93.4] and 104.0 [102.5–105.5], respectively $P < 0.05$). Multiple regression analysis shows that low asthma quality of life is associated with having CRS ($P < 0.0001$), lower lung function ($P = 0.008$), current smoking ($P = 0.01$), BMI > 30 kg/m^2 ($P = 0.04$), high age ($P = 0.03$), and a negative SPT ($P = 0.04$).

Conclusions: Comorbid CRS was a significant and independent negative predictor of quality of life in asthmatics. Other negative factors were lower lung function, current smoking, obesity, advanced age, and having nonatopic asthma.

Asthma is a chronic disease that substantially affects daily activities and quality of life (1). It is also well established that quality of life is impaired in subjects with chronic rhinosinusitis (CRS) (2). It is known that asthmatics have a higher incidence of CRS (3) and that asthma is associated with sinonasal inflammation and nasal symptoms that impair quality of life (4).

Previous results from the Global Allergy and Asthma European Network (GA^{2}LEN) (5) show that CRS is a common disease in Europe with an overall prevalence of 11% (6). Symptoms such as chronic nasal congestion, facial pressure and pain, headache, hyposmia, and anosmia can significantly reduce quality of life (7). Quality of life is a very important outcome in the evaluation of CRS severity (8).

There are studies on quality of life in asthma and in CRS, but despite the high covariance between the two conditions, studies of quality of life in subjects who suffer from the combination of the two conditions are few. Studies have shown a

common association between CRS and asthma (5, 9), which may be ascribed to similar systemic inflammatory processes (10). It has been shown that asthma has a negative effect on the quality of life of patients with nasal polyposis, a subgroup of CRS (11). Additionally, it has been demonstrated that quality of life in asthmatics with unspecified sinusitis is lower than without (12). The aim of this study was to assess the impact of CRS and other relevant factors on quality of life in well-characterized asthmatic subjects.

Materials and methods

Study population

The GA^{2}LEN postal survey was conducted in 19 European centers, targeting symptoms of asthma, rhinitis, and CRS, and was distributed to a random population-based sample (5, 6). Among those who responded, randomly selected subgroups consisting of individuals with asthma, CRS, both asthma and CRS, or neither asthma nor CRS were invited for a clinical follow-up. In Sweden, four centers participated, Gothenburg, Stockholm, Uppsala, and Umeå, and 27 866 persons responded to the postal survey in 2008 (13, 14), of whom 1329 persons participated in the follow-up during 2009 and 2010.

Group allocation and definitions

Patient group allocations were based on the answers given in the follow-up interview.

Asthma was defined as self-reported diagnosis of asthma and either asthma symptoms (wheezing, attack of shortness of breath, and/or awakening at night with breathlessness in the previous 12 months) or asthma treatment (taking any asthma medication during the last 12 months; $n = 605$).

CRS was defined according to the European Position Paper on Rhinosinusitis and Nasal Polyps (EP_3OS) criteria (15), that is, the presence of at least two of the following symptoms for at least 12 weeks in the past year: (i) nasal blockage, (ii) nasal discharge, (iii) facial pain or pressure, and (iv) reduction in the sense of smell with at least one of the symptoms being nasal blockage or nasal discharge ($n = 240$).

Subjects who were not classified as having asthma or CRS either in the first postal survey or in the follow-up interview and who did not report attacks of shortness of breath, wheezing, use of asthma medicines, or CRS symptoms, constituted the control group ($n = 226$).

Subjects who did not completely fulfill the criteria for any of the groups above ($n = 388$) were not included in the present analysis.

Subjects were invited for a clinical visit, including an oral interview (symptoms of asthma and atopic disease, smoking, medication use, and medical history).

Skin prick test

Skin prick test (SPT) was performed on the inside of the forearm using a standard set of allergens standardized for the GA^{2}LEN network including timothy grass, mixed grass, *Dermatophagoides pteronyssinus*, cat, birch, blattella, olive, *Alternaria*, dog, *Artemisia*, Parietaria, *Dermatophagoides farinae*, histamine (positive control), and diluent (histamine control). A positive SPT was defined as a wheal at least 3 mm at the widest diameter. Atopy was defined as the presence of at least one positive SPT finding.

Fraction of exhaled NO (FeNO)

FeNO was assessed using NIOX MINO (NIOX MINO®; Aerocrine, Stockholm, Sweden) according to the American Thoracic Society (ATS) and European Respiratory Society (ERS) recommendations (16).

Smell test

Sniffin' Sticks test kit (Burghart Messtechnik, Wedel, Germany) includes 12 pens. The pen was placed at a distance of 2 cm in front of both nostrils, and the participant was asked to sniff for 3–4 s. Using four alternative cards, odor identification was assessed for 12 common odors. The subject's scores represent the sum of correct identifications.

Peak nasal inspiratory flow (PNIF)

Peak nasal inspiratory flow was carried out using the PNIF meter (Clement Clarke International, Essex, UK). Three maximal inspirations were obtained, and the highest value was recorded. Data are expressed in l/min.

Spirometry

Lung function measurement was performed using the EasyOne™ Spirometer (ndd Medizintechnik AG, Zurich, Switzerland) according to the ATS spirometry standards (17). Forced vital capacity (FVC) and forced expiratory volume in one-second (FEV_1) were registered before and at least 15 min after bronchodilatation (inhalation of 200 μg salbutamol). The European Community for Steel and Coal equations were used as reference values (18).

The Mini Asthma Quality of Life Questionnaire (mAQLQ)

All subjects fulfilling the criteria for asthma in the postal survey completed the Juniper Mini Asthma Quality of Life Questionnaire (19), assessing the impact of asthma on quality of life. The questions in the mAQLQ are divided into four domains: symptoms, activity limitations, emotional functions, and effects of environmental stimuli. Each domain is scored from 1 to 7, where 1 indicates maximal impairment and 7 no impairment. The overall score is the mean value based on all questions.

Euro Quality of Life (EQ-5D) health questionnaire

All subjects completed the EQ-5D health questionnaire (20), which comprises five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression). The descriptive system is then converted into a single summary

index, and we used the United Kingdom time trade-off (TTO) value set (21). An index of 1.0 corresponds to full health. The visual analog score (VAS) component uses a scale in which 100 is defined as 'best' and 0 as 'worst' imaginable health.

Statistical analyses

All analyses were performed using STATA 12 (STATA Corp, College Station, TX, USA). The results are given as mean or geometric mean values and 95% confidence intervals (CI). Smell test scores, FeNO, and PNIF were log-transformed. The differences between groups were tested using either a chi-square test or an analysis of variance (ANOVA) with the Bonferroni test. Student's two-sample t-test was used to analyze the difference in lung function between the two groups: asthma *vs* asthma and CRS. Multiple linear regressions were used in the multivariate analyses. A *P*-value <0.05 was considered significant.

Ethics

The study was approved by the Regional Ethical Review Board in Stockholm, Sweden (Dnr 2008/1100-31/4), and the collected personal data were treated according to the Swedish personal data act.

Results

Subject characteristics

In total, 941 individuals (123 from Gothenburg, 263 from Stockholm, 268 from Umeå, 287 from Uppsala) 17–76 years of age were included in the study population (Table 1). The body mass index (BMI) was higher in subjects with asthma, and also in subjects with asthma and CRS, than in controls ($P < 0.001$). FeNO levels were higher in the asthma group than in controls ($P < 0.001$).

Subjects with CRS (with or without asthma) had significantly lower scores in the smell test than controls and those with asthma only. Peak nasal inspiratory flow values were significantly lower in the CRS group compared with controls or those with asthma only ($P < 0.01$), and a multiple regression analysis showed that PNIF values were associated with age ($P < 0.001$), gender ($P < 0.0001$), and having CRS ($P = 0.01$).

Furthermore, lung function was impaired in subjects with asthma and asthma in combination with CRS, compared with controls (Fig. 1). Subjects with asthma and CRS had lower $FEV_{1\%}$pred and FVC%pred than subjects with asthma only ($P < 0.05$).

Comparing the number of five asthma symptoms in the previous 12 months (wheezing, waking with chest tightness, attack of shortness of breath, attack of shortness of breath after strenuous activity, awakening at night with breathlessness),

Table 1 Characteristics of a total of 941 individuals in the range of 17–76 years of age. Allergic rhinitis is defined as a positive answer to 'Do you have any nasal allergies, including hay fever?'

	Control	CRS	Asthma	Asthma and CRS	Comparisons (*P*)
Subjects *n*	226	110	475	130	
Females (%)	51	46	60*§§	57	0.02
Age (years) Mean (95% CI)	47.5 (45.5–49.5)	45.4 (42.5–48.3)	44.7 (43.3–46.0)	44.6 (42.1–47.2)	0.10
BMI (kg/m^2) Mean (95% CI)	25.0 (24.5–25.5)	26.4 (25.4–27.4)	26.6*** (26.1–27.0)	27.1*** (26.3–28.0)	0.0001
Waist (cm) Mean (95% CI)	89.8 (88.0–91.6)	93.3 (90.9–95.7)	92.2 (90.8–93.5)	94.5* (91.9–97.1)	0.02
Never smoked (%)	57	53	54	49	0.59
Ex-smokers (%)	34	31	36	37	
Current smokers (%)	10	16	9	14	0.14
Skin prick test positivity%	31	32	71***§§§	64***§§§	<0.0001
Allergic rhinitis (%)	23	41***	69***§§§	72***§§§	<0.0001
Inhaled asthma medicines (%)	0	11***	75***§§§	82***§§§	<0.0001
Inhaled steroids last 12 months (%)	0	5***	49***§§§	63***§§§##	<0.0001
*Fe*NO (ppb) geometric mean (95% CI)	15.6 (14.3–16.9)	17.0 (15.4–18.7)	19.3*** (18.2–20.5)	18.8 (16.6–21.3)	0.0004
Smell test score geometric mean (95% CI)	9.6 (9.4–9.9)	8.8** (8.3–9.3)	9.8§§§ (9.6–9.9)	9.0*## (8.5–9.5)	<0.0001
PNIF (L/min) geometric mean (95% CI)	117 (111–122)	100** (91–110)	115§§ (111–119)	111 (103–118)	0.007

BMI, body mass index; CRS, chronic rhinosinusitis; PNIF, peak nasal inspiratory flow.
*$P < 0.05$,**$P < 0.01$,***$P < 0.001$ compared with control; §§$P < 0.01$, §§§$P < 0.001$ compared with CRS; ##$P < 0.01$ compared with asthma.

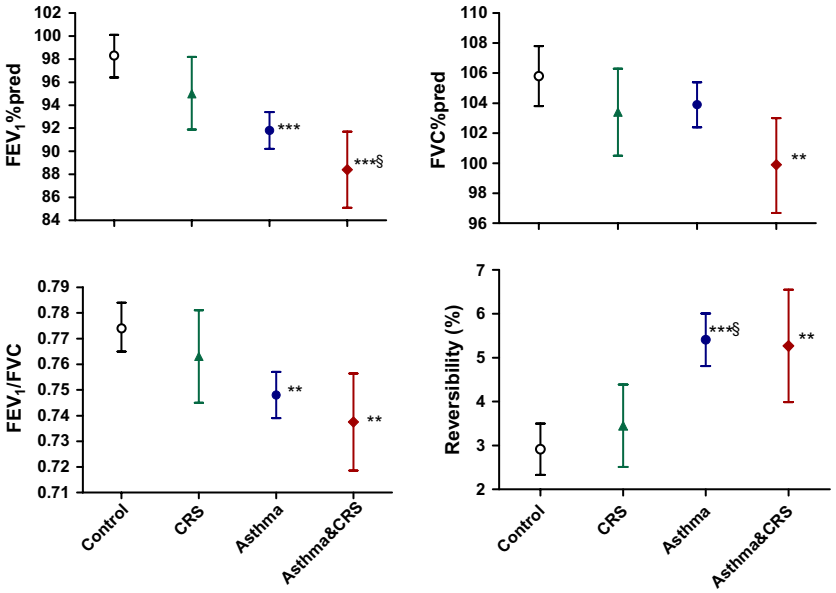

Figure 1 Lung function data in the control group ($n = 215$), chronic rhinosinusitis (CRS) group ($n = 100$), asthma group ($n = 434$) and asthma and CRS group ($n = 120$) based on pre-bronchodilator values. Reversibility represents (postFEV1-pre FEV1)/preFEV1 expressed as % change. Mean value and 95% CI. ANOVA FEV1% pred $P < 0.0001$ $F = 12.5$; ANOVA FVC%pred $P = 0.007$ $F = 4.1$; ANOVA FEV1/FVC $P = 0.0004$ $F = 6.1$; ANOVA Reversibility $P < 0.0001$ $F = 9.6$. Bonferroni tabulate $^{**}P < 0.01$, $^{***}P < 0.001$ compared to control; §$P < 0.05$ compared to CRS. T-test between asthma and asthma and CRS results in $P < 0.05$ for FEV1%pred and FVC% pred.

we find that 37% of subjects with both asthma and CRS have 3–5 asthma symptoms compared with 19% of those with asthma only ($P < 0.0001$). Subjects with both asthma and CRS were also more likely to have had an asthma attack (39 *vs* 29%, $P = 0.03$ and nocturnal asthma awakening 36 *vs* 22%, $P = 0.001$) within the last 3 months and an emergency room visit because of breathing problems within the last 12 months (16 *vs* 9%, $P = 0.03$) than subjects who only had asthma.

mAQLQ

The mAQLQ overall score and the scores of each of the four domains were significantly lower in subjects having both asthma and CRS compared to those with asthma only ($P < 0.01$; Fig. 2). Impaired quality of life assessed by the overall mAQLQ in asthmatics was associated with CRS, impaired lung function, current smoking, BMI > 30 kg/m^2, high age, and a negative SPT (Table 2). After adjusting for the asthma symptoms above (3–5 symptoms compared with 0–2), the association with CRS remained (mAQLQ overall coef = −0.36 (−0.57–[−0.15]); $P = 0.001$). The association between the mAQLQ overall score and having both asthma and CRS remained highly significant ($P < 0.001$) also after adjusting for asthma attack and nocturnal asthma awakening within the last 3 months and an emergency room visit because of breathing problems within the last 12 months.

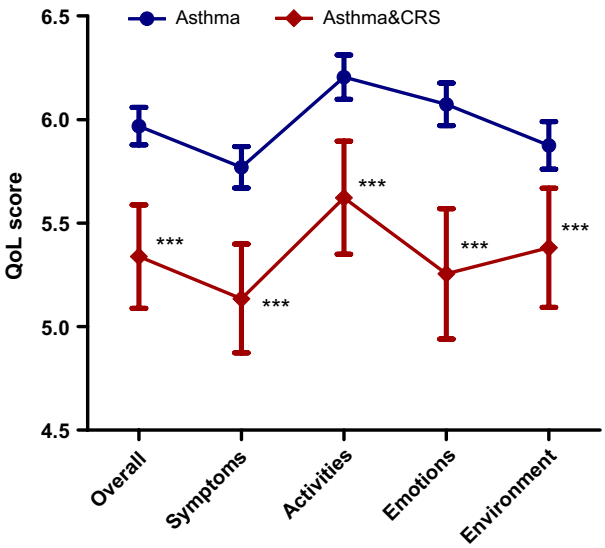

Figure 2 Mini Asthma Quality of Life Questionnaire for the four domains and the overall score in the asthma group ($n = 401$) and the asthma with chronic rhinosinusitis group ($n = 98$). Mean value and 95% confidence interval. $^{***}P < 0.001$ compared to asthma.

EQ-5D

The mean EQ-5D index value based on all five dimensions and the mean EQ VAS score were higher in the control group than in the other groups ($P < 0.01$; Table 3). The

Table 2 Association between quality of life assessed as the overall score from the mAQLQ and lung function, having CRS, and other subject characteristics in asthmatics (n = 432) after adjusting for all the variables in the table, as well as centre, and inhaled steroids use during the last 12 months. Gender represents comparison with males. A negative value indicates lower quality of life

	Coef overall mAQLQ score (95% CI)	*P*	Coef symptoms mAQLQ score (95% CI)	*P*	Coef activities mAQLQ score (95% CI)	*P*	Coef emotions mAQLQ score (95% CI)	*P*	Coef environment mAQLQ score (95% CI)	*P*
FEV1%pred/10	0.08 (0.02–0.13)	0.008	0.10 (0.04–0.16)	0.002	0.10 (0.04–0.17)	0.002	0.05 (−0.02 to 0.11)	0.19	0.03 (−0.04 to 0.10)	0.41
Asthma										
Asthma and CRS	−0.49 (−0.71–[−0.27])	0.000	−0.49 (−0.74–[−0.25])	0.000	−0.46 (−0.72–[−0.20])	0.001	−0.65 (−0.92–[−0.37])	0.000	−0.37 (−0.66–[−0.08])	0.013
Gender	−0.08 (−0.27 to 0.11)	0.40	−0.05 (−0.26 to 0.15)	0.61	−0.06 (−0.28 to 0.15)	0.57	−0.04 (−0.27 to 0.18)	0.72	−0.18 (−0.43 to 0.06)	0.14
Age										
17–32										
32–47	0.01 (−0.23 to 0.24)	0.95	0.02 (−0.24 to 0.27)	0.89	0.06 (−0.22 to 0.33)	0.69	0.12 (−0.17 to 0.41)	0.40	−0.19 (−0.50 to 0.12)	0.22
47–62	−0.13 (−0.38 to 0.12)	0.33	−0.17 (−0.44 to 0.11)	0.24	−0.11 (−0.40 to 0.18)	0.46	0.03 (−0.28 to 0.34)	0.83	−0.24 (−0.57 to 0.09)	0.15
62–76	−0.37 (−0.71–[−0.04])	0.03	−0.25 (−0.62 to 0.11)	0.17	−0.28 (−0.67 to 0.11)	0.16	−0.24 (−0.66 to 0.17)	0.24	−0.81 (−1.25–[−0.38])	0.000
BMI										
20–25										
25–30	−0.14 (−0.35 to 0.06)	0.18	−0.09 (−0.32 to 0.13)	0.43	−0.22 (−0.46 to 0.02)	0.07	−0.12 (−0.38 to 0.13)	0.34	−0.14 (−0.41 to 0.13)	0.31
>30	−0.26 (−0.50–[−0.02])	0.04	−0.30 (−0.56–[−0.03])	0.03	−0.24 (−0.52 to 0.04)	0.09	−0.20 (−0.50 to 0.10)	0.19	−0.28 (−0.59 to 0.04)	0.08
<20	−0.02 (−0.46 to 0.42)	0.94	0.13 (−0.36 to 0.61)	0.61	−0.06 (−0.57 to 0.45)	0.82	−0.16 (−0.70 to 0.38)	0.56	−0.05 (−0.62 to 0.53)	0.87
Never smoked										
Ex-smokers	−0.12 (−0.32 to 0.07)	0.22	−0.19 (−0.40 to 0.02)	0.08	−0.21 (−0.44 to 0.02)	0.08	−0.09 (−0.33 to 0.15)	0.48	0.06 (−0.19 to 0.32)	0.64
Current smokers	−0.45 (−0.79–[−0.11])	0.01	−0.61 (−0.98–[−0.24])	0.001	−0.40 (−0.80–[−0.005])	0.05	−0.59 (−1.01 to [−0.17])	0.006	−0.09 (−0.53 to 0.36)	0.71
Skin prick test positive	0.21 (0.01–0.41)	0.04	0.24 (0.02–0.46)	0.04	0.18 (−0.06 to 0.42)	0.14	0.15 (−0.10 to 0.39)	0.25	0.26 (−0.01 to 0.52)	0.06
logFeNO	0.06 (−0.09 to 0.20)	0.43	0.03 (−0.13 to 0.19)	0.71	0.18 (0.01–0.35)	0.04	−0.06 (−0.24 to 0.12)	0.50	0.07 (−0.12 to 0.26)	0.48

BMI, body mass index; CRS, chronic rhinosinusitis.

Table 3 Euro Quality of Life EQ-5D health questionnaire. EQ VAS and EQ-5D index values (mean, 95% CI) based on the UK EQ-5D index tariff and the distribution (%) of respondents reporting problems in different dimensions

	Control (n = 226)	CRS (n = 108)	Asthma (n = 472)	Asthma and CRS (n = 129)	Comparison (P)
EQ VAS Mean (95% CI)	85 (83–87)	76*** (73–79)	79*** (78–81)	71***###§ (67–74)	<0.00001
EQ-5D index value Mean (95% CI)	0.92 (0.91–0.94)	0.85** (0.81–0.88)	0.85*** (0.83–0.87)	0.74***###§§ (0.69–0.79)	<0.00001
EQ-5D domains					
Mobility	5.8	8.3	10.8*	14.7***	0.04
Self-care	0.9	1.9	2.3	3.1	0.50
Usual activities	4.0	9.3	7.2	17.7***###	<0.0001
Pain/discomfort	23.5	47.2***	42.9***	62.3***§###	<0.0001
Anxiety/depression	12.4	25.0**	26.6***	36.4***#	<0.0001

CRS, chronic rhinosinusitis.
EQ-5D index value ANOVA $P < 0.0001$ $F = 17.3$; EQ VAS ANOVA $P < 0.0001$ $F = 20.7$. $^{**}P < 0.01$, $^{***}P < 0.001$ compared with control; $^{\S}P < 0.05$, $^{\S\S}P < 0.01$ compared with CRS; $^{\#}P < 0.05$, $^{\#\#\#}P < 0.001$ compared with asthma.

group with asthma and CRS had a lower EQ-5D index value and mean EQ VAS score compared to the group with asthma only ($P < 0.001$; Table 3).

A lower EQ-5D index value was related to lower FEV_1, current smoking, high BMI (>30 kg/m^2), age (the age group 47–62 years compared with the age group of 17–32 years), a negative SPT, and gender (being a woman) (Table 4). The gender difference was significant only in the domains pain/discomfort ($P < 0.0001$) and anxiety/depression ($P = 0.002$).

Table 4 Association between quality of life assessed as the EQ-5D index value and lung function and other subject characteristics; n = 812 after adjusting for all the variables in the table and center. Gender represents comparison with males. Inhaled steroids represent its use during the last 12 months. A negative value indicates lower quality of life

	EQ-5D index coef (95% CI)	P
FEV1%pred/10	0.01 (0.001–0.02)	0.03
Control		
CRS	−0.07 (−0.11–[−0.02])	0.007
Asthma	−0.08 (−0.12–[−0.04])	0.000
Asthma and CRS	−0.16 (−0.21–[−0.11])	0.000
Gender	−0.06 (−0.09–[−0.3])	0.000
Age		
17–32		
32–47	0.004 (−0.03 to 0.04)	0.82
47–62	−0.06 (−0.09–[−0.02])	0.004
62–76	−0.02 (−0.06 to 0.03)	0.48
BMI		
20–25		
25–30	−0.03 (−0.06 to 0.01)	0.10
>30	−0.07 (−0.10–[−0.03])	0.001
<20	0.03 (−0.03 to 0.10)	0.27
Never smoked		
Ex-smokers	−0.02 (−0.05 to 0.01)	0.19
Current smokers	−0.05 (−0.10–[−0.005])	0.03
Skin prick test positive	0.05 (0.02–0.08)	0.002
Inhaled steroids	−0.01 (−0.04 to 0.02)	0.62
logFeNO	0.01 (−0.02 to 0.03)	0.52

BMI, body mass index; CRS, chronic rhinosinusitis.

Discussion

In this clinical follow-up of the Swedish multicenter GA^{2}LEN survey, we found that subjects who suffer from both asthma and CRS have more impaired quality of life and lung function than subjects with asthma but no CRS. Furthermore, in asthma, multiple regression analysis showed that impaired quality of life was independently associated with having CRS, lower lung function, current smoking, obesity, high age, and a negative SPT.

Having CRS is an independent negative predictor of quality of life in asthmatics. We found that subjects having both asthma and CRS have more asthma symptoms than subjects with asthma only. This is confirmed by the West Sweden Asthma Study which showed that CRS symptoms were associated with multisymptom asthma, a marker of more severe disease (22). Active medical treatment of CRS has been shown to benefit concomitant asthma (23) and significantly improve quality of life (7). One possible explanation for the association between low asthma-related quality of life and CRS could be related to poor sleep quality. We recently showed that having both asthma and nasal blockage is more related to poor sleep than having asthma only (24).

Our results show that FEV_1 and FVC are lower in individuals with both asthma and CRS compared to those with only asthma, which is in agreement with a study that described lower FEV_1 in patients with asthma who suffered from rhinosinusitis compared to asthma patients without rhinosinusitis (25). Our study showed that there was a direct association between asthma-specific quality of life and lung function in individuals with asthma. The association of quality of life with lung function found in this study is confirmed by the results of the EQ-5D, a generic quality-of-life health questionnaire.

We found that in asthma, current smoking was associated with lower quality of life, assessed both with mAQLQ and EQ-5D, and lower lung function. In particular, we found that the impact of smoking is significant in the mAQLQ domains

emotions, symptoms, and activities. A study by Tan et al. (26) showed that patients with asthma who smoked had lower emotional function scores in the asthma quality of life questionnaire with more frequent symptoms, particularly at night, which could affect their sleep. This result underlines the importance of smoking cessation in asthma-related quality of life.

In this study, we found that obesity is associated with a lower asthma-related quality of life in the domain asthma symptoms. This is consistent with findings that obese adults report poor asthma-specific quality of life and have more severe asthma, more frequent exacerbations and more asthma-related hospitalizations (27, 28). Assessed with EQ-5D, we found, in accordance with other authors, that obesity was associated with lower quality of life in the domains mobility, pain/discomfort and anxiety/depression, and lower EQ-5D VAS values (data not shown) (29).

One of the strengths of this study is the large age range, representing individuals up to 76 years of age. We found that asthmatics from 62 to 76 years of age have lower asthma quality of life compared with 17- to 32-year-old asthmatics in the domain environment. The general quality of life assessed by the EQ-5D index in this group is not reduced compared with the younger asthmatics (data not shown). Other studies show that elderly patients may underestimate symptom severity and attribute breathlessness to age and other comorbidities (30). A possible drawback of this study is that the criteria for defining CRS were based on subjective symptoms only, which may have led to some of the participants being misallocated. The definition was, however, based on the EP_3OS criteria (15), which have been shown to be significantly associated with nasal endoscopy findings (31, 32). Another drawback is that the effect size for some of the associations was relatively small, which might decrease the clinical significance of certain associations with health-related quality of life.

Furthermore, one-third of the subjects having both asthma and CRS were nonatopic, assessed with SPT. We found that atopy was related to higher quality of life in asthmatics. This is in accordance with Ehrs et al. (33), who found that quality of life was improved in atopic asthma compared with nonatopic asthma. Taken together, patients with CRS constitute a clinically heterogeneous group, and the inflammatory phenotype seems to influence quality of life.

Surprisingly, we found no gender differences in the asthma-related quality of life. However, women with asthma, CRS or the combination of both, have lower EQ-5D index values than men, and this is significant in the domains pain/discomfort and anxiety/depression. Women with asthma report lower quality of life scores, which seems to be related to a more subjective disease state in women than in men with asthma (34). Gender differences have also been reported for patients with CRS (35), which seemed to be restricted to the evaluation of aspects of general health-related quality of life, whereas the disease-specific quality of life was not judged differently between men and women (36).

In conclusion, having asthma in combination with CRS results in lower quality of life and lung function than having asthma only. Our data show that asthma-related quality of life is related to factors such as having CRS, reduced lung function, smoking, high age, obesity, and a negative SPT. Several of these factors are modifiable and should be considered when discussing quality of life with the asthmatic patient. In the therapeutic approach of patients with asthma, both upper and lower airways need to be evaluated and treated.

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Author contributions

AE and CJ analyzed the data and wrote the manuscript; AE, HB, LE, and RM collected data; RM, CJ, KL, and SED supervised the study and contributed to the design of data analyses; AB, AM, and PS contributed to data analysis; all co-authors contributed to drafting the manuscript or revised it critically.

Conflict of interest

None of the authors has declared any conflict of interest.

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