

Original article

United airways: the impact of chronic rhinosinusitis and nasal polyps in bronchiectatic patient's quality of life

Background: The nose and the bronchi belong, in anatomical and physiopathological terms, to the concept of united airways. Associations between upper and lower airways diseases have been demonstrated in allergic rhinitis and asthma, nasal polyposis (NP) and asthma, chronic rhinosinusitis (CRS) and chronic obstructive pulmonary disease, and more recently CRS/NP and bronchiectasis (BQ).

Objective: To evaluate the impact of CRS on quality of life (QoL) of patients with BQ, and to correlate these findings with the pulmonary status, nasal symptoms, and general health status.

Methods: In a prospective study, patients with BQ ($n = 80$) were evaluated for CRS and NP using EP³OS criteria, and severity of BQ using chest high resolution computed tomography (HRCT)-scan. Quality of life was assessed in all patients by using specific [Sinonasal Outcome Test-20 (SNOT-20), St George Respiratory Questionnaire (SGRQ)], and generic (Short Form-36; SF-36) questionnaires.

Results: Using SNOT-20, patients with CRS had worse QoL (2.1 ± 0.1 ; $P < 0.001$) than patients without CRS (0.4 ± 0.06). Using SGRQ total score, patients with CRS had worse QoL (43.7 ± 2.2 ; $P < 0.001$) than patients without CRS (24.7 ± 2.5). Using SF-36, patients with CRS had worse QoL, both in the physical summary (64 ± 3.4 ; $P < 0.05$) and the mental summary (65.5 ± 4.7 ; $P < 0.05$), than patients without CRS (physical summary [PS]: 76.2 ± 3.3 ; mental summary [MS]: 78.3 ± 5.3 , respectively). Sinonasal Outcome Test-20 was correlated with SGRQ total score ($r = 0.72$; $P < 0.01$), and SF-36 physical summary ($r = -0.63$; $P < 0.01$). St George Respiratory Questionnaire was correlated with SF-36 on physical summary ($r = -0.58$; $P < 0.05$) and with forced expiratory volume in 1 s ($r = -0.41$; $P < 0.05$).

Conclusion: These results suggested that CRS, measured by both specific and generic questionnaires, has a considerable impact on the QoL of patients with BQ.

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Key words: bronchiectasis; chronic rhinosinusitis; nasal polyposis; quality of life; Short Form-36 questionnaire; St George Respiratory Questionnaire; Sinonasal Outcome Test-20.

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Bronchiectasis (BQ) consists of a permanent and irreversible dilatation of bronchi and bronchioles caused by retained secretions and recurrent infections that cause inflammation, obstruction, and damage of the lower airway. Bronchiectasis is a consequence of a variety of different diseases in which airway infection and obstruction appear to be the most important contributory factors. Bronchiectasis is frequently associated with cystic fibrosis, primary ciliary dyskinesia, immunodeficiency, rheumatoid arthritis, and inflammatory bowel diseases (1).

Chronic rhinosinusitis (CRS), one of the most common chronic diseases (2), is an inflammatory disease of the

nose and sinus mucosa that is still little understood, despite various hypotheses about its cause (3). Chronic rhinosinusitis with nasal polyps (NP) is considered a subgroup of CRS. Chronic rhinosinusitis with or without NP is often taken together as one disease entity, because it seems impossible to clearly differentiate both entities (4–6). The reason why polyps develop in some patients and not in others remains unknown. In the general population, the prevalence of NP is 4%. Although the cause of NPs is still unknown, it has been reported to be associated with asthma and other pulmonary disorders, such as cystic fibrosis, primary ciliary dyskinesia, aspirin

sensitivity (7, 8), and more recently BQ (9). Almost four out of five patients with BQ (77%) presented criteria for CRS, and one out of every four patients had NP on nasal endoscopy (25%) (9).

Bronchiectasis is a disease with the potential to cause devastating complications. The patients with BQ present cough and chronic sputum production, which have a great impact on patient's quality of life (QoL) (10). Most patients undergo slow and progressive health deterioration over decades. Chronic rhinosinusitis and BQ can have detrimental effects on physical, psychological, and social aspects of patients' lives, significantly worsening their QoL. Symptoms and lung function do not reflect the impact of the disease on the patient's health status, which should be supplemented by the use of QoL questionnaires (11). Studies have reported that patients with CRS have more bodily pain (BP) and worse social functioning (SF) than for example patients with chronic obstructive pulmonary disease (COPD), congestive heart failure, diabetes, and back pain (12, 13).

There are two major types of QoL instruments used in clinical trials: specific and generic questionnaires (14, 15). Specific questionnaires are usually focussed on one particular area such as a disease state, a selected population, or a certain function or problem. The St George Respiratory Questionnaire (SGRQ) has been used to assess the QoL in patients with asthma, COPD, α_1 -antitrypsin deficiency, interstitial lung diseases, and BQ (16). The Sinonasal Outcome Test (SNOT-20) is also a validated, disease-specific, health-related QoL questionnaire for upper airway pathology (17). This has been used in a number of studies of CRS (18, 19). Rhinosinusitis-related impairment of QoL was assessed with the SNOT-20 questionnaire in allergic asthmatic, nonallergic asthmatic, and COPD patients. Patients with allergic and nonallergic asthma and COPD show increased nasal symptoms, more nasal inflammation, and significant impairment of their QoL related to rhinosinusitis (20). No studies have reported the impact of upper airway disease on QoL in patients affected by BQ on the basis of specific questionnaires such as SNOT-20 and SGRQ.

Generic QoL questionnaires are also available and may be administrated to any individual, thereby making it possible to assess the burden of illness in various conditions. The Short Form-36 Health Survey (SF-36) is the most widely used generic instrument for measuring health status. This questionnaire has been adapted for the Spanish-speaking general population in accordance with the International Quality of Life Assessment project and has demonstrated a good reproducibility and validity (21–23). In a previous study performed by our group with SF-36, we demonstrated that patients with BQ and CRS have a significantly impaired QoL compared with the Spanish general population with no differences between CRS, either with or without NP (24). The aim of this study was to evaluate the impact of CRS, with or without NP, on the QoL of patients with

BQ using a specific QoL questionnaire (SNOT-20, SGRQ), and to correlate the findings with: SF-36, nasal symptoms, and lung function.

Material and methods

Study population

Patients with noncystic fibrosis BQ in a stable phase of their illness ($n = 80$) were included in this prospective study from January 2005 to February 2006. Sixty patients fulfilled EP³OS criteria (2) for CRS, 20 of whom with NP (9).

Design

The diagnosis of BQ was performed on the basis of characteristic clinical symptoms and chest-CT scanning (Siemens Emotion Duo Two-slice 5 mm with high resolution slices 1 mm for pulmonary parenchyma; Siemens, Munich, Germany). The stability of the BQ condition was assessed with a complete clinical evaluation, a forced spirometry, and wherever necessary also with a thorax radiology. Stable BQ condition was defined as the absence of fever, no impairment of airflow limitation, no increase in sputum overproduction or change in the macroscopic characteristics (purulence), and no increase in chronic cough. In summary, no increase in respiratory symptoms or modifications in the treatment over the previous 6 weeks. The Ethics Committee of our institution approved the study and signed informed consent was obtained from all the patients.

Exclusion criteria were hospitalization in the previous 2 months, use of antibiotics in the last 4 weeks, *pseudomonas* colonization, or presence of a serious concomitant illness.

To characterize the involvement of upper airway disease in patients with BQ, the following diagnostic tools were used in the study: nasal symptom score, nasal endoscopy, sinonasal CT-scan (Siemens Somatom P4 Unislice 3 mm). Nasal congestion/obstruction/blockage, reduction or loss of the sense of smell, anterior rhinorrhea, postnasal drip, facial pain/pressure, itching, and sneezing were scored using the Rasp classification (0–3) (25). Polyp size was scored from 0 to 3 for each nasal cavity using nasal endoscopy, following Lildholdt's classification (26). A radiologist blindly staged sinus occupation for each patient, using CT scanning and the Lund-MacKay score system (0–24) (27). All these results have been already published in a previous study (9).

To characterize the involvement of lower airway disease, a chest HRCT-scan was performed during the 3-month period prior to the sinonasal examination and the extent of BQ in each lobe was graded, using a scale from 0 to 3 (0, no involvement; 1, segment involved; 2, more than one segment involved; and 3, gross cystic BQ involving the entire lobe) (28).

After a 4-week washout period for oral and intranasal steroids, SNOT-20, SGRQ, and SF-36 questionnaires were completed by all patients (29, 30).

Quality of life

- 1 The SNOT-20 comprises 20 items that assess symptoms of CRS and the impact that they have on health status. Each item is graded from 0 to 5. Higher scores represented a worse impairment of health status because of upper airway symptoms. A control group without CRS, studied to validate the questionnaire, had a mean score of 0.6 (17).

Table 1. Epidemiologic characteristics of BQ patients included in the study

	All BQ patients	Non-CRS	CRS	CRS without NP	CRS with NP
Patients, <i>n</i> (%)	80	20 (25)	60 (75)	40 (50)	20 (25)
Age (years)†	56.6 ± 1.8	58.7 ± 3.2	55.5 ± 2.1	57 ± 2.5	51.2 ± 4
Female subjects, % F/M ratio	71 2.4 : 1	50 1 : 1	81* 4.4 : 1	89* 8.3 : 1	60** 1.5 : 1
FEV ₁ , %†	80.8 ± 2.8	90 ± 4	75.8 ± 3*	77.6 ± 3.6*	71 ± 8*

BQ, bronchiectasis; CRS, chronic rhinosinusitis; NP, nasal polyposis; M, male; F, female; FEV₁, forced expiratory volume in 1 s.

Unpaired Student's *t* test: **P* < 0.05, when compared with non-CRS patients; ***P* < 0.05, when compared with patients with CRS without NP.

†Data presented as mean ± SEM.

- The SGRQ is a disease-specific instrument designed to measure impact on overall health, daily life, and perceived well-being. The SGRQ was developed for use by patients with fixed and reversible airway obstruction, and has been widely used in COPD, asthma and more recently in BQ research, including 56 items (76 weighted responses) across three domains: symptoms (frequency and severity), activity (activities that cause or are limited by breathlessness), and impact (SF, psychological disturbances resulting from airways disease). Scores range from 0 to 100, with higher scores indicating poorer QoL.
- The Medical Outcomes Study SF-36 consists of 36 self-administered questions and was developed to measure eight health domains: physical functioning (PF), role physical, BP, general health (GH), vitality, role emotional (RE), SF, and mental health. Two summary scales are also included: the physical component summary (PCS) and the mental component summary (MCS). We needed a generic questionnaire to assess QoL in pathology potentially involving both upper and lower airways: BQ and CRS (with or without NP). The Spanish version of the SF-36 Health Survey was used (21). This version is very similar to the original US questionnaire in absolute values, age, and gender. Scale scores in each domain and summaries range from 0 to 100, higher scores indicating better QoL (31). Data on SF-36 has already been published and will be used here only to correlate with specific QoL questionnaires, and to support our objectives including a subgroup of patients with BQ with no nasal pathology; given that only the PCS and the MCS will be reported here.

Statistical analysis

Statistics were performed using spss for Windows (spss 11.0; SPSS Inc., Chicago, IL, USA). All analyses were performed using two-tailed tests significance at the 0.05 level. The data are presented as mean ± SEM. All data were assessed for normal distribution and the Bonferroni correction for multiple comparisons was used. Unpaired Student's *t*-test was used to compare SNOT-20, SGRQ, and SF-36 of patients with BQ with and without CRS, and between patients with or without NP. Pearson correlation coefficients were used to examine the association between QoL scores (SNOT-20, SGRQ, SF-36) with nasal symptoms, and lung function.

Results

Demographic data

The mean age of BQ patients was 56.6 ± 1.8 years, 8% were smokers and 27% ex-smokers. No significant differences exist on the presence of CRS depending on

smoking history. Patients with CRS (81% female subjects) had a significantly higher female ratio (4.4 : 1), and this was even higher in patients with CRS without NP (8.3 : 1), when compared with patients without CRS (1 : 1) (Table 1).

Quality of life

- SNOT-20.** Patients with CRS had significantly higher total scores (2.1 ± 0.1; *P* < 0.001) than patients without CRS (0.4 ± 0.06) (Fig. 1). No significant differences were observed between patients with or without NP and depending on the BQ aetiology (idiopathic vs postinfectious).
- SGRQ.** Patients with CRS had significantly higher scores in total score (43.7 ± 2.2; *P* < 0.001), symptoms (56.7 ± 3; *P* < 0.001), activities (41.6 ± 2.4; *P* < 0.001), and impact (33 ± 2.5; *P* < 0.001), than patients with no CRS (total: 24.7 ± 2.5; symptoms: 35.9 ± 3.2; activities: 18.2 ± 3; impact: 19.9 ± 2.7) respectively (Fig. 1). No significant differences were found between patients with or without NP or between those with a different BQ aetiology (idiopathic vs postinfectious).

St George Respiratory Questionnaire total score (*r* = 0.72; *P* < 0.01), symptoms (*r* = 0.56; *P* < 0.01), activities (*r* = 0.72; *P* < 0.01), and impact (*r* = 0.64; *P* < 0.01) were correlated with the SNOT-20 total score.

- SF-36.** Patients with CRS had significantly lower scores in PCS (64 ± 3.4; *P* < 0.05), and MCS (65.5 ± 4.7; *P* < 0.05) than patients with no CRS (PS: 76.2 ± 3.3; MS: 78.3 ± 5.3) respectively (Fig. 1). No significant differences were found between patients with or without NP and depending on the BQ aetiology (idiopathic vs postinfectious).

SF-36 PCS (*r* = -0.63; *P* < 0.01), and SF-36 MCS (*r* = -0.43; *P* < 0.01) correlated with SNOT-20 total score, while only PCS (*r* = -0.58; < 0.05) correlated with SGRQ total score.

- Correlation of QoL questionnaires (SNOT-20, SGRQ, SF-36) with nasal symptoms, lung function**

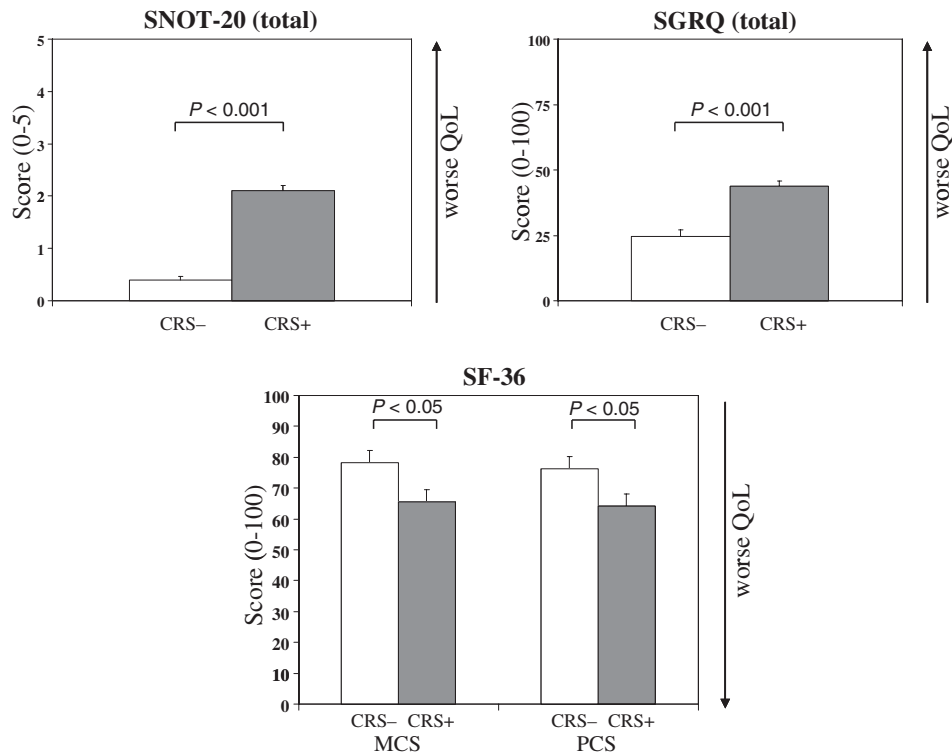


Figure 1. Quality of life depending on the existence (CRS+, gray bars) or absence (CRS-, white bars) of chronic rhinosinusitis, measured by SNOT-20, SGRQ, and SF-36 (MCS, PCS) questionnaires.

(forced expiratory volume in 1 s; FEV₁), and BQ severity (chest HRCT-scan).

- (i) *Nasal symptoms.* Total nasal symptom score correlated with SNOT-20 total score ($r = 0.8$; $P < 0.01$), SGRQ total score ($r = 0.67$; $P < 0.01$), as well as with the SF-36 PCS ($r = -0.72$; $P < 0.01$), and MCS ($r = -0.48$; $P < 0.01$).
- (ii) *Lung function.* A mild but significant correlation was observed between FEV₁ and SGRQ total score ($r = -0.41$; $P < 0.05$), but not with SGRQ total score and SF-36 component summaries.
- (iii) *Chest HRCT-scan.* Patients with CRS (6.2 ± 0.5 ; $P < 0.001$) showed a higher BQ severity score than patients with no CRS (4.2 ± 0.7). No differences were observed between patients with and without NP. A mild but significant correlation was observed between extension of BQ and SGRQ total score ($r = 0.4$; $P < 0.05$), but not with SNOT-20 total score and SF-36 component summaries.

Discussion

The main findings of our study were: (i) patients with BQ and CRS had an impaired QoL when compared with BQ

patients with no CRS measured by SNOT-20, SGRQ, and SF-36; (ii) NP had no additional impact on QoL in patients with BQs; (iii) upper airway QoL (SNOT-20) have been shown to correlate with both the lower airways QoL (SGRQ) and the GH QoL (SF-36). This study demonstrates that CRS contributed to the impairment of health status in patients with BQ.

The mean SNOT-20 score in patients with BQ who fulfill EP³OS criteria for CRS, with or without NP, was 2.1. This was higher than the score registered in a population of patients with CRS, studied during the validation of the SNOT-20 questionnaire, who had a mean score of 1.9 (17). Moreover, the SNOT-20 score in patients with BQ without CRS (0.4) was similar to that previously reported in normal control patients (0.6) (17). There were no differences between patients with CRS with or without NP, although the SNOT-20 questionnaire does not include sections on nasal congestion or smell disorders. Although SNOT-22, which includes both items, could be more adequate for differentiating between CRS with NP and CRS without NP, this questionnaire has not yet been validated. The absence of a relationship between current smoking status and the nasal or SNOT-20 scores is interesting as active smoking is known to be associated with symptoms of CRS (32).

Quality of life measured by the SGRQ in patients with BQ assessing the pulmonary function and the presence of colonization (with *pseudomonas* or other microorganisms)

has shown that patients with BQ colonized with *pseudomonas* have worse pulmonary function and QoL than uncolonized patients. Moreover, patients having microorganisms other than *pseudomonas* have a worse QoL than those without microorganisms (33). In our study, none of the patients with BQ were colonized by *pseudomonas*. With respect to the aetiology (idiopathic vs postinfectious), no differences in QoL were found in patients with BQ.

Patients with NP have shown lower scores in all SF-36 domains except for PF and RE than patients with coronary artery disease (34), COPD (22), and asthma (35). Nasal polyps are often an indicator of airway disease involving both the upper and lower respiratory tracts (36). Radenne et al. (37) have investigated the impact of NP on QoL demonstrating that NPs impaired QoL in all SF-36 domains. Other studies have shown statistically significant differences in seven of the eight domains of the SF-36, the exception being PF (12, 28, 38). More recently our group has demonstrated that asthma – but not aspirin sensitivity – has an additional negative impact on the QoL of patients with NP (29).

A previous study by our group demonstrated that patients with BQ and CRS present a significantly impaired QoL when compared with the Spanish general population with no differences between CRS with NP and CRS without NP (24). In this study, patients with BQ with CRS showed an important negative impact on QoL when compared with patients with BQ without CRS, with no additional impact from the presence of NPs. Upper airway QoL (SNOT-20) have been shown to correlate with both the lower airways QoL (SGRQ) and the GH

QoL (SF-36). This study provides additional evidence that the degree of abnormality in nasal symptoms is associated with the impairment of QoL in SNOT-20, SGRQ, and SF-36. Patients of the group CRS with NP had a higher loss of sense of smell, without provoking any significant differences in QoL (SNOT-20, SGRQ, and SF-36), when compared with patients of the group CRS without NP. Otherwise, there was no significant correlation between the SNOT-20 and SGRQ total score ($r = 0.21$, $P < 0.09$), or between the SNOT-20 and the individual impact, activity, or symptoms domains of the SGRQ in patients with upper airway symptoms and COPD (39).

In conclusion, these results are the first to suggest that CRS with and without NP have a considerable impact on the QoL of patients with BQ. Hence, our data also confirm that the ‘united airway’ concept goes beyond the scope of asthma and COPD. In addition, treating the nose might also have beneficial effects on the health status of patients with BQ.

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