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Rhinosinusitis - Its Impact on Quality of Life

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1. Introduction

Chronic rhinosinusitis (CRS) is one of the most common chronic diseases, affecting about 15% of the western population. This disease is connected with a significant health care burden having direct annual costs of about 5.8 billion dollars (Anand, 2004). These direct costs do not cover other important expenses to the individual, the community and society, such as lost time from work and / or school and the associated decreased productivity (Benninger, 2010).

CRS is an inflammatory process involving the sinonasal mucosa and defined as the presence of two or more symptoms one of which should be either nasal blockage/obstruction/congestion or nasal discharge (anterior or posterior) with

± facial pain (pressure)

± reduced smell

for more than 12 weeks, together with pathologic endoscopic findings in the middle nasal meatus (Figure 1) and/or CT changes within the ostiomeatal complex and/or sinuses (Fokkens et al., 2007). Nasal polyposis is considered a subgroup of CRS (Figure 2).

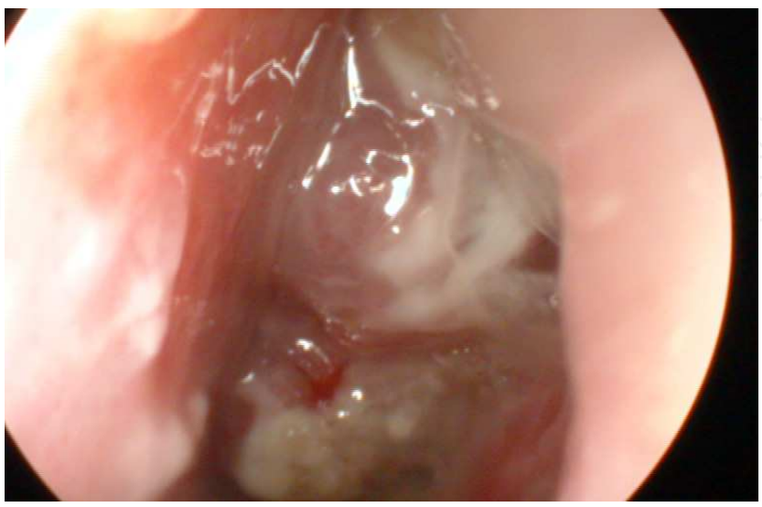


Fig. 1. Endoscopic view of chronic rhinosinusitis- edema and purulent secretion in the middle nasal meatus

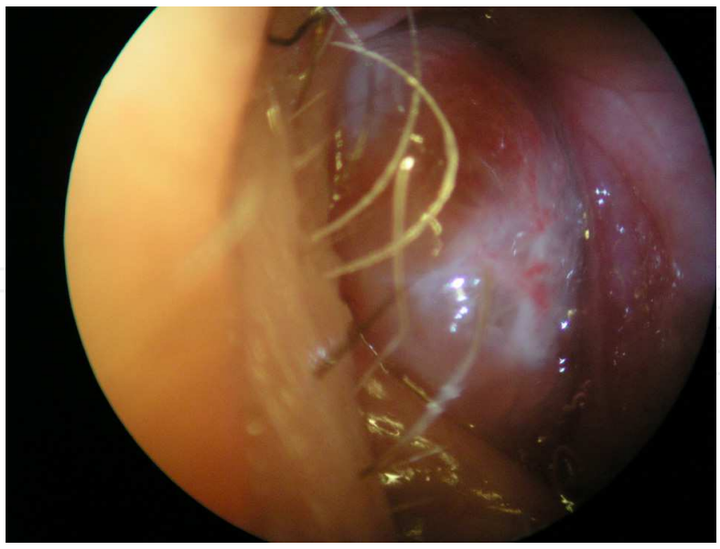


Fig. 2. Endoscopic view of nasal polyposis

Quality of life (QoL) is a unique personal experience that reflects not only health status but other factors in a patient's life which can only be described by each individual patient (Piccirillo, 2002). Quality of life may also be defined as the difference between expectations and experience (Calman, 1984). A part of the overall quality of life is health related quality of life (HRQoL), which is influenced by the health of patients and can be changed through treatment. Health related QoL may also be defined as those aspects of an individual's subjective experience that relate both directly and indirectly to health, disease, disability and impairment (Carr et al., 2001). The HRQoL is influenced by the patient's age, culture, expectations and physical and mental capabilities.

It has been shown that CRS has a significant impact on quality of life (Hopkins et al., 2009). Although the symptoms of rhinosinusitis are not life threatening they are associated with a dramatic reduction in QoL (van Oene, et al., 2007). Comparisons with other common chronic diseases revealed significantly lower scores for bodily pain and social functioning in patients with CRS compared to patients with congestive heart failure, angina, chronic obstructive pulmonary disease or back pain (Gliklich & Metson, 1995a).

When disease severity was measured using imaging and the endoscopic grading system, it was found that patients with nasal polyps (NP) appeared to have a more serious medical condition compared to CRS patients without polyps (Bhattacharyya, 2005); however, when measured using QoL instruments, and except for symptoms related to nasal congestion, patients with polyps seem to have a lighter disease burden than those without polyps (Soler & Smith, 2010).

Although there are many diagnostic methods currently available for evaluating sinonasal disease, it can not be said that the results clearly correlate with quality of life, as it is perceived by patients (Lund, 2001).

The way chronic rhinosinusitis affects daily life, from the patient's point of view, is far more important than the results of CT scans or the presence of a small polyp in an ethmoid cell (Schalek et al., 2010).

2. Instruments for quality of life assessment

The last two decades have been characterized by increasing interest in assessing the quality of life, which is related to the systematic development and validation of QoL questionnaires. Tools used to evaluate the quality of life are either generic health instruments for assessing general conditions or disease-specific questionnaires focused on symptoms of a disease.

Creation of a questionnaire is a relatively complex process involving several steps, each of which can significantly affect the final quality of the questionnaire.

The basic criteria which must be met by the questionnaire are: (i) reliability, (ii) validity, (iii) responsiveness and (iv) ease of use or feasibility.

Confirming that a particular instrument meets those criteria is a process called validation of the questionnaire. Validation studies must be performed on patients who have the same characteristics as the target population and there must be enough patients included in the validation study to make it statistically relevant.

Reliability

Reliability concerns the extent to which the questionnaire is free of random or systematic error.

Internal reliability (consistency) reflects the way individual items relate to each other. This property is determined by calculating Cronbach's α (range 0 – 1). If scale has an alpha of at least 0.7 it is considered to be reliable for group level comparisons and a value of 0.9 or more means it is suitable for assessment at the individual level (Bland & Altman, 1997).

Test-retest reliability (reproducibility) reflects stability over time with repeated testing. Questionnaires with good reproducibility should give similar results under similar conditions. This property of the questionnaire may be tested using the t- test and a Pearson or Spearman correlation coefficient or the intra-class correlation coefficient.

Validity

The questionnaire can be called valid when it measures what it is supposed to measure. Different levels of validity are distinguished.

Construct validity means that the instrument behaves according to an underlying hypothesis, i.e. the measured variables behave in a consistent way relative to theoretical and clinical expectations.

Convergent validity reflects the degree of correlation with other instruments of the same concept.

Discriminant validity reflects the ability of the questionnaire to distinguish between disease-affected groups of patients and those who are disease free.

Content validity is appropriateness and redundancy of items and scales of the instrument.

Responsiveness

Responsiveness is the sensitivity to change over time, i.e. the ability of the questionnaire to detect a change when it occurs. There are many responsiveness statistics, often it is measured by a standardized response mean- SRM (> 0.8 - high sensitivity to change).

Feasibility

Feasibility depends on a patient's understanding and willingness to complete the questionnaire. Complex, time-consuming questionnaires are usually not well received by patients, which will affect the meaningfulness of results. The feasibility can be assessed by pretesting with real patients in order to get feedback.

2.1 General health instruments

General (generic) health instruments are applicable in different diseases that can be compared regarding their impact on QoL. The following overview includes only a few of the most commonly used questionnaires, which are also frequently used to assess QoL in patients with CRS.

Short form 36 health survey (SF-36)

This questionnaire is one of the most widely used general QoL instruments. It consists of 36 items forming 8 scales (Ware & Sherbourne, 1992). The scales are: physical function, role physical, bodily pain, general health, vitality, social function, role emotional, and mental health.

Short form 12 health instrument (SF-12)

This is a shortened version of the SF-36 that contains questions from all eight SF-36 scales. Two summary scales are constructed: (i) physical and (ii) mental summary scores.

Glasgow benefit inventory (GBI)

This questionnaire was developed in 1996 (Robinson et al., 1996) and is designed to measure outcomes of surgical procedures in the field of otorhinolaryngology. The questionnaire consists of 18 items assessing the quality of life. Patients evaluate each item using the 5-grade scale: extremely positive, positive, no change, negative, extremely negative. GBI overall score the ranges from −100 to +100. Positive values indicate improvement, 0 no change of the state and negative values indicate deterioration of QoL.

2.2 Disease-specific questionnaires

This type of tool is frequently used to assess QoL in patients with CRS. Compared with general instruments they are able to capture symptoms in greater detail and are more sensitive in detecting changes after therapeutic intervention (Hopkins et al., 2009). The most frequently used validated questionnaires are listed below and their properties are summarized in Table 1.

Nasal symptom questionnaire (also Fairley nasal symptom score)

This instrument was the first (1993) validated QoL questionnaire for patients with sinonasal disease. The questionnaire consists of 12 items rated on a four-point scale (0-3). A validation study was performed on 411 patients with very good results for reliability and validity (Fairley et al., 1993). This questionnaire is not widely used, possibly due to a paucity of general health correlations.

Instrument	Developed	Language	Items	Scale	MS of CRS	Reliability	Validity	Responsiveness	Completion (min)
Fairley NSS	1993	English	12	0-3	yes	yes	yes	yes	5
RSOM-31	1995	English	31	1-5,VAS	yes	yes	yes	yes	20
SNOT-20	2002	English, German, Japan	20	0-5	no	yes	yes	yes	7
SNOT-16	1999	English	16	0-5	no	yes	yes	yes	5
SNOT-22	2003	English, Swedish, Chnese, Czech, Danish	22	0-5	yes	yes	yes	yes	7
RSDI	1997	English, Turkish	30	0-5	yes	yes	No data	No data	5
CSS	1995	English, Chinese, Norwegian	6	0-100	no	yes	yes	yes	5
RhinoQoL	2005	English, French	17	1-5	no	yes	yes	yes	7
RSI	2003	English	20	0-5	yes	No data	yes	yes	5

Table 1. Properties of disease-specific QoL questionnaires (MS of CRS-major symptoms of CRS)

Rhinosinusitis Outcome Measure (RSOM-31), Sinonasal Outcome Test-16 (SNOT-16), SNOT-20 and SNOT-22

The RSOM-31 was developed by Piccirillo, in 1995, and contains 31 disease-specific and general items. A condensed version of this questionnaire is the SNOT-20 which has also been validated (Piccirillo et al., 2002). This questionnaire contains 20 questions, which can be divided into five subgroups (nasal symptoms, paranasal symptoms, sleep-related symptoms, and social and emotional impairment). Patients rate individual items on a six-point scale (0 - no problem, 5 - most serious problem) and in addition, they can mark which of the five items they consider to be the most important. SNOT-20 is one of the most frequently used tools and is particularly popular for its high patient compliance.

Addition questions, regarding nasal obstruction and disorders of smell, were added to SNOT-20 to produce the SNOT-22 (Figure 3). The added questions are very significant because problems with olfaction and nasal obstruction are directly related to the quality of life of patients with CRS and therapeutic interventions are designed to positively influence these two annoying symptoms. The Royal College of Surgeons of England used SNOT-22 in a National Comparative Audit of Surgery for nasal polyposis and chronic rhinosinusitis. Data for this study came from 3128 patients using questionnaire SNOT-22; the questionnaire was found easy to use and provided good discriminant validity (Hopkins et al., 2006). In 2009 the SNOT-22 was validated and recommended for routine clinical practice (Hopkins et al., 2009).

Also a 16-item version of the SNOT questionnaire has been validated. This version proved to have excellent discriminant and construct-related validity, but it does not cover all major CRS symptoms and has not gain general acceptance.

Sino-nasal outcome test-22 questionnaire

Name: **Date:**

Below you will find a list of symptoms and social/emotional consequences of your nasal disorder. We would like to know more about these problems and would appreciate you

answering the following question to the best of your ability. There are no right or wrong answers, and only you can provide us with this information. Please rate your problems, as they have been over the past two weeks. Thank you for your participation.

A: Considering how severe the problem is when you experience it and how frequently it happens, please rate each item below on how 'bad' it is by circling the number that corresponds with how you feel using this scale ➔	**No problem**	**Very mild problem**	**Mild or slight problem**	**Moderate problem**	**Severe problem**	**Problem as bad as it can be**
1. Need to blow nose	0	1	2	3	4	5
2. Sneezing	0	1	2	3	4	5
3. Runny nose	0	1	2	3	4	5
4. Cough	0	1	2	3	4	5
5. Post nasal discharge (dripping at the back of your nose)	0	1	2	3	4	5
6. Thick nasal discharge	0	1	2	3	4	5
7. Ear fullness	0	1	2	3	4	5
8. Dizziness	0	1	2	3	4	5
9. Ear pain	0	1	2	3	4	5
10. Facial pain/pressure	0	1	2	3	4	5
11. Difficulty falling asleep	0	1	2	3	4	5
12. Waking up at night	0	1	2	3	4	5
13. Lack of a good night's sleep	0	1	2	3	4	5
14. Waking up tired	0	1	2	3	4	5
15. Fatigue	0	1	2	3	4	5
16. Reduced productivity	0	1	2	3	4	5
17. Reduced concentration	0	1	2	3	4	5
18. Frustrated/restless/ irritable	0	1	2	3	4	5
19. Sad	0	1	2	3	4	5
20. Embarrassed	0	1	2	3	4	5
21. Sense of taste/smell	0	1	2	3	4	5
22. Blockage/congestion of nose	0	1	2	3	4	5

Fig. 3. The SNOT-22 questionnaire

Chronic sinusitis survey (CSS)

One of the most frequently used instruments was developed by Gliklich and Metson in 1995 (Gliklich & Metson, 1995b). The CSS consists of two parts, symptom-based and medication-based (Figure 4). When using the CSS, patients do not assess the severity of symptoms, but their duration, which, together with a limited number of questions can be regarded as a disadvantage (Morley & Sharp, 2006). Furthermore the questionnaire does not include any questions related to olfaction.

Chronic Sinusitis Survey-CSS

1. During the past 8 weeks, how many weeks have you had:
   a. Sinus headaches, facial pain or pressure
      0 weeks 1-2 weeks 3-4 weeks 7-8 weeks
   b. Nasal drainage or postnasal drip
      0 weeks 1-2 weeks 3-4 weeks 7-8 weeks
   c. Nasal congestion or difficulty breathing through the your nose
      0 weeks 1-2 weeks 3-4 weeks 7-8 weeks
2. During the past 8 weeks, how many weeks have you taken
   a. Antibiotics
      0 weeks 1-2 weeks 3-4 weeks 7-8 weeks
   b. Nasal sprays prescribed by your doctor
      0 weeks 1-2 weeks 3-4 weeks 7-8 weeks
   c. Sinus medications in pill form (such as antihistamines,deconestants)
      0 weeks 1-2 weeks 3-4 weeks 7-8 weeks

Fig. 4. Chronic Sinusitis Survey-CSS

Rhinosinusitis disability index (RSDI)

The questionnaire (Figure 5) was developed in 1997 by Benninger and Senior (Benninger & Senior, 1997). RSDI uses three subscales (emotional, physical and functional) to combine measurements of general health status and disease-specific QoL. The questionnaire is characterized by excellent test-retest reliability, good internal consistency, good construct, discriminant and content validity.

The rhinosinusitis disability index (RSDI) domains and items

Physical

The pain or pressure in my face makes it difficult for me to concentrate
3. The pain in my eyes makes it difficult for me to read
4. I have difficulty stooping over to lift objects because of face pressure
5. Because of my problem I have difficulty with strenuous yard work and housework
6. Straining increases or worsens my problem
7. I am inconvenienced by my chronic runny nose
8. Food does not taste good because of my change in smell
9. My frequent sniffing is irritating to my friends and family
10. Because of my problem I don't sleep well
11. I have difficulty with exertion due to my nasal obstruction
12. My sexual activity is affected by my problem

Functional

Because of my problem I feel handicapped
13. Because of my problem I feel restricted in performance of my routine daily activities
14. Because of my problem I restrict my recreational activities

15. Because of my problem I feel frustrated
16. Because of my problem I feel fatigued
17. Because of my problem I avoid traveling
18. Because of my problem I miss work or social activities
19. My outlook on the world is affected by my problem
20. Because of my problem I find it difficult to focus my attention away from my problem and on other things

Emotional

Because of my problem I feel stressed in relationships with friends and family

21. Because of my problem I feel confused
22. Because of my problem I have difficulty paying attention
23. Because of my problem I avoid being around people
24. Because of my problem I am frequently angry
25. Because of my problem I do not like to socialize
26. Because of my problem I frequently feel tense
27. Because of my problem I frequently feel irritable
28. Because of my problem I am depressed
29. My problem places stress on my relationships with members of my family or friends

Fig. 5. Rhinosinusitis disability index- RSDI

Rhinosinusitis symptom inventory (RSI)

One of the more recent questionnaires (Bhattacharyya, 2005) was developed mainly to evaluate improvement of QoL after treatment. The instrument assesses major and minor symptoms of CRS on a six-point scale. Simultaneously, medication use, doctor visits and work absences (directly related to CRS) are recorded.

Rhinosinusitis quality of life survey (RhinoQoL)

This 17-item questionnaire is based on the CSS and the questioning system of both instruments is identical. The RhinoQoL does not contain questions regarding olfaction disturbances, which is one of major symptoms of CRS. The questionnaire was validated by Atlas on a population of 50 patients (Atlas et al., 2005).

There is also one important question concerning QoL measurement: How is a clinically significant change of health-related QoL defined? Statistically significant improvement does not always mean clinically relevant improvement as perceived by an individual patient. A concept called the minimal important difference helps address this problem. It is defined as the smallest change in QoL that patients perceive as beneficial, in the absence of side effects or excessive cost (Juniper at al., 1994). Prior studies measuring acute pain have shown that the minimal important difference for acute pain is between 0.9 and 1.3 on a 10-point scale. Recent studies reporting scaled symptom scores by Ling and Kountakis (Ling & Kountakis, 2007) and Bhattacharyya (Bhattacharyya, 2005) easily reach this threshold of clinical relevance. For the general health instrument SF-36, 10 to 12.5 points (100-point scale) represents the minimum change believed to be clinically relevant (Wyrwick et al., 2005).

Using statistical constructs, the minimal important difference has been defined as greater than half a standard deviation of the baseline QoL value for the given population. Recently Soler and Smith (Soler & Smith, 2010) summarized minimal important differences for disease specific QoL instruments (Table 2).

Questionnaire	Score Range	MCID
RSDI total	0-120	≥10.35
RSDI Physical	0-44	≥3.80
RSDI Functional	0-36	≥3.45
RSDI Emotionals	0-40	≥4.20
CSS total	0-100	≥9.75
CSS Symptoms	0-100	≥13.25
CSS Medications	0-100	≥12.60
SNOT-22	0-110	≥8.90

Table 2. Minimal important differences (MCID) for disease-specific QoL questionnaires (Soler & Smith, 2010)

Another important issue may be how to choose a particular tool for evaluating QoL in patients, regarding assessment of therapeutic effects or comparison of two or more therapeutic modalities on QoL.

A review of Chester and Sindwani, from 2007 (Chester & Sindwani, 2007), demonstrates that of the 18 QoL instruments used to evaluate the outcomes of endoscopic sinus surgery (ESS), only 5 were used more than twice: CSS (12 studies), SNOT-20 (11 studies), SF-36 (10 studies), RSI (4 Studies) and RSDI (3 studies).

Gill et al. proposed three recommendations to improve the measurement of quality of life: (i) use of global ratings, ideally one for general QoL and one for disease-specific QoL; (ii) severity and importance of symptoms must be rated; (iii) a possibility for patients to add other annoying symptoms (Gill & Feinstein, 1994). This recommendation takes into account the study of Morley et al, which suggests the SNOT-22 was the best tool for treatment evaluation, especially the after ESS (Morley & Sharp, 2006). This study was published in 2006, before the SNOT-22 had been validated. SNOT-22 fully corresponds to the recommendation of Gill and his co-workers – it includes questions regarding sinonasal symptoms, covers the major symptoms of CRS and also includes questions assessing the overall quality of life. It allows patients to easily assess the severity of symptoms and select the symptoms that are most important from their point of view. In addition, patients have the opportunity to present other troublesome symptoms that are not listed in the questionnaire.

The study of van Oene et al. focused on the issue of quality of disease specific QoL instruments (van Oene, 2007). Only questionnaires that clearly meet the following criteria were included in the study: (i) the questionnaire must be designed for adults with CRS and (ii) must cover all three aspects of HRQL-physical, functional and psychosocial. Parameters of the questionnaire, i.e. construction, description, feasibility, validation study and psychometric properties are all ranked using a points system. Criteria were fulfilled only for

RSOM-31, SNOT-16, SNOT-20, RSDI and RhinoQoL. The highest scores were achieved by RSOM-31 and SNOT-20. The questionnaire SNOT-22 was not enrolled because it had not yet been validated. CSS and RSDI did not meet the definition of a HRQL questionnaire. The authors point out the importance of the relationship between the characteristics of the questionnaire and the purpose for which it should be used. For example, for use in clinical practice, reliability of the instrument is essential, while for the purposes of clinical research, responsiveness (for longitudinal study) or discriminant validity (for cross-sectional studies) may be critical.

3. How the Rhinosinusitis afffects the quality of life

Symptoms of CRS can be disabling and lead to significant impairment of QoL. The most common reported symptom in CRS is nasal congestion/obstruction (Bhattacharyya, 2003). This symptom is accompanied by nasal discharge (anterior or posterior), reduction or loss of olfaction, facial pain or pressure and headaches, which were reported as the most disabling (Soler et al., 2008). These symptoms can impact all activities (work, leisure and sleep) of CRS patients. It is reasonable to expect that individual CRS symptoms can result in more complex problems such as sleep disturbances, psychological disorders (changes in mood, depression, and anxiety), fatigue, and sexual dysfunction.

3.1 Sleep disturbance and fatigue

Although sleep impairment has been studied less in CRS compared to allergic rhinitis, it is obvious that CRS is associated with this problem as well (Craig et al., 2008).

Also, a recent study by Benninger demonstrated that patients with CRS have significantly reduced sleep activity scores on the Rhinosinusitis Disability Index (Benninger et al., 2010).

In a population-based, case-control study, patients with nasal polyposis had a 2-fold higher risk of sleep disturbances than controls (Serrano et al., 2005). This is further supported by a study that approached it from the other way around; in a study of general medical outpatients, an increased prevalence of CRS symptoms in patients with unexplained chronic fatigue was observed (Chester, 2003). Thus, sleep impairment is a significant issue for CRS patients and questions regarding quality of the sleep have been incorporated in many disease-specific QoL questionnaires.

Nasal congestion/obstruction is thought to be a major cause of sleep impairment. This bothersome CRS symptom is usually worse at night, which is result of the lower position of the patient's head. Additionally, the overnight decline of serum cortisol levels can contribute to night-time nasal congestion. Nasal obstruction in healthy subjects leads to apneas and hypopneas (Suratt et al., 1986). Other CRS symptoms (e.g. discharge, facial pain and headache) can also reduce sleep quality.

It is also assumed that inflammatory mediators of CRS probably play a direct role in sleep disturbances (Craig et al., 2008).

There is a clear relationship between sleep impairment and daily fatigue. Poorly sleeping patients would be expected to experience fatigue and improved sleep should have a positive influence on fatigue.

3.2 Depression

Brandsted and Sindwani demonstrated that 25% of consecutively diagnosed CRS patients were also treated for depression, which is higher than in the general population (10 – 16%) (Brandsted & Sindwani, 2007). In this study the authors also compared the QoL of CRS patients with depression to a control group of CRS patients without depression. The results showed significantly poorer disease-specific and overall QoL scores in depressed CRS patients (both pre- and postoperatively).

Additionally, Mace reported lower preoperative and postoperative QoL scores in CRS patients with depression compared to non-depressed patients but with comparable improvements after endoscopic sinus surgery in both groups (Mace et al., 2008).

Wasan identified high levels of anxiety and depression in patients who undergo evaluation for CRS using the Rhinosinusitis Symptom Inventory and the Hospital Anxiety and Depression Scale (Wasan et al., 2007).

In conclusion depression is frequently associated with CRS and contributes to lower overall QoL in CRS patients, although it is likely that the diseases are independent (Rudmik & Smith, 2011).

3.3 Sexual dysfunction

Sexual activity is another important aspect of QoL. It is not hard to imagine that patients with nasal obstruction, discharge, reduced olfaction, facial pressure and sleep deficits would have an altered sex life compared to healthy controls. The Rhinosinusitis Disability Index (RSDI) is a disease-specific QoL questionnaire which has one question which directly addresses the impact of sinonasal disease on sexual function.

There are few studies dealing with sexual function in patients with sinonasal disease. Two trials investigating the influence of allergic rhinitis on sexual function, demonstrated lower scores for sexual function in patients suffering from allergic rhinitis compared those without sinonasal disease or with non-allergic rhinitis or anatomical obstruction. Although CRS was not specially evaluated in these studies, the results suggest that CRS may have similar negative effects on sexual function. (Benninger & Benninger, 2009; Kirmaz et al., 2005).

Benninger, using the Rhinosinusitis Disability Index, has provided data (on level of evidence IIIb) showing that functional endoscopic surgery for CRS has a positive impact on sexual function (Benninger et al., 2010).

3.4 Olfactory dysfunction

Smell disturbance is a common symptom affecting 61 – 83% of patients with CRS. Patient with olfactory impairment often report problems preparing food, decreased appetite, and a decreased sense of self-hygiene. Patients are also not able to detect spoiled foods and safety hazards such as smoke, chemicals, and gas leaks (Litvack et al., 2009). Moreover there are some professions dependent on good olfactory function (chefs, professional tasters, fireman, plumbers, etc.) and loss of smell in those occupations can be debilitating.

Although humans and other primates are regarded as primarily "optical animals" with a relatively undeveloped sense of smell, recent studies indicate that humans seem to use olfactory communication, particularly, in interpersonal relationships (Grammer et al., 2005). Perception of substances such as pheromones may modulate changes in interpersonal perception and individual mood, behavior and physiology (Havlicek et al., 2010).

4. Effect of rhinosinusitis treatment on quality of life

The effect of surgical treatment on QoL in patients with CRS has been documented fairly well (Metson & Glicklich, 1998; Salhab et al., 2004; Smith et al., 2005; Ling & Kountakis, 2007).

A review by Smith et al. assessed the effect of surgical treatment of CRS on symptoms and QoL in patients with CRS. Improvement of quality of life or symptoms was demonstrated in all 45 enrolled studies, 11 studies were prospective, and in five, a validated QoL questionnaire was used (Smith. et al., 2005).

Ling and Kountakis (Ling & Kountakis, 2007) showed a greater than 80% improvement in symptoms of CRS from baseline, when measured using a visual analogue scale, 12 months after ESS. These authors also used SNOT-22 scores that showed improvement by as much as 77%, postoperatively.

Improvement of both major and minor symptoms of CRS after ESS was also shown by Bhattacharyya (Bhattacharyya, 2005) using the RSDI (100 patients, average follow-up = 19 months).

Litvack (Litvack et al., 2007) showed that both primary and revision endoscopic surgery equally improved QoL (the RSDI and CSS questionaires were the QoL instruments used in the trial).

A prospective audit conducted on 3128 patients undergoing surgery for CRS also demonstrated a significant improvement of QoL over a 36-month follow-up (SNOT-22) (Hopkins et al., 2006).

Proimos (Proimos et al., 2010) demonstrated improvement of QoL in 86 patients with CRS with nasal polyps and asthma, 12 months after ESS. In this study SNOT-22 was used and additionally, the 5 most important items of SNOT, from the patient's point of view, were evaluated. The results confirmed that ESS satisfied expectations of patients regarding control of most of the important symptoms and a positive influenced on their overall QoL.

In a recent multi-institutional, prospective study, Smith et al. (Smith et al., 2010) demonstrated clinically significant improvement of QoL (CSS and RSDI questionnaires were used in 302 patients, mean ESS follow-up = 17.4 months). Authors of this study also tried to find predictive factors for QoL outcomes after ESS. They used a multivariate logistic regression model to examine predictors of clinically significant improvement of QoL. In this predictive model, after all co-factors were evaluated (e.g. comorbidities, demographic factors, and results of diagnostics tests), surprisingly, only primary or revision surgery was clearly predictive. The authors concluded that clinical phenotype did not provide outcome-predictive information and other factors with possible predictive importance should be investigated.

There is a relative lack of documentation regarding improvement of QoL after medical treatment of CRS. Similarly, there are insufficient data regarding comparisons of effects of different medical and surgical treatments on QoL. The lack of well-formed, prospective, randomized, controlled trials, concerning medical treatment can lead to the idea that surgical treatment of CRS has a better effect on QoL than medical treatments (Ragab et al., 2010).

Also the fact that surgical treatment should only be indicated for patients with a more severe course of disease, resistant to medical treatment, makes any comparison of effect of treatment on QoL more complicated.

A study by Lund et al. (Lund et al., 2004) showed no significant difference in the score on a disease-specific questionnaire (Chronic Sinusitis survey-CSS) in patients with CRS without NP, treated for 20 months with intranasal budesonide compared to placebo. In the same study, a significant difference between the two groups was found only in the general health subscale of SF-36 General Health Questionnaire, but no significant difference in the other subscales were observed.

Alobid et al. (Alobid et al., 2006) assessed the effect of treatment with oral and intranasal steroids on the quality of life of patients with CRS with nasal polyposis. The patients, after a short-course of oral prednisone, demonstrated a significant improvement in QoL in all domains (compared with base line and the control group) using the general-health QoL instrument SF-36. The improvement was sustained by intranasal steroids after 12, 24 and 48 months. The study was conducted on 60 patients who were compared with a control group (18 patients) without treatment.

The same group (Alobid et al., 2005) compared, in a randomized trial, medical treatment (53 patients, oral prednisone for two weeks) and surgical treatment (56 patients undergoing ESS) of CRS with nasal polyps. Both groups received intranasal budesonide for 12 months after intervention. At 6 and 12 months, a significant improvement in the QoL, measured again using the SF-36, was observed in both the medical and surgical group.

Ragab et al. in a recent prospective, randomized, controlled trial evaluated and compared the effect of medical and surgical treatment of CRS on QoL (Ragab et al., 2010). The study was conducted on ninety CRS patients with and without polyps randomized into medical and surgical groups. The medical group was treated with erythromycin (12 week course), alkaline nasal douches and intranasal steroids. In addition, 3 patients with polyps were prescribed a course of short-term oral steroids. The extent of endoscopic sinus surgery was tailored to the extent of the disease in the surgical group. Following ESS, all patients were prescribed a two-week course of erythromycin and alkaline douches and intranasal steroids as long-term therapy. Quality of life was assessed using the disease specific instrument SNOT-22 and the general health instrument SF-36 before randomization and after 6 and 12 months. A significant improvement in the SNOT score was recorded, without statistically significant difference between medical and surgical group after 6 and 12 month. Also, the SF-36 demonstrated a significant improvement in the QoL in seven out of eight domains. Only physical functioning did not change significantly from the baseline. Furthermore this study does not support the fact that polyps represent a poor prognostic factor for efficacy of treatment, as has been suggested in previous studies (Kennedy, 1992; Sobol et al., 1998).

In conclusion, the presented data provides evidence that both maximal medical and surgical therapy improve the QoL of CRS patients. CRS should be targeted with maximal medical therapy as the first step and surgery should be reserved for refractory cases.

5. The correlation between quality of life and the results of other measurements in chronic rhinosinusitis

The relationship between health-related QoL and the results of other examinations of CRS is not entirely clear. Although we might intuitively expect that patients with worse CT and endoscopic findings would have a lower quality of life, results of available studies do not confirm this fact. Also, the influence of CRS symptoms on QoL, relative to treatment, cannot be predicted from endoscopic or CT scores.

The lack of correlation between objective assessment and subjective perception of QoL is not unique to CRS, but can also be seen in such disorders as bronchial asthma, obstructive sleep apnea and low back pain (Soler & Smith 2010).

5.1 Imaging methods

Bhattacharyya et al. failed to demonstrate a correlation between CT scores and the SNOT-20 (Bhattacharyya et al., 1997) in 221 patients referred for CT scans.

Wabnitz et al. failed to demonstrate a significant correlation between CT scores based on the commonly used Lund-Mackay staging (score range 0-24) and the SNOT-20 QoL questionnaire in 221 patients indicated for CRS surgery; the study also found no correlation between the SNOT-20 and symptom scores (visual analog scale-VAS) (Wabnitz et al., 2005).

In a study by Holbrook et al., they tried to correlate the RSOM-31 questionnaire and the Lund Mackay CT scores. In this study patients were also asked to locate their sinus pain and pressure. The study was not able to demostrate a correlation between QoL scores and CT findings or between CT findings and areas of facial pain (Holbrook et al., 2005).

Hopkins et al. found a small, clinically insignificant association between Lund-Mackay scores and SNOT-22. In the study, CT findings from 1840 patients with CRS were reviewed and the results were consistent with the above mentioned studies. In this study, a small but significant association between CT scores and postoperative improvement on the SNOT-22 was found, which indicates that patients with lower preoperative CT scores benefit more from surgical treatment (Hopkins et al., 2007).

In conclusion CT scans measure a different aspect of CRS than QoL and, of itself, cannot be an indication for surgery. It is necessary for preoperative assessment of the extent of disease and identification of anatomical landmarks, but it should not be used for prediction or localization of CRS symptoms.

5.2 Rhinoendoscopy

A varying degree of correlation has been shown between improvement of sinonasal symptoms and results from endoscopic examinations after ESS (Giger et al., 2004; Wright & Agrawal, 2007).

Wright et al. showed a slight correlation between endoscopic scores based on the Lund-Kennedy and Sinus Symptom Questionnaire, 1, 3 and 6 months after ESS. However, this study did not show a significant correlation between postoperative endoscopic examination and the CSS (Wright & Agrawal, 2007). Studies evaluating the effect of non-surgical treatment also demonstrated no correlation between RSDI and endoscopic scores (Birch et al., 2001).

A recent study by Mace et al. focused on the correlation between endoscopic scores and HRQOL in patients after ESS. This study evaluated the results of endoscopic scores based on the Lund-Kennedy (score range 0 – 20) and two HRQoL questionnaires, RSDI, and CSS, in 102 patients preoperatively and 12 months after ESS. Changes in endoscopic scores were significantly correlated with improvement in RSDI total scores, physical RSDI subscale scores and functional RSDI subscale scores and CSS symptom scores. On the contrary, no correlation was observed among RSDI emotional subscale scores and CSS medication subscale scores and CSS total scores. When the groups of patients with and without nasal polyps (NP) were assessed separately, patients with CRS + NP (36 patients) demonstrated a significantly stronger correlation. In contrast, the group of patients without NP demonstrated no correlation between improved endoscopic scores and any of the HRQoL instruments. The authors concluded that the reason for the significant increase in quality of life in patients with NP was related to improvement in nasal breathing, olfaction, and relief of the facial pressure. The results of multivariate modeling used in this study revealed that the amount of improvement on the HRQoL can be explained by relatively small improvements on the endoscopic score. For example, with a single point improvement in the endoscopic score, RSDI total scores would be expected to improve by 1.03 units (Mace et al., 2010).

In conclusion the improvement on HRQoL is a complex process that cannot be explained only by improved endoscopic findings.

5.3 Histopathologic findings

The studies in this issue are focused primarily on the correlation between eosinophilic inflammation of the paranasal sinus mucosa and other parameters indicative of disease severity (particularly CT scan, endoscopy, examination of olfaction). The presence of eosinophilic inflammation, defines a subgroup of CRS, which is refractory to conservative and surgical treatment and knowledge of the eosinophilic status can provide information regarding the severity of the disease and help in choosing an appropriate treatment strategy.

Studies by Kountakis and Baudoin failed to demonstrate a correlation between the eosinophil count and the severity of CRS symptoms (Kountakis et al., 2004; Baudoin et al., 2006).

Soler et al. showed mucosal eosinophilia correlated with disease severity expressed by CT, endoscopy and Smell Identification Test (SIT). In contrast to this finding, they did not demonstrate a correlation between eosinophilia and two disease-specific QoL questionnaires (RSDI, CSS) or with the general QoL instrument, Short Form Health Survey, SF-36. Moreover, the study showed no correlation between QoL and any other cell, stromal and epithelial marker of inflammation (Soler et al., 2009).

Another study by Soler et al. focused on the comparison of quality of life in patients with and without eosinophilia after ESS. In accordance with the previous study, no baseline differences were observed for any QoL Instrument (RSDI, CSS, SF-36) between patients with and without eosinophilia. Although both groups showed improved quality of life after surgery, a clear trend towards less improvement in patients with eosinophilia was observed (Soler et al., 2010).

A recent study by Hai (Hai et al., 2010) indicated that patients with biofilm CRS significantly improved their QoL after ESS, however the degree of biofilm reduction did not correlate with QoL.

From the above, the QoL measurement, in the context of histopathological findings, again shows some differences between other parameters, which are often used as indicators of disease severity.

5.4 Olfactory function

It is generally considered that the loss of smell, a typical CRS symptom, significantly contributes to reduced quality of life (Deems et al., 1991; Temmel et al., 2002; Miwa et al., 2001; Bramerson et al., 2007). From this perspective, the work of Litvack et al., which deals with correlations of olfaction disturbances with other parameters of CRS severity, is interesting. Not surprisingly, endoscopic and CT scores correlated moderately with olfactory scores. In contrast, however, there was no correlation between olfactory function and disease-specific (RSDI, CSS) QoL questionnaires or the general health-related (SF-36) QoL questionnaire (Litvack et al., 2009). In this particular study the reason for these results may be the relatively limited ability of the selected questionnaires to assess olfactory function. Neither the CSS nor the SF-36 contains any questions regarding olfaction, and only one question on the RSDI addresses this issue. A similar deficiency can be found in other CRS-specific validated instruments including the RSOM and SNOT-20.

5.5 Mucociliary transport

It can be assumed that improved mucociliary transport should positively affect the symptoms of CRS. Boatsman et al. conducted a study that examined the correlation between the results of SNOT-20 and the saccharine test of mucociliary transport. In this study no significant correlation between the parameters was demonstrated. Moreover, no correlation between the individual domain scores and mucociliary clearance time was shown (Boatsman et al. 2006).

Similar research by Naxakis, also failed to demonstrate a correlation between mucociliary velocity, and QoL (SNOT-20) in patients after surgical and conservative treatment of CRS (Naxakis et al., 2009).

Clinicians are used to basing their diagnostic and therapeutic decisions on the results of objective tests, particularly CT and endoscopic findings while letting patient specific symptoms slip into the background. It is important to realize, however, that it is the symptoms that force patients to seek medical care and it is the symptoms of CRS that significantly influence and reduce their quality of life. The above listed data clearly shows that quality of life is a unique, multidimensional tool that can be used to assess the severity

of the disease. The relationship between QoL measured results and results of other "objective" investigations clearly supports the fact that QoL evaluation measures different aspects of the disease.

6. Barriers and limitations of the quality of life measurement

Despite the undeniable benefit of evaluating the quality of life in diagnosis and treatment of CRS, there are some opposition regarding the routine use of this tool in clinical practice. Specific objections include:

Measurement of QoL takes too much time

Completing the most frequently used questionnaire takes less than 10 minutes. When the patient takes the questionnaire for the first time, it is necessary to educate them; therefore, the first measurement may take a little longer. The time devoted to patient instruction will be appreciated during repeated examinations, which are usually less time consuming. Inclusion of QoL measurements in routine practice is also a function of organization; it is time-effective, for example, to ask patients to fill out the questionnaire while they are waiting to be seen.

Examination of quality of life is too subjective and therefore unreliable

Outcomes rated by a clinician may be thought to be more reliable than measures rated by a patient. However, we should realize that grading of the symptoms by a clinician is prone to error. A study comparing the severity of a disease from the patient's viewpoint vs. a doctor's viewpoint, demonstrated that patients evaluate their condition as being more serious (Scadding & Wiliams, 2008); 124 patients with allergic rhinitis participated in the study; however, it can be assumed that similar results would be observed in patients with CRS as well.

We should always keep in mind that it is the symptoms that reduce the quality of life for the patient, and it is the symptoms that motivate the patient to see the doctor; no one else other than the patients, is more competent to comment on how they perceive their symptoms and how the symptoms impact their life.

The results of QoL measurements do not correlate with outcomes of objective tests

As already mentioned the evaluation of quality of life evaluates a different aspect of the disease. Symptoms and QoL are the result of interactions between many factors, of which, measurable biological and physiological variables are only a part (Figure 6) (Wilson & Clearly, 1995). For these same reasons, measurement of QoL cannot serve as a predictor of treatment outcomes.

Limitations of QoL measurements

It should be emphasized that QoL measurement is only a part of the rhinology examination and cannot substitute for other tests. For instance, a preoperative CT scan is always necessary, as well as imaging in cases of impending complication from sinusitis, which may endanger the patient's life while causing relatively minor subjective complaints. Surgery to improve nasal patency should be always associated with an objective parameter (rhinomanometry, inspiratory peak flow) and so on.

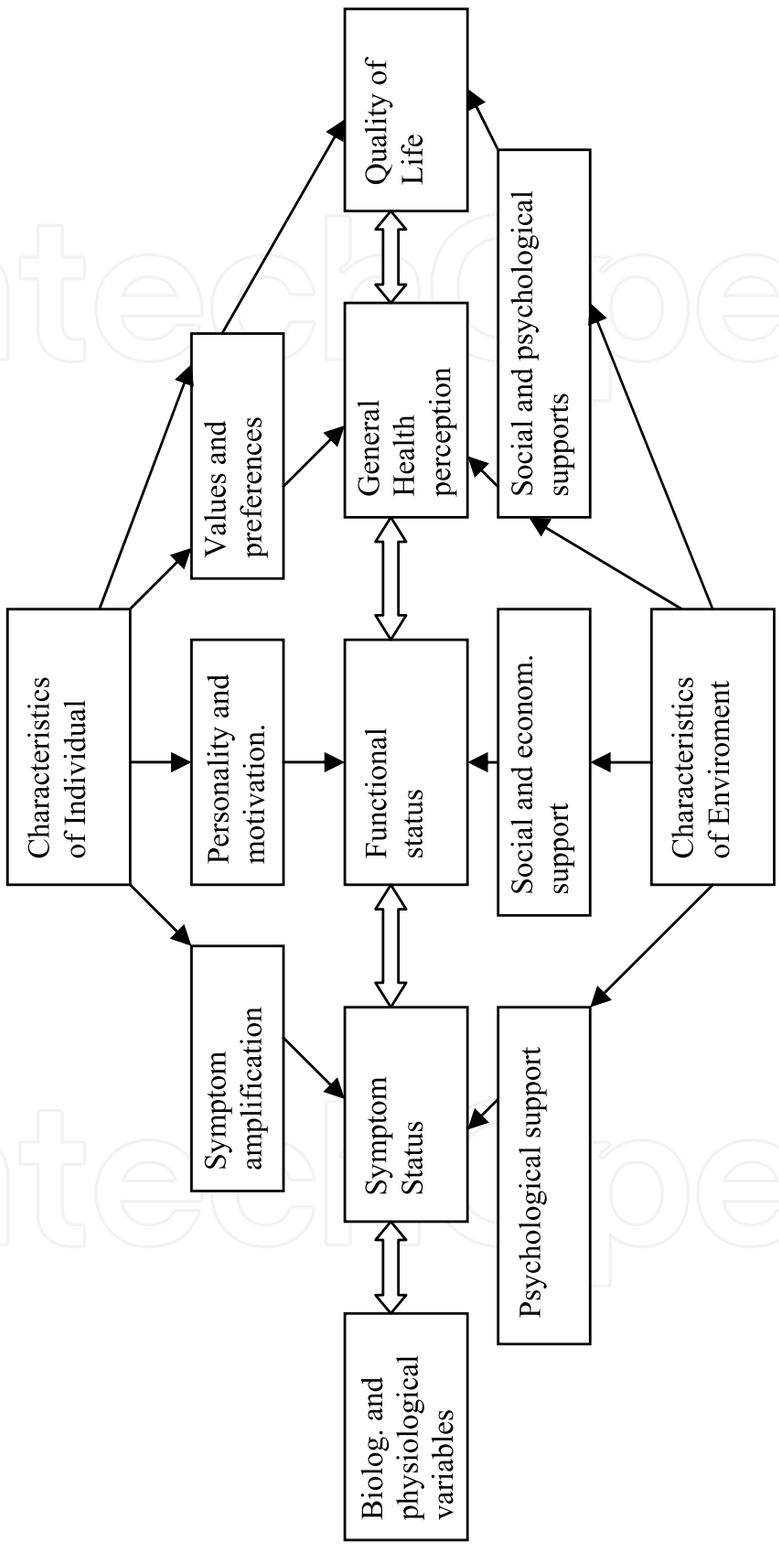


Fig. 6. Interactions between factors influencing quality of life (Wilson & Clearly, 1995)

7. Conclusion

CRS is a disease with a high incidence, which significantly affects the quality of life. Quality of life of patients is negatively influenced not only by CRS symptoms (nasal congestion, discharge, facial pain and pressure, headache, anosmia), but it is also accompanied by elevated rates of depression, anxiety, sexual and sleep disturbances and fatigue. The primary interest of treatment of rhinologic diseases is to improve the quality of life of patients.

In the last two decades there has been a significant increase in interest in measuring quality of life using specially developed, validated questionnaires. These tools allow the patient to express how CSR affects their daily life. In addition, by measuring the quality of life, we can evaluate the effect of treatment or compare different treatment methods.

Quality of life is the result of interactions among many factors and "measurable" biological and physiological factors are only part of the QoL equation. It is therefore not surprising that the quality of life does not always correlate with results of other tests that we perform on CRS patients.

The available data shows that both conservative and surgical treatments lead to improvement in the quality of life.

We can conclude by saying that measurement of quality of life should become a routine part of our everyday practice and the results should be considered in context with other indicators of disease severity. Moreover, in some countries, the data obtained by measuring the quality of life of CRS patients may be compulsory for use in evaluating treatment effectiveness and can thus influence payments to medical care providers.

8. Abbreviations

CRS	Chronic Rhinosinusitis
CSS	Chronic Sinusitis Survey
ESS	Endoscopic Sinus Surgery
GBI	Glasgow Benefit Inventory
HRQoL	Health-related Quality of Life
NP	Nasal Polyposis
QoL	Quality of Life
RhinoQoL	Rhinosinusitis Quality of Life Survey
RSOM	Rhinosinusitis Outcome Measures
RSDI	Rhinosinusitis Disability Index
RSI	Rhinosinusitis Symptom Inventory
SF-12	Short Form 12 Health Instrument
SF-36	Short Form 36 Health Survey
SNOT	Sinonasal Outcome Test
SRM	Standardized Response Mean

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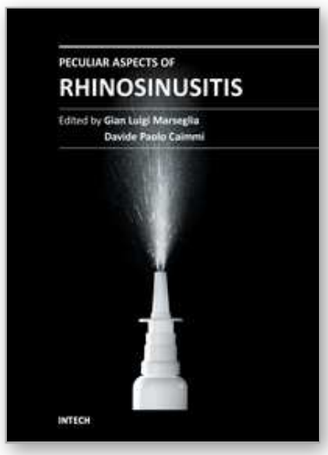
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Rhinosinusitis has both a great practical interest and a broad significance due to the scientific complexity of the pathogenetic problems related to the disease, not yet completely resolved, and their implications for clinical treatment. This book highlights certain specific topics that usually are not clarified in other resources. The first chapter is devoted to the impoverished quality of life experienced by patients suffering from rhinosinusitis. The second chapter focuses on the microbiological aspects of rhinosinusitis, while the two subsequent chapters explain the peculiar aspects of chronic rhinosinusitis and of recurrent chronic rhinosinusitis. The first chapter of the second section of the book is dedicated to the imaging techniques used to visualize the nasal sinuses and the other to a medical topical type of treatment.

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