

Evaluation of chronic rhinosinusitis management using the SNOT-22 in adult cystic fibrosis patients

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Abstract. – OBJECTIVES: Sinonasal disease (SND) is a common finding in subjects with Cystic Fibrosis (CF). Even though it does not play a key role in the life expectancy of these patients, it increases the morbidity rate of CF, with deterioration of the quality of life and of general health status. The aim of this study is the evaluation of the impact of sinonasal disease and Extensive Endoscopic Sinus Surgery (eESS) on the quality of life (QoL) of CF patients by means of the 22 item Sino-Nasal Outcome Test (SNOT-22) and define if there is a correlation between SNOT-22 and the Lund-Mackay score.

PATIENTS AND METHODS: We performed a prospective study in 33 CF patients with medically refractory SND. The extent of polyposis was graded both endoscopically and on computed tomography images in accordance with the Lund-Mackay score. All patients underwent eESS. The SNOT was administered in order to assess the quality of life related to SND both before surgery and during follow-up at 6 months, 1 year and 2 years postoperatively.

RESULTS: The SNOT-22 and Lund-Mackay score showed a remarkable mean improvement during follow-up. The differences between the initial examination and last score were significant ($p < 0.001$), but there was no statistic correlation between SNOT-22 and Lund-Mackay.

CONCLUSIONS: More attention should be paid to sinonasal symptoms in CF patients and SNOT-22 is a simple and effective tool for this purpose. This score is also important for indicating the outcome of the eESS procedure. In all patients SNOT showed a significant improvement in QoL.

Key Words:

Cystic fibrosis, Chronic rhinosinusitis, QoL (Quality of life), SNOT-22 (Sino-Nasal Outcome Test), Lund-Mackay staging, eESS (Extensive endoscopic sinus surgery).

Introduction

Cystic fibrosis (CF) is the most frequent autosomal recessive disease affecting Caucasians, with an incidence of 1:2500-3000 healthy new-

borns^{1,2}. The incidence in Italy is approximately 1:-3400, with an estimated carrier rate of 1-27^{3,4}.

The involvement of the paranasal sinus in CF is almost universal⁵⁻⁷, especially involvement of the anterior (100% of cases) and posterior (57% of cases) sinus compartment⁸. Chronic rhinosinusitis (CRS), with or without nasal polyposis, usually occurs in adult patient with CF with a prevalence varying between 90-100%⁹. The pathogenesis of sinonasal disease in CF is due mainly to the visco-elastic properties of the mucus and to the impaired mucociliary clearance which contribute to the mechanical obstruction of the sinuses. Furthermore, the ciliary dysfunction and consequent stasis of thick mucus lead to CRS. Nasal polyps may originate from multifocal benign inflammatory transformation of the sinus mucosa^{10,11}, and their histopathology shows infiltration by neutrophils rather than by eosinophils^{10,11}.

Sinonasal disease is a source of significant morbidity in CF, even if only relatively few patients complains of symptoms.

The treatment of sinonasal disease has progressed significantly over recent years thanks to an increase in the use of endoscopic endonasal surgical procedures, which have proved to be safe when performed in specialized centres with a team of paediatricians, pulmonologists, and infectious disease specialists^{10,12,13}.

Although neither medical nor surgical treatment on their own are able to achieve complete remission, extensive endoscopic sinus surgery (eESS) plus medical treatment represents an essential approach to sinonasal disease in CF resulting in an improvement in symptoms and a drastic reduction in recurrences^{10,12,13}.

Several studies have attempted to correlate CT findings with symptoms using different symptom scales in patients suffering from CRS without CF and immunodeficiency^{11,14,15}.

A number of questionnaires have been developed and validated to assess QoL in adults with

chronic rhinosinusitis¹⁶⁾ The most popular of these are the rhinosinusitis disability index (RSDI)¹¹ the 16¹⁷-20¹⁸ and 22¹⁹-items sino-nasal outcome test (SNOT) and the visual analogic scale (VAS)¹¹.

However, no significant correlation between CT score calculated by Lund Mackay^{11,14,15} or Nair¹⁴ system and symptoms as well as culture and surgical findings were observed²⁰⁻²³.

The latter is a patient reported measure of outcome developed for use in CRS with or without nasal polyposis. It consists of 22 items and is a modification of SNOT-20. It covers a broad range of health and health-related quality of life issues including "physical problems, functional limitations and emotional consequences". In addition to the normal 20-item version of the score, another two items were measured: nasal blockage, and loss of sense of taste and smell¹⁹. Moreover, to our knowledge, the correlation between the degree and severity of symptoms and radiological score was not assessed in any CF adult series complicated by CRS.

The aim of our report was to evaluate the impact of eESS on QoL in a group of CF adult patients affected by CRS using SNOT-22 and comparing it with the Lund-Mackay score.

Patients and Methods

This prospective study group consisted of 33 patients with cystic fibrosis (21 males and 12 females, M:F 1.75:1; mean age 32 yrs; range 18-46 yrs). All subjects had chronic rhinosinusitis (CRS) and nasal polyposis. All patients underwent surgery in the ENT division of the Department of Pediatrics of "Sapienza" University of Rome between 2006 and 2009.

Patients previously operated on were excluded from the study.

The diagnosis of CF was confirmed by constantly high values in sweat sodium or sweat chloride test results and by an analysis of mutations in the cystic fibrosis transmembrane regulator (*CFTR*) gene as set out in the Cystic Fibrosis Foundation (CFF) guidelines²⁴.

In all of the patients rigid or flexible videonasendoscopy and computed tomography (CT) of the paranasal sinuses without contrast medium were performed through volume acquisition and multiplanar reconstruction with bone algorithm. These techniques enabled us to calculate the endoscopic score and radiological grade according to the Lund-Mackay staging system^{11,20,21}.

Finally, the Sino-Nasal Outcome Test (SNOT-22 test)¹⁹ was used to assess the QoL related to sinonasal disease. The patient were asked to score a list of 22 symptoms, social and emotional consequences.

Outcomes were graded as 0 (no problem), 1 (very mild problem), 2 (mild or slight problem), 3 (moderate problem), 4 (severe problem), or 5 (problem as bad as it could be). The list included: need to blow nose, sneezing, dripping nose, cough, postnasal drip, dense nasal drip, ear fullness, dizziness, ear pain, facial pain/pressure, difficulty falling asleep, wake up at night, lack of a good night's sleep, wake up tired, fatigue, reduced productivity, reduced concentration, frustrated/restless/irritable, sad, embarrassed, decrease in smell and taste, nasal obstruction.

The symptom and Lund-Mackay scores were evaluated preoperatively and again after 6 months, 1 and 2 years.

Statistical Analysis

The mean scores, standard deviations of the SNOT-22 and Lund-Mackay were calculated. Differences in means were verified using the two-sided T test; *p*-values have been adjusted for multiplicity through Bonferroni correction²⁵, and we report an adjusted *p*-value, so that an adjusted *p* < 0.05 can be deemed to be statistically significant. Finally, the statistical relationship between SNOT-22 and Lund-Mackay scoring system was evaluated using the Spearman correlation index.

Results

The correlation of each item with the total SNOT-22 is reported in Table I.

At the initial check-up, the mean final SNOT-22 score was 30.5 ± 14.5 versus 12.2 ± 6.4, 13.6 ± 6.3; and 13.8 ± 7.2 after 6 months, 1 year and 2 years respectively. A remarkable improvement in mean scores, between the pre and postoperative values, was observed, although the overall improvement declined over time, increasing the mean SNOT-22 scores. In order to evaluate whether the improvements observed between the initial and follow-up visits were statistically significant, Student's t-test was applied to the mean scores and was significant for all of the follow-up visits (*p* < 0.001).

Table I. SNOT-22 pre-operative visit. 6 months. 1 and 2 years individual item and total scores.

	Preoperative		6 months		1 Year		2 Years	
	MEAN	SD	MEAN	SD	MEAN	SD	MEAN	SD
Need to blow nose	2.6	1.3	1.2	1.0	1.2	1.1	1.3	1.2
Sneezing	1.1	1.3	0.6	0.9	0.6	0.8	0.6	0.9
Dripping nose	2.1	1.6	0.7	0.6	0.8	0.8	0.8	0.8
Cough	2.5	1.6	1.4	1.4	1.6	1.5	1.7	1.5
Postnasal drip	2.1	1.5	1.0	1.2	0.9	1.0	1.1	1.2
Dense nasal drip	2.7	1.5	1.2	1.1	1.2	1.0	1.3	1.2
Ear fullness	0.7	1.4	0.1	0.3	0.1	0.4	0.1	0.5
Dizziness	0.3	0.8	0.1	0.4	0.1	0.3	0.1	0.4
Ear pain	0.4	1.0	0.1	0.4	0.2	0.6	0.2	0.6
Facial pain/pressure	1.8	1.8	0.5	0.7	0.7	0.8	0.6	0.9
Difficulty falling asleep	0.5	1.4	0.0	0.0	0.0	0.2	0.0	0.0
Wake up at night	1.0	1.7	0.2	0.8	0.3	0.9	0.3	0.9
Lack of a good night's sleep	0.6	1.2	0.2	0.6	0.3	0.7	0.3	0.7
Wake up tired	0.4	1.0	0.0	0.2	0.1	0.4	0.1	0.4
Fatigue	1.1	1.5	0.6	1.1	0.8	1.1	0.7	1.1
Reduced productivity	0.5	1.2	0.1	0.4	0.1	0.4	0.1	0.4
Reduced concentration	0.9	1.5	0.5	1.0	0.6	1.0	0.5	1.0
Frustrated/restless/irritable	1.4	1.7	1.0	1.3	0.9	1.1	1.0	1.3
Sad	0.7	1.4	0.5	0.9	0.4	0.9	0.5	1.0
Embarassed	0.3	0.8	0.1	0.4	0.1	0.3	0.1	0.4
Decrease in smell and taste	2.9	2.1	0.9	1.0	1.5	1.5	1.3	1.5
Nasal obstruction	3.9	1.4	1.1	1.0	1.1	0.8	1.1	1.0
Tot.	30.5	14.5	12.2	6.4	13.6	6.3	13.8	7.2

At the initial examination, a higher score was observed in 6 items (nasal obstruction, decrease in smell and taste, dense nasal drip, post-nasal drip, need to blow nose, dripping nose, cough). Only 4 of these items showed a significant improvement ($p < 0.001$): need to blow nose, dripping nose, dense nasal drip, nasal obstruction (Table II). The remaining items had lower mean scores ranging from 1.8 to 0.3. They remained not statistically significant throughout the entire follow-up.

The distribution of the Lund-MacKay stage is shown in Table II. The mean score \pm the standard deviations at the initial examination and after 6 months, 1 year, and 2 years were 18.0 ± 4.4 ; 6.9 ± 3.0 ; 7.3 ± 3.0 ; and 7.8 ± 4.3 respectively. The differences between the initial score and later scores were significant ($p < 0.001$).

Although both SNOT-22 and Lund-Mackay showed a significant postoperative improvement, they did not correlate statistically. The data of the Spearman correlation index were not significant throughout the whole follow-up period (preoperative $\text{cor} = 0.12$ and $p = 0.46$; after surgery at 6 months $\text{cor} = 0.07$ and $p = 0.66$; at 1 year $\text{cor} = 0.09$ and $p = 0.59$; at 2 years $\text{cor} = 0.03$ and $p = 0.86$).

Table II. Differences between the initial (t0) score and later scores (6m: 6 months; 1y: 1 year; 2y: 2 years).

Item	t0v6m	t0v1y	t0v2y
1 Need to blow nose	0.00	0.01	0.03
2 Sneezing	1.00	1.00	1.00
3 Dripping nose	0.00	0.02	0.02
4 cough	0.80	1.00	1.00
5 Postnasal drip	0.34	0.07	0.74
6 Dense nasal drip	0.01	0.00	0.03
7 Ear fullness	1.00	1.00	1.00
8 Dizziness	1.00	1.00	1.00
9 Ear pain	1.00	1.00	1.00
10 Facial pain/pressure	0.03	0.24	0.15
11 Difficulty falling asleep	0.98	1.00	0.98
12 Wake up at night	1.00	1.00	1.00
13 Lack of a good nights sleep	1.00	1.00	1.00
14 Wake up tired	1.00	1.00	1.00
15 Fatigue	1.00	1.00	1.00
16 Reduced productivity	1.00	1.00	1.00
17 Reduced concentration	1.00	1.00	1.00
18 Frustrated/restless/irritable	1.00	1.00	1.00
19 Sad	1.00	1.00	1.00
20 Embarassed	1.00	1.00	1.00
21 Decrease in smell and taste	0.00	0.51	0.15
22 Nasal obstruction	0.00	0.00	0.00

For each Lund's unit of decrement compared to baseline SNOT decrease of 0.03 with $p = 0.67$ (statistically not significant).

Discussion

It is well known that CF complicated by CRS represents a great challenge in the overall management of these patients. The importance of this topic is demonstrated by the increasing number of papers devoted to its study. Intense investigations were specifically designed to analyze the clinical and QoL evolution of this subtype of CRS, particularly in the light of the introduction of ESS into surgical practice. In addition, the improved life expectancy has been another important impulse in this direction. There is no doubt that nasal polyposis has a negative impact on disease remission and the need for re-interventions. Some authors observed that polyposis recurred in a series of adults with more clearly worsening findings^{26,27}.

In the literature, several outcome measures for this topic have been proposed, including the rhinosinusitis quality of life questionnaire, the chronic sinusitis survey, the symptom score instrument, and the rhinosinusitis disability index¹⁶⁻¹⁹. We adopted the SNOT to analyze our current series because it is reliable in routine clinical practice and, more importantly, it is easily understandable by the patients. We considered the SNOT-22 to be more suitable than the SNOT-20 because the extra two symptoms (nasal obstruction and the loss of taste and smell) were important for assessing the patients' QoL. To our knowledge no other studies used this type of questionnaire for evaluating adult patients with CF. The data that emerged from our experience are in general agreement with previously reported series employing other tools. The positive impact of surgery on the postoperative SNOT-22 score should be emphasized. ESS was well tolerated by CF patients. Although significant improvements during the entire period of follow-up were observed confirming the effectiveness of treatment on the QoL of CF patients, there was a clear and constant worsening of the symptom scores. The analysis of the single items confirmed this trend. Four items showed a statistically significant postoperative improvement.

Note that one of these symptoms (nasal obstruction) is only taken into consideration by SNOT-22. This allowed us to focus on this spe-

cific symptomatic aspect. The remaining items were statistically not significant throughout the entire follow-up. These observations confirmed that SNOT-22 is a valid indicator of ESS outcomes for adult patients undergoing sinonasal surgery due to CRS and nasal polyposis, as stated by Hopkins et al¹⁹.

Many studies have reported a possible correlation between the Lund-Mackay and the symptom score^{11,14,15} but their results are controversial. In fact, some authors indicate a significant relationship while others failed to detect it. Our findings confirm these latter results. These data indicate that a significant improvement in the objective findings (Lund-Mackay score) was not followed by an analogous improvement in the subjective responses (SNOT-22). Hence, the behavior of clinical signs was not directly proportional to that of symptoms.

Clinically, our data suggest that these patients require adequate support during the consultation phase to reduce their psychological discomfort given the troublesome potential complications and the need for repeated surgeries.

The ultimate shortcoming is, of course, the small number of patients in our series and the limited period of follow-up. Future prospective studies must include long-term surgical outcomes in larger series enrolled from more than one geographical regions of our country.

Conclusions

The SNOT-22 showed an improvement in symptoms resulting in a better quality of life.

It can be used to facilitate routine clinical practice to highlight the impact of CRS on the quality of life of patients with CF.

It is also a valid indicator for measuring the outcome of surgical intervention.

The behavior of the clinical signs measured using the Lund-Mackay score was not directly proportional to that of the SNOT-22.

Table III. Mean Lund-Mackay staging change score.

Lund-Mackay staging	Mean	SD
Preoperative	18.0	4.4
6 months	6.9	3.0
1 year	7.3	3.0
2 years	7.8	4.3

Conflict of Interest

The Authors declare that there are no conflicts of interest.

References

- 1) WELSH MJ, TSUI LC, BOAT TF, BEAUDER AL. The metabolic and molecular basis of inherited diseases. Volume 3. 7th ed. New York: McGraw-Hill, 1995; pp. 3799-3876.
- 2) SAKANO E, RIBEIRO A, BARTH L, CONDINO NETO A, RIBEIRO JD. Nasal and paranasal sinus endoscopy, computed tomography and microbiology of upper airways and the correlations with genotype and severity of cystic fibrosis. *Int J Pediatr Otorhinolaryngol* 2007; 71: 41-50.
- 3) BOSSI A. Report 2004 del Registro Italiano Fibrosi Cistica. *Orizzonti FC* 2006; 2: 4-28.
- 4) PIGNATTI PF, MASTELLA G. FIBROSI CISTICA. IN: CAO A, DALLAPICCOLA B, NOTARANGELO LD *Malattie Genetiche, Molecole e Geni*. Padova: Piccin Editore, 2004; pp. 195-228.
- 5) SLIEKER MG, SCHILDER AG, UITERWAAL CS, VAN DER ENT CK. Children with Cystic Fibrosis. Who should visit the otorhinolaryngologist. *Arch Otolaryngol Head Neck Surg* 2002; 128: 1245-1248.
- 6) YANKASKAS JR, MARSHALL BC, SUFIAN B. Cystic Fibrosis Adult Care – Consensus Conference Report. *Chest* 2004; 125: 1s-39s.
- 7) GIBSON RL, BURNS JL, RAMSEY BW. Pathophysiology and management of pulmonary infections in cystic fibrosis. *Am J Respir Crit Care Med* 2003; 168: 918-951.
- 8) BRIHAYE P, CLEMENT PAR, DAB I, DESPRECHIN B. Pathological changes of the lateral nasal wall in patients with cystic fibrosis (mucoviscidosis). *Pediatr Otorhinolaryngol* 1994; 28: 141-147.
- 9) 9-RYAN MW. Diseases associated with chronic rhinosinusitis: what is the significance? *Curr Opin Otolaryngol Head Neck Surg* 2008; 16:231-236.
- 10) CROCKETT DM, MCGILL TJ, HEALY GB, FRIEDMAN EM, SALKELD LJ. Nasal and paranasal sinus surgery in children with cystic fibrosis. *Ann Otol Rhinol Laryngol* 1987;96: 367-72.
- 11) FOKKENS W, LUND V, MULLOL J; European position paper on rhinosinusitis and nasal polyps 2007. European Position Paper on Rhinosinusitis and Nasal Polyps group. *Rhinol Suppl* 2007; 20: 1-136.
- 12) KINGDOM TT, LEE KC, FITZSIMMONS SC, GROPP GJ. Clinical characteristics and genotype analysis of patients with cystic fibrosis and nasal polyposis requiring surgery. *Arch Otolaryngol Head Neck Surg* 1996; 122: 1209-1213.
- 13) SHATZ A. Management of recurrent sinus disease in children with cystic fibrosis: A combined approach. *Otolaryngol Head Neck Surg* 2006; 135: 248-252.
- 14) NAIR S. Correlation between symptoms and radiological findings in patients of chronic rhinosinusitis: a modified radiological typing score. *Rhinology* 2009; 47: 181-186.
- 15) ZHENG Y, ZHAO Y, LV D, LIU Y, QIAO X, AN P, WANG D. Correlation between computed tomography staging and quality of life instruments in patients with chronic rhinosinusitis. *Am J Rhinol. Allergy* 2010; 24: e41-45.
- 16) ALOBID I, BERNAL-SPREKELSEN M, MULLOL J. Chronic rhinosinusitis and nasal polyps: the role of generic and specific questionnaires on assessing its impact on patient's quality of life. *Allergy* 2008; 63: 1267-1279.
- 17) ANDERSON ER. Clinimetric evaluation of the sinonasal outcome test-16. *Otolaryngol Head Neck Surg* 1999; 121: 702-707.
- 18) PICCIRILLO JF, MERRITT MG JR, RICHARDS ML. Psychometric and clinimetric validity of the 20-Item Sino-Nasal Outcome Test (SNOT-20). *Otolaryngol Head Neck Surg* 2002; 126: 41-47.
- 19) HOPKINS C, GILLET S, SLACK R, LUND VJ, BROWNE JP. Psychometric validity of the 22-item Sinonasal Outcome Test. *Clin Otolaryngol* 2009; 34: 447-454.
- 20) HOPKINS C, BROWNE JP, SLACK R, LUND V, BROWN P. The Lund-Mackay staging system for chronic rhinosinusitis: how is it used and what does it predict? *Otolaryngol Head Neck Surg* 2007; 137: 555-561.
- 21) HOPKINS C, BROWNE JP, SLACK R, LUND V, TOPHAM J, REEVES B, COPLEY L, BROWN P, VAN DER MEULEN J. The national comparative audit of surgery for nasal polyposis and chronic rhinosinusitis. *Clin Otolaryngol* 2006; 31: 390-398.
- 22) JONES JW, PARSON DS, CUYLER JP. The results of functional endoscopic sinus (FES) surgery of the symptoms of patients with cystic fibrosis. *Int J Pediatr Otorhinolaryngol* 1993; 28: 25-32.
- 23) KHALID NA, MACE J, SMITH T. Outcomes of sinus surgery in adults with cystic fibrosis. *Otolaryngol Head Neck Surg* 2009; 141: 358-363.
- 24) Cystic Fibrosis Foundation, Clinical practice guidelines for cystic fibrosis, Bethesda, Maryland, 1997.
- 25) FARCOMENI A. A review of modern multiple hypothesis testing, with particular attention to the false discovery proportion, *Stat Meth Med Res* 2008; 17: 347-388.
- 26) KECK T., ROZSASI A. Medium-term Symptom outcome after paranasal sinus surgery in children and young adults with cystic fibrosis. *Laryngoscope* 2007; 117: 475-479.
- 27) ROWE-JONES JM, MACKAY IS. Endoscopic sinus surgery in the treatment of cystic fibrosis with nasal polyposis. *Laryngoscope* 1996; 106: 1540-1544.