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Rhinology

Prognostic value of the Sinonasal Outcome Test 22 (SNOT-22) in chronic rhinosinusitis

Valore prognostico del Sinonasal Outcome Test 22 (SNOT-22) nella rinosinusite cronica

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SUMMARY

Previous studies have highlighted that baseline Sinonasal Outcome Test 22 (SNOT-22) score affects surgical outcomes in chronic rhinosinusitis (CRS) and suggested that a SNOT-22-based approach might ameliorate patients' understanding of expectations after treatment. Our study aimed at verifying this hypothesis in an Italian CRS population. In 457 CRS patients treated with endoscopic sinus surgery after failure of maximal medical therapy, the percentage of achieving a minimal clinically important difference (MCID) and the percentage of relative improvement after surgery were calculated. Moreover, the impact of several factors on preoperative and postoperative SNOT-22 score was investigated. Symptom improvement occurred in the majority of patients and was directly proportional to baseline SNOT-22. 79,7% of patients achieved the MCID and the percentage of relative improvement was 50,1%. Psychological and social-functioning implications significantly affected SNOT-22 scores. Multiple regression analysis showed that history of previous surgery, asthma, preoperative endoscopic and SNOT-22 scores predicted the postoperative SNOT-22 score (R2 = 0,298). Submitting CRS patients to SNOT-22 prior to surgical treatments might help to inform about probable outcomes, although it is strongly influenced by individual perception. Further studies are needed to identify an effective set of subjective and objective parameters for evaluation of outcomes.

KEY WORDS: Sinonasal Outcome Test-22 (SNOT-22), chronic rhinosinusitis, endoscopic sinus surgery, outcome prediction, quality of life

RIASSUNTO

Studi in letteratura hanno evidenziato che il punteggio basale del Sinonasal Outcome Test 22 (SNOT-22) influenza l'outcome chirurgico nella rinosinusite cronica (CRS) ed hanno suggerito che un approccio SNOT-22-mediato potrebbe migliorare la comprensione delle aspettative dei pazienti dopo il trattamento. Il presente studio mirava a verificare questa ipotesi in una popolazione italiana di CRS. In 457 pazienti con CRS, trattati con chirurgia endoscopica endonasale dopo fallimento della terapia medica massimale, sono stati calcolati la percentuale di raggiungimento della differenza minima clinicamente rilevabile (MCID) e la percentuale di miglioramento relativo dopo l'intervento chirurgico. Inoltre, è stato studiato l'impatto di diversi fattori sul punteggio dello SNOT-22 preoperatorio e postoperatorio. Il miglioramento dei sintomi si è verificato nella maggior parte dei pazienti ed era direttamente proporzionale alla SNOT-22 basale. Il 79,7% dei pazienti ha raggiunto l'MCID e la percentuale di miglioramento relativo è stata del 50,1%. Le implicazioni psicologiche e sociali hanno influenzato significativamente i punteggi dello SNOT-22. Un'analisi di regressione multipla ha mostrato che la storia di precedenti interventi chirurgici, asma, score endoscopico preoperatorio e SNOT-22 basale hanno statisticamente predetto il punteggio dello SNOT-22 postoperatorio (R2 = 0,229). Sottoporre i pazienti con CRS a SNOT-22 prima dei trattamenti chirurgici potrebbe quindi aiutare ad informarli sui probabili esiti, sebbene sia fortemente influenzato dalla percezione individuale. Sono necessari ulteriori studi per identificare un set efficace di parametri soggettivi e oggettivi per la valutazione dei risultati.

PAROLE CHIAVE: *Sinonasal Outcome Test-22 (SNOT-22), rinosinusite cronica, chirurgia endoscopica nasosinusale, previsione dell'outcome, qualità della vita*

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Introduction

Since the advent of nasal endoscopy, the evaluation of treatment outcomes in patients affected by chronic rhinosinusitis (CRS) has been a matter of debate. The pioneers of endoscopic sinus surgery (ESS) demonstrated surgical success rates of around 90-95% [1]. However, these results are far from the actual rates reported in literature. This is easily explained in two ways. As ESS was introduced recently in the 1980s and it was not in widespread practice, there was a lack of long-term follow-up studies that described the actual surgical effects [2]. Moreover, evaluation method of outcomes was based on qualitative scales, often estimating changes only on one or a few items of the CRS symptoms criteria, lacking a global assessment of improvement [3,4]. Finally, and this is partly also a current issue, the cohorts of patients were inhomogeneous, including cases of acute rhinosinusitis, massive nasal polyposis, or recurrent sinusitis after external procedures [5]. The 1990s witnessed the clinical application of the biopsychosocial model [6]. This theory supported that, in order to understand and respond adequately to patient suffering, clinicians should consider the biological, psychological and social dimensions of illness simultaneously. In practice, this was a way of considering the patient's subjective experience as an essential contributor to accurate diagnosis, health outcomes and humane care. In accordance with this philosophy, a "quality of life revolution" was observed in different areas of medicine [7] and several quality of life (QoL) questionnaires have been developed to quantify the individual and societal burden of chronic diseases. This paradigm shift also occurred for CRS. Since then, rhinologists have used several specific symptom-based scores to evaluate treatment outcomes in CRS patients, such as the Sinonasal Outcome Test 22 (SNOT-22) [8]. Applying these tools, it emerged that around 20-30% of CRS patients do not experience significant improvement after surgery, although the impact of ESS on QoL is generally reported as positive [9]. Moreover, other studies have quantified the 5-year risk of revision surgery to be 10-20%, while the presence of certain comorbidities, such as asthma and aspirin sensitivity, along with other factors like high baseline CT stage or incomplete sinus dissection, have been associated with elevated revision rates of 25-40%. However, despite the presence of known risk factors for revision surgery, evidence for several of these clinical characteristics has failed to reliably predict ESS outcomes [9]. Contrarily, it seems from previous regression studies that baseline SNOT-22 is one of the most important factors affecting the outcome [10] and several studies suggested its prognostic role in terms of achievement of improvement and risk of revision surgery [11]. In light of these observations, the presented study aimed at verifying in an Italian CRS population whether SNOT-22 could assist physicians in predicting surgical outcomes, improving shared decision-making process and ameliorating patients' understanding of their QoL expectations after treatment. The primary outcomes included measurement of the percentage of patients receiving a minimal clinically important difference (MCID) and the percentage of relative improvement (RI) after surgical treatment.

Materials and methods

This prospective study was conducted according to the declaration of Helsinki and was previously approved by the Institutional Review Board of the hospital (n. 109/2016).

Clinical data were obtained from a population of 457 patients affected by CRS operated in the same tertiary care centre in the period 2015-2018.

Enrolled patients were adult subjects affected by bilateral CRS undergoing ESS as a primary procedure after failure of maximal medical therapy [12]. All study participants had completed previous medical therapy including, but not limited to, at least two courses of topical steroid (60 days each). Oral steroid or culture-directed antibiotics were added when necessary (at least one course of 15 and 10 days respectively). However, medical therapy was not suspended until surgery.

Exclusion criteria were previous trauma, congenital facial malformations, systemic autoimmune diseases, cystic fibrosis, ciliary dyskinesia, head and neck malignancies or history of previous radiotherapy, any other nasal surgery performed concomitantly.

All surgical procedures were performed by the same 4 surgeons with more than 10 years of experience in ESS.

Postoperative medical therapy consisted in nasal irrigation with saline solution and intranasal corticosteroid [12], delivered with a high-volume squeeze bottle device [13]. A perioperative short-term of oral corticosteroid was also administered. Non-standardised oral steroid or culture-directed antibiotic therapy were added in cases of recurrent infection or uncontrolled symptoms. Patients were followed at 15 days, 1, 3, 6 and 12 months after surgery.

Each patient was evaluated about 15 days before surgery and during follow-up visits using a set of objective and subjective (self-assessed) measurements. Data obtained in the preoperative assessment and during the last follow-up visit (12 months) were collected for analysis.

Concerning the objective evaluation, the Lund-Kennedy (LK) [14] and the Lund-Mackay (LM) [15] scales were used. The evaluation between preoperative and postoperative LM

scores was not possible, because CT scan is not routinely performed after surgery unless required for particular clinical conditions.

For subjective evaluation, the Italian version of the Sino-Nasal Outcome Test-22 (I-SNOT-22) [16] was used. It is the most frequently employed in clinical practice because it is simple, intuitive and takes only a few minutes to complete [17]. It represents a questionnaire structurally composed of 22 CRS-related items scored from 0 to 5 (total score range 0-110, higher scores represent worse symptoms), which evaluates the severity of complaints that patients have been experiencing over the past weeks due to CRS [18]. SNOT-22 items can be divided into 2 categories: questions about physical symptoms (items 1-12) which cover rhinologic as well as ear and facial symptoms, and questions about health and QOL (items 13-22) which cover sleep function and psychological issues [19].

Similar to Rudmik [20], the cohort of patients was divided into 10 groups according to baseline SNOT-22 score. These groups were based on 10-point increments of the SNOT-22 score (patients who scored less than 10 were excluded since they had no chance to receive an MCID). The percentage of patients reaching at least an MCID, which in SNOT-22 is defined as a reduction of around 9 points after ESS [21], was estimated. The percentage of RI for each preoperative SNOT-22 group was then calculated with the formula [(mean postoperative SNOT-22 score - mean preoperative SNOT-22 score)/mean preoperative SNOT-22 score] x 100 [20].

Statistical analysis

Results are given as arithmetic mean ± standard deviation. The Kolmogorov Smirnoff test was used to test the normality of distribution. Parametric tests were used to evaluate differences between groups. In particular, ANOVA test with Tukey post-hoc test and Chi-square test were used when appropriate to compare groups. A multiple regression analysis was run to predict the SNOT-22 postoperative score from age, sex, smoking habit, asthma, allergy, aspirin intolerance, LK score, LM score, history of previous surgery for CRS and preoperative SNOT-22 score. A significance level of 0.05 for all testing was used. Statistical analyses were performed using the SPSS 25.0 package.

Results

A total of 457 CRS patients were consecutively enrolled. Among these, 34 patients were lost to follow-up. The remaining 423 patients attended the scheduled follow-up visits for 12 months and were considered eligible for analysis. The mean age of the cohort was 47.4 ± 13.5 years (range 18-86 years). 112 patients were asthmatic (26.5%) and 156 patients were allergic to common inhalants (36.9%), while 31 patients complained aspirin intolerance (7.3%). 225 patients were affected by CRS with nasal polyps (CRSwNP) (53.2%), while the remaining 198 (46.8%) were affected by CRS without nasal polyps (CRSsNP).

The mean preoperative SNOT-22 score was 48.9 ± 20.8 (range 13-106), and the mean preoperative SNOT 1-12 score was 30.8 ± 10.3 (range 9-56). The preoperative SNOT 1-12 score accounted for the total SNOT-22 for 67.4% (percentage of the SNOT-22 related to rhinologic symptoms). The mean preoperative LK score was 5.6 ± 2.8 (range 0-12), while the mean preoperative LM score was 11.5 ± 6.6 (range 0-24). The mean postoperative SNOT-22 score was 22.9 ± 17.9 (range 1-75), and the mean postoperative SNOT 1-12 score was 14.3 ± 9.5 (range 1-41). The postoperative SNOT 1-12 score accounted for the total SNOT-22 for 70.7%. The mean postoperative LK score was 1.7 ± 2.1 (range 0-10). These differences were significant at Student's t test ($p = 0.001$ for SNOT-22 score; $p = 0.001$ for SNOT 1-12 score; $p = 0.001$ for the percentage of SNOT-22 related to rhinologic symptoms, and $p = 0.001$ for LK score).

Based on baseline SNOT-22 score, 10 different groups of patients were defined. The sample sizes for each preoperative SNOT-22 group appeared to follow a normal distribution ($p = 0.132$ at Kolmogorov-Smirnoff test), with the largest groups composed of patients with baseline SNOT-22 scores between 20-69 (Fig. 1). Clinical characteristics, as well as preoperative subjective and objective scores, are depicted in Table I.

Postoperative SNOT-22 score was significantly improved in each of the 10 groups at paired Student's t test ($p = 0.001$ for all comparisons). 79.7% of the total cohort achieved a MCID improvement after ESS. Among the patients who achieved a MCID, the percentage of RI was 62.7%. When considering the total cohort (including also those who did not achieved a MCID) the percentage of RI was 50.1%. The MCID and the percentage of RI obtained from each of the 10 groups, as well as pre- and postoperative SNOT-22 scores are reported in Table II. A clear distinction of behaviour was observed between patients with baseline SNOT-22 score greater or less than 30. In particular, the mean percentage of achieving a MCID in groups 3-10 is 91.6% with an average 56.8% of RI. Contrarily, the mean percentage of achieving a MCID in groups 1-2 is 44.2% with an average of 38.9% of RI.

Significant differences in the number of patients achieving the MCID were demonstrated by the chi-square test ($p = 0.001$). In detail, patients in groups 1-2 achieved a

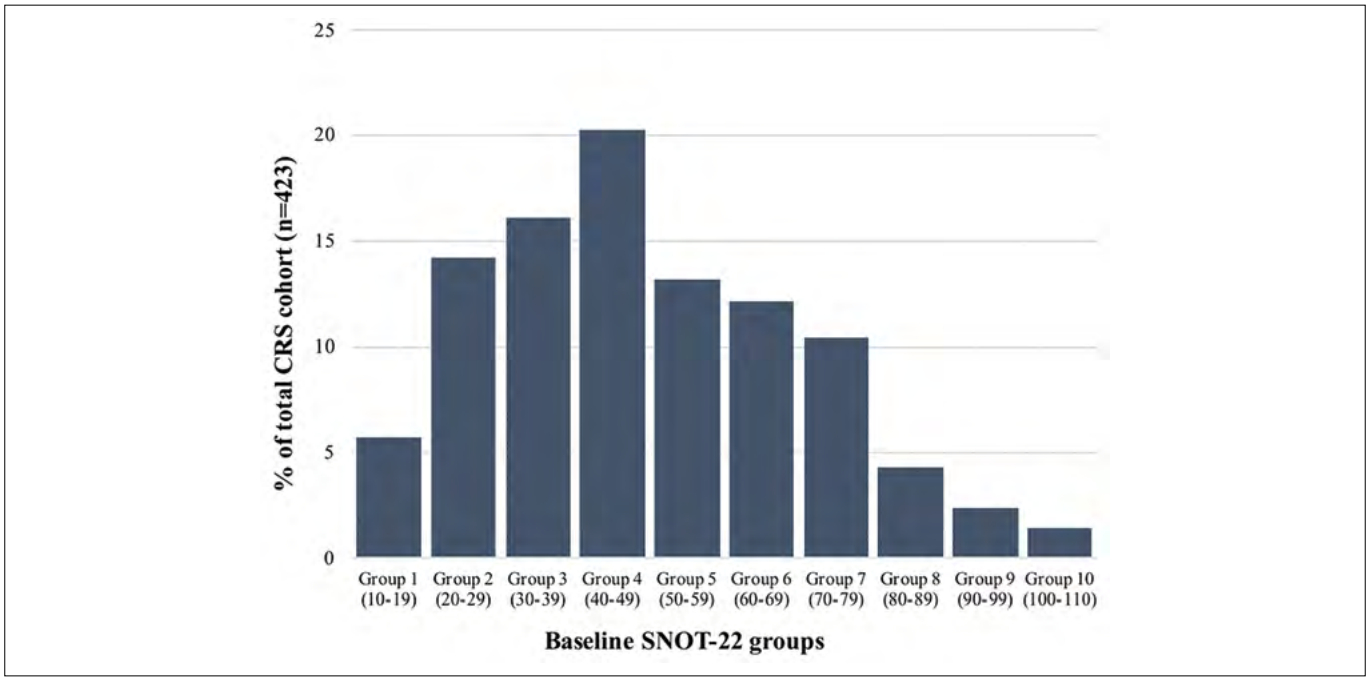

Figure 1. Distribution of the study population according to baseline SNOT-22 score.

Table I. Pre-treatment clinical features of the study population classified in 10 groups based on baseline SNOT-22 score.

	Group 1 (10-19)	Group 2 (20-29)	Group 3 (30-39)	Group 4 (40-49)	Group 5 (50-59)	Group 6 (60-69)	Group 7 (70-79)	Group 8 (80-89)	Group 9 (90-99)	Group 10 (100-110)
N (%)	24 (5.7)	60 (14.2)	68 (16.1)	86 (20.3)	56 (13.2)	51 (12.1)	44 (10.4)	18 (4.3)	10 (2.4)	6 (1.4)
Age	48.3 ± 16.6 (18-73)	49.1 ± 15.4 (18-71)	47.7 ± 16.5 (18-80)	50.4 ± 12.3 (21-86)	47.1 ± 12.7 (22-77)	46.2 ± 11.1 (27-67)	43.6 ± 10.9 (24-65)	42.1 ± 11.1 (24-61)	42.2 ± 6.6 (34-53)	47.3 ± 9.1 (41-59)
Sex (M:F)	16:8	52:26	44:24	54:32	28:28	33:18	22:22	8:10	2:8	2:4
Asthma, n (%)	10 (41.7%)	14 (23.3%)	18 (26.5%)	18 (20.9%)	18 (32.1%)	8 (15.7%)	14 (31.8%)	4 (22.2%)	8 (80%)	0 (0%)
Allergy, n (%)	8 (33.3%)	25 (41.7%)	22 (32.6%)	18 (20.9%)	26 (46.4%)	23 (45.1%)	20 (45.5%)	10 (55.6%)	4 (40%)	0 (0%)
Aspirin intolerance, n (%)	2 (8.3%)	4 (6.7%)	2 (2.9%)	8 (9.3%)	6 (10.7%)	5 (9.8%)	0 (0%)	4 (22.2%)	0 (0%)	0 (0%)
CRSwNP, n (%)	14 (58.3%)	33 (55%)	36 (52.9%)	36 (41.9%)	30 (53.6%)	26 (50.9%)	26 (59.1%)	12 (66.7%)	6 (60%)	6 (100%)
LK score	4.9	4.9	6	6.1	5.8	5.4	5.3	5.4	5.6	5.7
LM score	11.3	10.6	11.5	13.6	11.6	11.3	7.8	12.4	14.6	10.3

M: male; F: female; CRSwNP:chronic rhinosinusitis with nasal polyps; LK: Lund-Kennedy; LM: Lund-Mackay.

MCID with a significant less frequency than those in the other groups. Furthermore, the percentage of RI among the 10 groups was also significantly different at ANOVA test ($p = 0.002$) and patients in group 2 scored significantly lower than those in group 6, 8 and 10 ($p = 0.013$, $p = 0.022$ and $p = 0.039$, respectively, Tukey post-hoc test). Interestingly, the percentage of the SNOT-22 score related to nasal symptoms was significantly different among the 10 groups in both the pre- and post-treatment conditions ($p = 0.001$ and $p = 0.001$, respectively, ANOVA test). In particular, at baseline, the SNOT 1-12 score accounted for 88.5% of the SNOT-22 total score in group 1, while it accounted for the 51.9% in group 10. These differences were significant with Tukey's post-hoc test. In the post-treatment assessment, the SNOT 1-12 score ranged from 88.0% of the SNOT-22 total score in group 1 to 54.5% in group 9. These differences were significant by Tukey's post-hoc test.

Each of the 10 groups was further divided into two subgroups according to the presence of polyps. The results of SNOT-22 scores obtained before and after the surgery,

Table II. Probability of patients with CRS achieving MCID after ESS based on preoperative SNOT-22 score group.

	Preop. SNOT-22 score	% SNOT 1-12 over preop. SNOT-22	Postop. SNOT-22 score	% SNOT 1-12 over postop. SNOT-22	Probability of achieving MCID (%)	RI (%)
Group 1 (10-19) n = 24	16 ± 2.2	88.5%	8.7 ± 3.8	88.0%	33.3% (n = 8)	- 44%
Group 2 (20-29) n = 60	24.8 ± 2.9	82.1%	16.3 ± 12.2	75.6%	55% (n = 33)	- 33.8%
Group 3 (30-39) n = 68	34 ± 2.7	76.4%	17.5 ± 13.6	79.9%	82.4% (n = 56)	- 49%
Group 4 (40-49) n = 86	44.5 ± 3.1	67.2%	22.9 ± 16.8	66.8%	86.1% (n = 76)	- 48.9%
Group 5 (50-59) n = 56	54.2 ± 2.8	58.9%	25.9 ± 15.8	63.8%	85.7% (n = 48)	- 52%
Group 6 (60-69) n = 51	65.4 ± 3.2	57.5%	23.1 ± 19.2	69.9%	92.1% (n = 47)	- 64.6%
Group 7 (70-79) n = 44	73.9 ± 2.8	55.8%	35.6 ± 21.9	62.4%	86.3% (n = 38)	- 51.6%
Group 7 (80-89) n = 18	82 ± 2	53.7%	32.8 ± 21.4	68.6%	100% (n = 18)	- 60.2%
Group 9 (90-99) n = 10	94.6 ± 3.6	53.5%	43.8 ± 21.6	54.5%	100% (n = 10)	- 53.8%
Group 10 (100-110) n = 6	104 ± 2.4	51.9%	26.7 ± 14.5	69.4%	100% (n = 6)	- 74.3%
Total n = 423	48.9 ± 20.8	67.4%	22.9 ± 17.9	70.7%	79.7% (n = 338)	- 50.1%

MCID: minimal clinical important difference; RI: relative improvement.

as well as the probability of achieving a MCID and the percentage of RI are reported in Table III and Table IV. No differences between CRSwNP and CRSsNP patients in the postoperative SNOT-22 score ($p = 0.177$), the percentage of the SNOT-22 score related to rhinologic symptoms in the pre- ($p = 0.366$) and post-treatment ($p = 0.300$) conditions, and the percentage of the RI ($p = 0.162$) were demonstrated by Student's t test. Moreover, no difference in the probability of achieving a MCID was demonstrated at chi-square test ($p = 0.215$). On the contrary, a significant difference in the baseline SNOT-22 score was found with the Student's t test ($p = 0.010$). In particular, patients affected by CRSsNP scored significantly better than those affected by CRSwNP. A multiple regression analysis was run to predict the postoperative SNOT-22 score from gender, age, smoke, asthma, LK, LM, previous surgery, allergy, aspirin intolerance and preoperative SNOT-22 score. Some of these variables predicted the postoperative SNOT-22 score, $F(9, 423) = 6.423$, $p = 0.001$, $R2 = 0.298$. A history of previous surgery for CRS was the most important predictor ($B = 6.277$, $p = 0.009$). Other factors predicting ESS outcomes included the presence of asthma ($B = 5.286$, $p = 0.045$), preoperative LK score ($B = 0.937$, $p = 0.040$) and preoperative SNOT-22 score ($B = 0.326$, $p = 0.001$).

Discussion

Chronic rhinosinusitis affects a large portion of the world population leading to significant impairment of QoL [12]. Current studies report that about half of CRS patients remain symptomatic despite first-line pharmacological therapy [22]. Consequently, patients and physicians have to make a decision as whether to continue with medical therapy alone or undergo ESS followed by pharmacological therapy. On

Table III. Probability of patients with CRSwNP achieving MCID after ESS based on preoperative SNOT-22 score group.

	Preop. SNOT-22	Postop. SNOT-22	Probability of achieving MCID (%)	RI (%)
Group 1 (10-19) n = 14	16.9 ± 2.1	7.7 ± 4.5	42.9% (n = 6)	- 54.7%
Group 2 (20-29) n = 33	25.6 ± 2.7	16.9 ± 15.1	54.6% (n = 18)	-33.7%
Group 3 (30-39) n = 36	33.1 ± 2.5	17.1 ± 9.1	77.8% (n = 28)	- 48.1%
Group 4 (40-49) n = 36	44.5 ± 3.3	23.8 ± 18.1	88.9% (n = 32)	- 46.8%
Group 5 (50-59) n = 30	54.3 ± 2.7	27.4 ± 18.2	80% (n = 24)	- 48.9%
Group 6 (60-69) n = 26	64.3 ± 3.4	21.4 ± 19.2	92.3% (n = 24)	- 66.6%
Group 7 (70-79) n = 26	74 ± 2.9	36.6 ± 26.1	76.9% (n = 20)	- 50.1%
Group 7 (80-89) n = 12	81.5 ± 2.1	23.2 ± 16.2	100% (n = 12)	- 71.6%
Group 9 (90-99) n = 6	92 ± 3.8	39.7 ± 18.1	100% (n = 6)	- 56.8%
Group 10 (100-110) n = 6	104 ± 2.2	26.7 ± 14.5	100% (n = 6)	- 74.3%
Total n = 225	48.9 ± 20.7	22.9 ± 18.4	78.2% (n = 176)	- 50.9%

MCID: minimal clinical important difference; RI: relative improvement.

Table IV. Probability of patients with CRSsNP achieving MCID after ESS based on preoperative SNOT-22 score group.

	Preop. SNOT-22	Postop. SNOT-22	Probability of achieving MCID (%)	RI (%)
Group 1 (10-19) n = 10	14.8 ± 2.1	10.0 ± 1.9	25.0% (n = 2)	- 30.6%
Group 2 (20-29) n = 27	23.9 ± 2.7	15.4 ± 7.6	55.6% (n = 15)	- 33.8%
Group 3 (30-39) n = 32	35.1 ± 2.9	18.0 ± 17.5	87.5% (n = 28)	- 50%
Group 4 (40-49) n = 50	44.4 ± 3.1	22.2 ± 15.9	84.0% (n = 42)	- 50.3%
Group 5 (50-59) n = 26	54.2 ± 2.2	24.1 ± 12.7	92.3% (n = 24)	- 55.6%
Group 6 (60-69) n = 25	66.4 ± 2.5	24.9 ± 19.5	92.0% (n = 23)	- 62.5%
Group 7 (70-79) n = 18	73.8 ± 3.5	34.0 ± 14.9	100% (n = 18)	- 53.8%
Group 7 (80-89) n = 6	83 ± 3.1	52.0 ± 17.6	100% (n = 6)	- 37.4%
Group 9 (90-99) n = 4	98.5 ± 0.6	50.0 ± 27.7	100% (n = 4)	- 49.4%
Group 10 (100-110) n = 0	/	/	/	/
Total n = 198	47.6 ± 19.3	23.1 ± 17.3	82.8% (n = 162)	- 49.2%

MCID: minimal clinical important difference; RI: relative improvement.

one hand, Steele et al. showed that 57% of patients electing continued medical therapy failed to improve 1 MCID with a mean relative score improvement of 16%. Moreover, 1 in 5 patients experienced deterioration by > 1 MCID [23]. On the other hand, although surgical benefits are much more remarkable [1,8,9,24], the decision to face surgical cannot disregard evaluation of related risks and costs. To date, a tool that is able to identify patients who might benefit from surgery and the expected degree of improvement is still lacking. This is a natural consequence for not having a standardised staging system that drives treatment choices.

Many reports have investigated a number of factors that might influence the outcomes of CRS surgery. These include both patient-related factors (baseline SNOT-22, radiological extent of disease, presence of polyps, asthma or other comorbidities, gender, previous surgery) and surgical factors (experience of surgeon, timing of surgery, postoperative management) [25]. It seems from previous regression studies, and partly confirmed by our work, that baseline SNOT-22 is one of major factors affecting outcomes [10]. In this sense, the advantage of submitting CRS patients to SNOT-22 prior to any surgical treatment could, in theory, help physicians to inform them about their probable outcomes after ESS. For simplicity, explaining to a patient that he/she is likely to receive a 50% reduction in symptom load will aid informed consent and optimise preference-based decisions.

The fact is that, luckily, the majority of patients experience an improvement in symptoms after ESS, intended as a reduction of the SNOT-22 score after treatment ($p = 0.001$) [1,8,9,24]. We have shown that improvement of symptoms occurs in all groups and that the improvement is

directly proportional to the baseline SNOT-22 value. In other words, patients with worse preoperative symptomatology obtain the greatest range of score reduction after treatment. However, this statistical significance might not imply a clinical benefit. Indeed, the MCID has been proposed to combat this conceptual vice by defining a threshold value by which a statistically significant result may also offer a clinically meaningful result. The MCID is the lowest degree of change that a patient will notice, which for SNOT-22 score has previously been defined as 8.9 points in a 3-month postoperative score [18]. However, what represents a clinically important change may vary from one individual to another and may not necessarily reflect the patients' expectation for improvement after treatment. As an example, a patient reaching a MCID of 9 points in the postoperative SNOT-22 may not be satisfied with this outcome due to a persistent measurable burden of disease, despite achieving a noticeable improvement. To overcome the intrinsic limitations of MCID, a clinically significant change should be also outlined by a parameter expressing the true magnitude of postoperative improvement, i.e. the percentage of RI. Hence, integrating these measurements might optimise patient understanding and counselling. Rudmik et al. demonstrated that 80% of patients with a SNOT-22 score > 30 improved by an average of 48% following ESS [20]. Similarly, in our series, patients with SNOT-22 score >30 showed a 91.6% chance of achieving MCID with a mean 56.8% of RI. Also, a larger UK cohort showed a 66% chance of achieving a MCID with baseline SNOT-22 score > 30 [26]. On the other hand, patients with SNOT-22 < 30 have less than half the probability of achieving the MCID and a reduced degree of RI. That was evident in all the above-mentioned studies and confirmed in our series (44.2% mean MCID achievement, 38.9% mean RI). Therefore, although the baseline SNOT-22 score and chance of achieving the MCID is not intended to be used as an absolute threshold for eligibility for surgery, these global results suggest that a patient with low preoperative score might be less likely to benefit from surgery and caution should be paid when operating on patients with a score < 10. It is also true that only the categories of patients with lower baseline SNOT-22 values are likely to achieve a normal or near-normal status. Indeed, prior studies submitting SNOT-22 to patients with no sinus disease resulted in an average score of around 10 [16,18]; conversely, patients with higher baseline SNOT-22 values, despite a good RI, are still left with a significant burden of disease and remain more symptomatic than healthy controls. To be honest, SNOT-22 groups on either extreme of the scoring scale contained small sample size in all studies, which makes it difficult to provide accurate statistical results and introduce larger degrees of uncertainty around the means of these groups. Therefore, larger collaborative CRS databases should be developed to better define these categories of patients [26,27] and understand their behaviour.

Although our results are in line with the current literature, they should be interpreted with caution. First, though few in number, CRS patients with baseline SNOT-22 score < 10 were excluded from the analysis because of their near-normal status. Moreover, since all surgical procedures have been performed in the Day Surgery division, patients with severe comorbid asthma are not included in the study population. This choice obviously affected the overall mean values of percentage of MCID achievement and RI. Second, all surgeries were performed by specialist rhinologists, minimising the unfavourable outcomes due to surgical inexperience. Third, CRS is a dynamic disease characterised by fluctuating trends from quiescence to outbreaks. A one-off administration of a self-assessed questionnaire might not be enough reliable to assess the overall burden of the disease, especially considering a limited follow-up of 12 months.

In light of the above, two reflections arise. If we assume that a patient with a low baseline SNOT-22 score has a low probability of reaching the MCID and that a patient with a high baseline SNOT-22 score has a high probability of reaching the MCID, but not enough RI to become asymptomatic, either we are far from having an ideal treatment for CRS or SNOT-22 (in general QoL-based questionnaires) may not be a sufficiently effective tool to evaluate treatment outcomes. While, on the one hand, basic research efforts are aimed at discovering innovative targeted therapies [28], on the other, clinical practice efforts are focused on defining new comprehensive method of outcomes evaluation. In particular, the attempt is to incorporate subjective and objective parameters since symptom-based items are influenced by psychological habitus and show a wide inter-individual variability. Indeed, our data show that in groups with low baseline SNOT-22 almost all of the SNOT-22 score is given by rhinologic symptoms, while in groups with high baseline SNOT-22 score rhinologic symptoms account only for about 50% of the global SNOT-22 value, suggesting that psychological and social-functioning aspects significantly affect the SNOT-22 score. Furthermore, Hopkins et al. [18] demonstrated that when the sleep-psychological domain items dominate the total SNOT-22 score, ESS outcomes may be suboptimal. In fact, CRS patients that showed a moderately-severe total SNOT-22 score with high burden from sleep-psychosocial items may have less durable benefit after treatment, showing a statistically and clinically improvement at 3 months after ESS, followed by a worsening of symptoms at 6 months.

For this reason, these patients may be counselled to expect less benefit than those in whom nasal subdomain scores predominate [29].

In this context, Hopkins et al. obtained a long list of potential parameters revising the current literature. After intricate statistical analysis, the 54 initial items were distilled down to a final core set of 15 items, over 4 domains, including the SNOT-22 repeated over time with some additional questions and the Lund-Kennedy score [30]. This core outcome set (COS) represents the first "prototype" of an evaluation tool for CRS that is able to integrate subjective and objective parameters, but further work is still necessary to make it relevant for clinical practice. In this regard, a recent study highlighted a close correlation between symptoms and burden of inflammation. A cohort of CRSsNP patients undergoing ESS was clustered in 4 preoperative SNOT-22-based groups. These groups were significantly different with respect to primary versus revision ESS status, number of previous sinonasal surgeries, asthma prevalence and total SNOT-22 scores. More interestingly, the cluster of subjects with the highest total preoperative SNOT-22 score had the highest tissue eosinophilia compared to the other symptomatic groups and a more frequent diagnosis of asthma, suggesting that a high burden of inflammation correlates with worse symptomatology [29].

Conclusions

Submitting CRS patients to SNOT-22 prior to surgical treatments might help to inform about their probable outcomes, although it is strongly influenced by individual perception. Based on recent preliminary observations, the integration of SNOT-22 scores and tissue histopathology could represent an innovative method to predict treatment outcomes in CRS patients. Further studies are needed to define a simple and effective evaluation tool by implementing the knowledge of pathophysiological mechanisms underlying the different expressions of this disease. Eventually, this will lead to identify new histopathological-biomolecular pathways that are able to classify the CRS patients into homogeneous subgroups, to establish endotype-driven treatments and possibly provide objective predictors of response to therapy.

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