THE Laryngoscope
FOUNDED IN 1896

Quality of Life in Septal Perforation Compared to Chronic Rhinosinusitis and Controls

Journal:	*The Laryngoscope*
Manuscript ID	lscope-24-0397
Wiley - Manuscript type:	Original Report
Date Submitted by the Author:	21-Feb-2024
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Keywords - Combo:	Adult rhinology < Clinical < Allergy/Rhinology, Quality of Life < Clinical Research, Nose and paranasal sinuses < Head and Neck

Title

Quality of Life in Septal Perforation Compared to Chronic Rhinosinusitis and Controls

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CONFLICT OF INTEREST

Isam Alobid received consulting and speaking fees from: AstraZeneca, Viatris, Roche, Sanofi, GSK, MSD, Menarini, Salvat, Galensus Health, Olympus, Metronic, and Novartis.

Claire Hopkins received advisory board fees and consultation fees from GSK, AstraZeneca, Sanofi, and Lilly.

The other authors involved in this study do not declare a conflict of interest.

FUNDING

No funding was received to assist with the preparation of this manuscript.

ABSTRACT

***Objective*:** The aim of this study is to investigate the impact of septal perforation (SP) on QoL. SP is compared to the general population and patients with chronic rhinosinusitis with nasal polyposis (CRSwNP) using the Sino-Nasal Outcome Test 22 (SNOT-22).

***Methods*:** Prospective single centre study in a referral Rhinology Unit from January 2014 to March 2023.

***Results*:** A total of 392 patients were included in 3 groups: controls (n=141), CRSwNP (n=118) and SP (n=133). The mean score of the SNOT-22 was significantly higher in the CRSwNP group (42.4 / SD 24.4) and SP (46.5 / SD 22) compared to the control group (6.2 / SD 8.4). Scores by either items or domains were significantly higher in the CRSwNP and SP groups compared to the control group. There were no significant differences in the mean SNOT-22 between the CRSwNP and SP groups (p=0.26; 95% CI -1.68-9.99). In the comparison by domains, patients with SP reported worse QoL with higher scores (p<0.001) in the sleep and function domains and in all their items. Only one item of the emotion domain corresponding to being frustrated/restless/irritable was higher (p<0.001) in SP compared to CRSwNP.

***Conclusion*:** SP produces negative impact on QoL similar to CRSwNP. Moreover, sleep and function domains are significantly worse in SP. Aetiology and area of SP influence nasal and emotion domain, though more studies on SP using SNOT-22 and specific questionnaires are needed.

***Key words*:** septal perforation, quality of life, SNOT-22, domains, chronic rhinosinusitis with nasal polyps

LEVEL OF EVIDENCE: Level II

INTRODUCTION

Septal perforation (SP) is a defect in the total thickness of the nasal septum that causes a communication between both nostrils and affects 1-2% of the population [1,2]. The main causes are iatrogenic after sinonasal surgery, rhinotillexomania (nose picking), traumatic, intranasal drug abuse or idiopathic [3]. Although in most patients SP is an incidental finding or presents with mild symptoms, in some cases it generates great discomfort [4]. SP may produce nasal obstruction, inspiratory wheezing, epistaxis, crusts, rhinorrhoea, or loss of smell [4,5]. The symptomatology is caused by impaired airflow and nasal warming function [4]. Diagnosis is made by detailed medical history along with complete physical examination including evaluation of the nasal pyramid and a detailed endoscopic evaluation of the nasal cavity [6]. In addition, general blood tests with autoimmunity markers, urinalysis for detecting drugs, and chest x-ray are recommended, especially in those SP of undetermined aetiology [6]. The diagnostic study is completed by computed tomography. Biopsy is recommended in SP cases of undetermined aetiology to rule out malignancy or inflammatory diseases [6]. Symptomatic patients require treatment to improve quality of life (QoL). Initially, management is based on topical treatments to ensure adequate nasal hydration. However, in those patients' refractory to conservative treatment surgical repair will be necessary to restore nasal function and improve the patient's symptoms [6].

SP generates symptoms that affect QoL and require specific evaluation. Patient Reported Outcome Measures (PROMs) are instruments that quantify patient's perceptions of their health status and allow to measure the impact of the pathology on their QoL [7]. Sino-Nasal Outcome Test 22 (SNOT-22) is a widely used questionnaire for evaluating QoL in patients with sinonasal pathology [7-10]. It is well-established that patients with chronic rino-sinusitis with nasal polyposis (CRSwNP) report poor QoL with a complex range of symptoms apart from those related to the nose and paranasal sinuses as sleep impairment, anxiety, and depression [11-14]. There are few studies on QoL in patients with SP [8-10]. The NOSE-Perf questionnaire has recently been published and its translation into Spanish was carried out by our group [15,16].

The aim of this study is to investigate the impact of SP on QoL compared to the general healthy population and patients with chronic rhinosinusitis with nasal polyposis using the SNOT-22 and its domains.

MATERIALS AND METHODS

Study Design

Prospective single-center study in the Rhinology and Skull Base Unit of the Hospital Clínic Barcelona, from January 2014 to March 2023.

Population selection

Patients diagnosed with symptomatic SP who were referred to our center were included. In addition, we included patients with CRSwNP under medical treatment with intranasal corticosteroids. Control group was recruited by age and gender from healthy volunteers evaluated in our rhinology department without sinonasal disease. Only patients over 18 years of age have been included.

The exclusion criteria in the SP group were to have any other paranasal sinus or nasal cavity pathology as chronic rhinosinusitis, history of neoplasia, to have received radiotherapy of the head and neck or to suffer from autoimmune diseases with sinus involvement or potential involvement such as granulomatosis with polyangiitis.

The sample size was calculated based on the study by Leong SC et al. as a comparison of two independent means between the SP and CRSwNP groups (50.2 / SD 23.5 and 57.2 / SD 10.3 respectively) [17]. An alpha risk of 0.05 and a statistical power of 80% were accepted. The calculated sample size was 107 patients per group.

Data collection

Age and gender were described in all patients by groups.

Patients in all the 3 groups responded to visual analogue score (VAS) from 0 to 100 millimetres, 0 being no discomfort and 100 being the worst imaginable discomfort of the following symptoms: nasal obstruction, rhinorrhoea, loss of smell, and facial pain. Patients with SP responded to the VAS of nasal whiting, crusting, and epistaxis.

All patients answered the SNOT-22 during the face-to-face interview. The questionnaire was delivered in paper format and completed by the patient autonomously.

The SNOT-22 contains 22 questions grouped into 5 domains: nasal, ear/facial, sleep, function, and emotion. Each question is scored from 0 to 5 on a Likert scale, with 0 being no problem and 5 being the problem as bad as it can be [18]. The nasal domain includes 8 items scored from 0-40; the ear/facial domain 4 items scored from 0-20; the sleep domain 4 items scored from 0-20; the functional domain 3 items scored from 0-15; and finally, the emotion domain 3 items scored from 0-15 (Figure 1). The SNOT-22 has a total score of 0 to 110 points and is classified as 4 categories: no

alteration between (0-10), mild (11-20), moderate (21-50), and severe (over 50) [19].

The overall score of the SNOT-22 is expressed as an absolute value from 0 to 110 and the domains and items are expressed as a percentage.

Patients in the CRSwNP group were divided into 3 subgroups according to the severity of the disease using VAS: mild (0-30), moderate (>30-70), and severe (>70-100) [20]. The nasal polyposis was scored according to the Meltzer classification of 0-4 in each nostril [21].

The SP aetiology was recorded and classified in percentage in the following categories: surgery, intranasal drug abuse, traumatic, use of intranasal vasoconstrictors, rhinotillexomania or idiopathic. Measurements in millimetres (mm) of the SP were recorded: antero-posterior diameter (AP), supero-inferior (SI) and its approximate area (mm^2) obtained by multiplying AP x SI diameters.

Statistical analysis

Mean and standard deviation for continuous variables were calculated. The qualitative variables are expressed in frequencies and percentages. The normality of the continuous variables was evaluated through the Shapiro–Wilk test with a significance level of p=0.01. Chi-square test and Fisher's exact test were used to compare categorical variables.

Continuous variables were compared among the 3 groups with ANOVA test. Post-hoc Bonferroni correction was performed when SP and CRSwNP groups were compared.

Univariate and multivariate linear regressions were performed to analyse the relationship between SNOT-22 total score and its domains as dependent variable, and age, gender, SP areas or aetiology. Pearson or Spearman correlation coefficients were used to measure the relation between SNOT-22 total score and nasal symptomatology. Statistically significant correlation was stablished for Spearsman's rho negligible (0.01-0.19), weak (0.20-0.29), moderate (0.30-0.39), strong (0.40-0.69) and very strong (≥0.70) correlations.

All statistical testing was two-tailed. Alpha was set to 0.05 for significance. All statistical analyses were made using STATA soft- ware v.16.1 (StataCorp, TX, USA).

Ethics

The study was approved by the hospital's Drug Research Ethics Committee (CEIm) under number HCB/2017/0268. All study participants accepted and signed the informed consent. No financial compensation or additional specific post-study care has been granted.

RESULTS

Study Population

A total of 392 patients were included in 3 groups: controls (n=141), CRSwNP (n=118) and SP (n=133). The mean age was 45 years (range 18-90), 52.9 years (range 19-76) and 48.8 years (range 18-89) respectively. No significant differences were found by age or gender.

CRSwNP group

The mean severity of CRSwNP due to VAS was 57.2 (SD 33.7). They were divided into mild (19.8%), moderate (37.1%) and severe (43.1%). The mean nasal polyp score was 4.6 (SD 1.6).

SP group

The most frequent causes of SP were after surgery (n=53; 39.9%), followed by intranasal drug abuse (n=31; 23.3%), rhinotillexomania (n=26; 19.5%), idiopathic (n=11; 8.3%), traumatic (n=7; 5.2%) and use of intranasal vasoconstrictors (n=5; 3.8%) (Figure 2).

The AP and SI diameters of the SP were 20.2 mm (SD 9.6) and 14.1 mm (SD 6.6) respectively with an approximate area of 333.6 mm2 (SD 311.9).

Nasal sinus symptoms of VAS

The VAS of all variables evaluated in the control group was mild (0 to 30). In the CRSwNP group, the highest scores were loss of smell (65.5 / SD 26.4), nasal obstruction (57.2 / SD 33.7) and rhinorrhoea (43.4 / SD 28.8). In the SP group, nasal obstruction (62.6 / SD 28.9) was followed by the presence of crusts (60 / SD 35.7) and rhinorrhoea (44.2 / SD 34.0) (Table 1).

Quality of Life by SNOT-22

The mean score of the SNOT-22 was significantly higher in the CRSwNP group (42.4 SD 24.4) and SP (46.5, SD 22) compared to the control group (6.2 / SD 8.4). Scores by both items and domains were significantly higher in the CRSwNP and SP groups compared to the control group (Table 2).

No differences were observed in the 3 groups overall SNOT-22 score by gender ($p>0.05$).

There were no significant differences in the mean SNOT-22 between the CRSwNP and SP groups ($p=0.26$; 95% CI -1.68-9.99) (Table 2).

The mean score of the SNOT-22 by CRSwNP severity groups was mild 15.3 (SD 13.5), moderate 39.5 (SD 16.7) and severe 56.5 (SD 22.5).

Sub-analysis by Domains

Patients with SP obtained worse QoL with higher scores ($p<0.001$) in the sleep and function domains compared to CRSwNP group (Table 2 and Figure 3).

Sub-analysis by items

Patients with SP obtained worse QoL with higher scores ($p<0.001$) in all questions in the sleep domain corresponding to difficulty falling asleep (#11), wake up during the night (#12), lack of a good night's sleep (#13), and waking up tired (#14). Likewise, in the questions of the function domain corresponding to fatigue (#15), reduced productivity (#16) and reduced concentration (#17). Finally, significant differences were obtained in one of the items of the emotion domain corresponding to being frustrated/restless/irritable (#18) ($p<0.0253$) (Table 3).

Patients with CRSwNP had a higher score in the item corresponding to the loss of taste or smell of the nasal domain ($p=0.000$) (Table 3).

Sub-analysis in septal perforation group

No significant differences were found in the total SNOT-22 score in the SP group according to age ($p=0.970$), gender ($p=0.052$), area of the perforation ($p=0.536$), the aetiology ($p=0.156$). However, in the SP group there was a tendency for a higher questionnaire score in female SP (male 43.4/SD 2.3, female 50.9/SD3.2; $p=0.052$).

In the univariable analysis of SNOT-22 emotion domain, significant differences were found by aetiology; intranasal drug abuse ($p=0.007$), rhinotillexomania ($p=0.029$); cross sectional area ($p=0.019$) and female gender ($p=0.031$). The multivariable analysis of SNOT-22 emotion domain showed significant differences by SP's area ($p=0.048$) intranasal drug abuse ($p=0.039$) and rhinotillexomania ($p=0.018$).

Univariant analysis SP caused by intranasal drug abuse and use of vasoconstrictors obtained worse QoL on SNOT-22 nasal domain ($p=0.023$ and $p=0.002$ respectively). No differences were found by aetiology on ear/facial, sleep nor function domains, neither by SP's area or gender on nasal, ear/facial, sleep nor function domains. Age did not have significant differences on any domains.

A significant correlation was found between SNOT-22 total score and presence of crusts (0.27; $p=0.009$) and nasal whitling (0.21; $p=0.040$) measured by VAS. While negligible correlation was found with epistaxis (0.18; $p=0.087$).

DISCUSSION

The most relevant findings in our study were: 1) Patients with SP have worse QoL compared to the healthy population; 2) SP has a negative impact on QoL equal to CRSwNP; 3) Sleep and function domains are worse in SP than in CRSwNP; 4) Neither the area of the SP nor the cause does not influence QoL by total SNOT-22; 5) PS aetiology and area influence QoL measured by SNOT-22 nasal and emotion domains; 6) Nasal whistling and the presence of crusts is related to worse QoL in SP patients.

Few studies have investigated the effect of SP on QoL. Taylor CM et al. published the validation of the NOSE-Perf for patients with SP (n=202) reporting that the symptomatology that caused greater discomfort in these patients was the presence of nasal crusts, followed by rhinorrhoea, shortness of breath and nasal obstruction [22]. In our cohort, the symptom with the highest score measured by VAS was nasal obstruction, followed by the presence of crusts and rhinorrhoea [22]. Despite the fact that we found a weak correlation between worse QoL and nasal whistling or presence of crusts, it has to be considered that these specific symptoms are not included in SNOT-22.

In the cohort published in 2018 by Leong et al. describing QoL in patients with SP (n=27) using SNOT-22 the domains were described according to DeConde et al. published in 2014[17,23]. In our prospective study, in addition to having a much higher number of patients with SP (n=133), the analysis of SNOT-22 was performed through the domains based on psychometric analysis described by Khan et al. in 2022 for CRSwNP [18]. This mismatch between the domains and items included make the results partially comparable.

In line with previous publications, the mean of SNOT-22 score was higher in patients in the CRSwNP and SP groups compared to the control group [17]. The score obtained in the SNOT-22 was slightly higher in the SP group than in the CRSwNP group, differing from the results reported by Leong et al. In both cases, the differences were not significant [22]. This difference of greater involvement in patients with SP could be due to the fact that only symptomatic patient's refractory to conservative measures were included in our study. Furthermore, if we compare the SNOT-22 results of SP and CRSwNP groups according to the severity finding SP patients obtain scores between the moderate-severe CRSwNP, closer to the patients in the moderate group.

So far, in the previous analysis by domains, higher scores had been reported in the

group with CRSwNP in nasal, ear/facial and emotion, while in the present study a higher score has been obtained only in the nasal domain without reporting significant differences. Moreover, for the first time, significant differences have been obtained in the sleep and function domain with higher scores in the SP group [5,18,24]. Leong et al. also reported differences in the sleep domain but without obtaining significant differences [17].

In relation to the impairment of the sleep domain in patients with SP, the presence of psychopathology due to a history of substance abuse and obsessive spectrum disorders such as rhinotillexomania (total 42.8%) does not have any influence on the results. The alteration of the domain can be justified by SP symptoms such as turbulent discharge, crusting or nasal obstruction. In 2016, Boynuegri S et al. published a study in which they analysed sleep quality using polysomnography (PSG) in 19 patients with SP at baseline and after the placement of a septal button [25]. They found that SP did not impair the objective sleep parameters determined by the PSG, but also obtained a decrease in REM sleep duration and an increase in supine Apnea-Hypopnea Index (AHI). The alteration in supine AHI decreased after the intervention [25].

Although evidence has been published on the impairment of the sleep domain in patients with SP, this study provides evidence of not being determined by aetiology [17]. However, intranasal drug abuse and rhinotillexomania have a greater affectation of the emotion domain. More studies are needed to analyse the influence of the underlying psychopathology factors in emotion domain.

In our study, we observed no differences in the global SNOT-22 score according to the area or cause of SP. Likewise, the size and location of SP have been related to symptomatology [5,18,24]. Although some studies had linked anterior location with greater symptomatology, some authors described an increase in symptomatology in posterior and larger SPs, but no significant differences were reported [18,24]. Nonetheless, we found that SP area obtained worse QoL on emotion domain.

CRSwNP is a pathology that has been extensively studied at the clinical level. According to literature and due to the nasal inflammatory load, patients in this group had a higher score in the item corresponding to the loss of taste or smell of the nasal domain [10].

On the other hand, SNOT-22 score in SP patients is similar to those moderate CRSwNP according to the EPOS, which confirms the great impact of the SP on the

QoL of the patients [20].

As CRS and other diseases, female report higher SNOT-22 scores than males with SP [26,27]. Moreover, we found female with SP have a worse QoL related to emotion domain than male.

The strengths of the study are: 1) The large sample size of our cohort with a total of 392 patients with 133 patients SP diagnosed, as well as 118 diagnosed with CRSwNP with more than 80% of patients moderate-severe; 2) The use of domains based on psychometric analysis.

The limitations of the study are: 1) The patients included were referred because they presented symptoms in relation to SP, while in the population as a whole there may be a group of patients suffering from a SP that is asymptomatic; 2) There are specific symptomatology related to SP that are not reflected in the SNOT-22, such as nasal whistling, the presence of crusts, cacosmia or epistaxis, which are shown in questionnaires such as NOSE-Perf that Taylor CM et al. have already used to objectively characterize and establish the baseline symptomatology of SP [22]; 3) Limited sample size in less frequent SPs aetiologies requires caution with the interpretation of the scores of QoL.

The SNOT-22 was used, despite not being a specific questionnaire for SP, with the aim of comparing and making visible the involvement of QoL in these patients compared to another widely studied sinus disease such as CRSwNP. In addition, the SNOT-22 makes it possible to measure the emotion and function domains that are not assessed in the NOSE-Perf questionnaire, as well as the nasal domain extensively, since it only consists of one question in the specific questionnaire.

The results obtained in the study encourage the systematic use of SNOT-22 as a QoL questionnaire in patients with SP. Its use makes possible to assess the severity of symptoms, as well as the need for intervention and its outcome. The predominance of affectation in some domains could help targeting interventions in a personalized way.

A specific SP questionnaire adapted to the local socio-cultural environment is needed to include the most frequent symptoms as well as their impact on sleep, function, and frustration/irritability.

CONCLUSION

SP presents with physical and emotional signs and symptoms that negatively affect QoL. Patients with SP have worse QoL compared to the healthy population and equal to CRSwNP. Sleep and function domains are worse in SP than in CRSwNP. Nasal whistling and the presence of crusts is related to worse QoL in SP patients. Aetiology and area of SP influence nasal and emotion domain, though more studies on QoL and the creation of specific questionnaires for SP are needed.

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FIGURES

Figure 1. Domains and items of the Sino-Nasal Outcome Test questionnaire of 22 with their score by domains according to Khan et al. [18].

Figure 2. Aetiology of Septal Perforation in percentages.

Figure 3. Box plots of the total score of the SNOT-22 and by domains expressed as a percentage of the three cohorts.
CRSwNP: chronic rhinosinusitis with nasal polyposis. SP: septal perforation.

TABLES

Table 1. Visual Analogue Scale control group. CRSwNP and SP.

VAS of symptoms. mean (SD)	Control (n=141)	CRSwNP (n=118)	Septal Perforation (n=133)
Nasal obstruction	2.3 (4.9)	57.2 (33.7)	62.6 (28.9)
Rhinorrhoea	3.3 (6.6)	43.4 (28.8)	44.2 (34.0)
Loss of smell	2.0 (6.6)	65.5 (26.4)	34.6 (33.6)
Facial pain	0.1 (1.0)	25.3 (28.5)	28.4 (30.5)
Crusts	-	-	60.0 (35.7)
Nasal whistling	-	-	38.0 (33.6)
Epistaxis	-	-	33.7 (34.5)

Abbreviations: CRSwNP: chronic rhinosinusitis with nasal polyposis. SD: standard deviation.

Table 2. Comparison of the mean SNOT-22 questionnaire Score by Domains in CRSwNP and SP.

	Control (n=141)	**CRSwNP (n=118)**	**Septal Perforation (n=133)**	**p-value**
SNOT-22 mean (SD)	6.2 (8.4)	46.5 (22.0)*	42.4 (24.4)*	**p<0.0001**
Nasal domain, mean % (SD)	2.4 (3.5)	49.2 (22.2)*	44.4 (20.9)*	p=0.092
Ear/Facial domain, mean % (SD)	2.8 (8.5)	24.4 (23.8)*	25.0 (23.6)*	p=1.000
Sleep domain, mean % (SD)	12.0 (17.2)	38.4 (32.0)*	53.2 (29.3)*	**p=0.000**
Function domain, mean % (SD)	7.2 (14.2)	31.1 (28.5)*	44.3 (31.3)*	**p=0.000**
Emotion domain, mean % (SD)	6.9 (15.0)	36.5 (31.8)*	43.0 (32.0)*	p=0.173

Abbreviations: CRSwNP: chronic rhinosinusitis with nasal polyposis. SD: standard deviation.

*Significant difference between control group compared to CRSwNP and SP groups.

P-value: post-hoc Bonferroni comparison between CRSwNP and SP groups.

Table 3. Comparison of the SNOT-22 questionnaire score by items between the three groups expressed as a percentage.

Questionnaire	Control (n=141)	CRSwNP (n=118)	Septal Perforation (n=133)	p-value
SNOT-22 by items, mean % (SD)				
Nasal				
1. Need to blow nose	3.8 (7.9)	55.8 (33.1)*	53.7 (34.4)*	p=1
2. Sneezing	6.0 (9.2)	36.1 (29.7)*	35.1 (28.8)*	p=1
3. Think nasal discharge	3.0 (7.2)	50.9 (32.6)*	46.0 (32.3)*	p=0.818
4. Cough	2.1 (6.2)	30.6 (32.4)*	23.0 (30.1)*	p=0.056
5. Post-nasal discharge	1.1 (4.6)	46.2 (32.0)*	41.1 (35.2)*	p=0.420
6. Runny nose	0.1 (1.7)	41.9 (32.7)*	48.3 (37.2)*	p=0.217
21. Decreased sense of taste/smell	0.3 (2.4)	67.1 (34.4)*	41.7 (36.0)*	**p=0.000**
22. Nasal blockage	2.9 (7.0)	67.4 (32.4)*	68.3 (39.7)*	p=1
Ear/Facial				
7. Ear fullness	4.8 (14.5)	33.1 (29.5)*	32.6 (33.6)*	p=1
8. Dizziness	4.1 (14.6)	19.8 (27.4)*	19.2 (28.6)*	p=1
9. Ear pain	0.3 (2.4)	15.9 (28.8)*	17.0 (28.3)*	p=1
10. Facial pain/pressure	0.3 (2.4)	28.6 (33.6)*	31.8 (32.9)*	p=1
Sleep				
11. Difficulty falling asleep	11.4 (19.5)	33.9 (35.7)*	47.4 (35.8)*	**p=0.002**
12. Wake up at night	13.2 (20.4)	40.7 (34.7)*	53.7 (33.1)*	**p=0.002**
13. Lack of good night's sleep	12.7 (20.2)	39.3 (36.3)*	57.0 (35.0)*	**p=0.000**
14. Wake up tired	14.0 (21.6)	40.3 (35.1)*	55.6 (33.2)*	**p=0.000**
Function				
15. Fatigue	8.2 (16.0)	35.3 (32.1)*	49.8 (34.4)*	**p=0.000**
16. Reduced productivity	6.7 (15.6)	29.1 (32.1)*	41.4 (35.1)*	**p=0.002**
17. Reduced concentration	6.7 (15.2)	29.3 (31.7)*	42.4 (34.4)*	**p=0.001**
Emotion				
18. Frustrated/restless/irritable	7.1 (16.6)	33.4 (34.3)*	48.1 (35.7)*	**p=0.000**
19. Sad	5.1 (14.2)	31.5 (35.6)*	39.4 (34.9)*	p=0.106
20. Embarrassed	8.5 (18.9)	44.9 (36.6)*	41.8 (37.9)*	p=1

Abbreviations: CRSwNP: chronic rhinosinusitis with nasal polyposis. SD: standard deviation.

*Significant difference between control group compared to CRSwNP and SP groups.

P-value: post-hoc Bonferroni comparison between CRSwNP and SP groups.

Domains	Items	Score
Nasal	*Need to blow nose* *Sneezing* *Think nasal discharge* *Cough* *Post-nasal discharge* *Runny nose* *Decreased sense of taste/smell* *Nasal blockage*	40
Ear/Facial	*Ear fullness* *Dizziness* *Ear pain* *Facial pain/pressure*	20
Dream	*Difficulty falling asleep* *Wake up at night* *Lack of good night's sleep* *Wake up tired*	20
Function	*Fatigue* *Reduced productivity* *Reduced concentration*	15
Emotion	*Frustrated/restless/irritable* *Sad* *Embarrassed*	15

Figure 1. Domains and items of the Sino-Nasal Outcome Test questionnaire of 22 with their score by domains according to Khan et al. (18).

150x169mm (300 x 300 DPI)

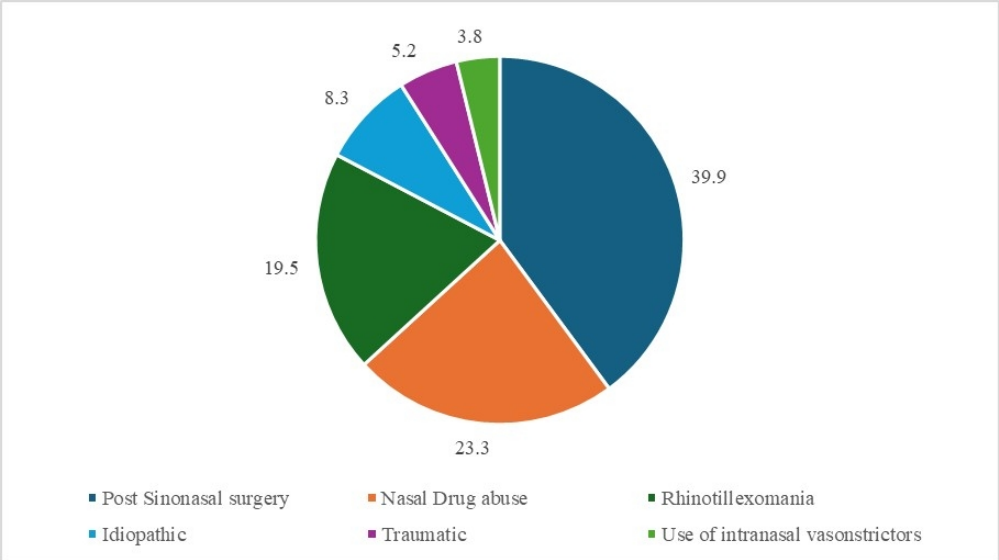

Figure 2. Aetiology of Septal Perforation in percentages.

154x86mm (150 x 150 DPI)

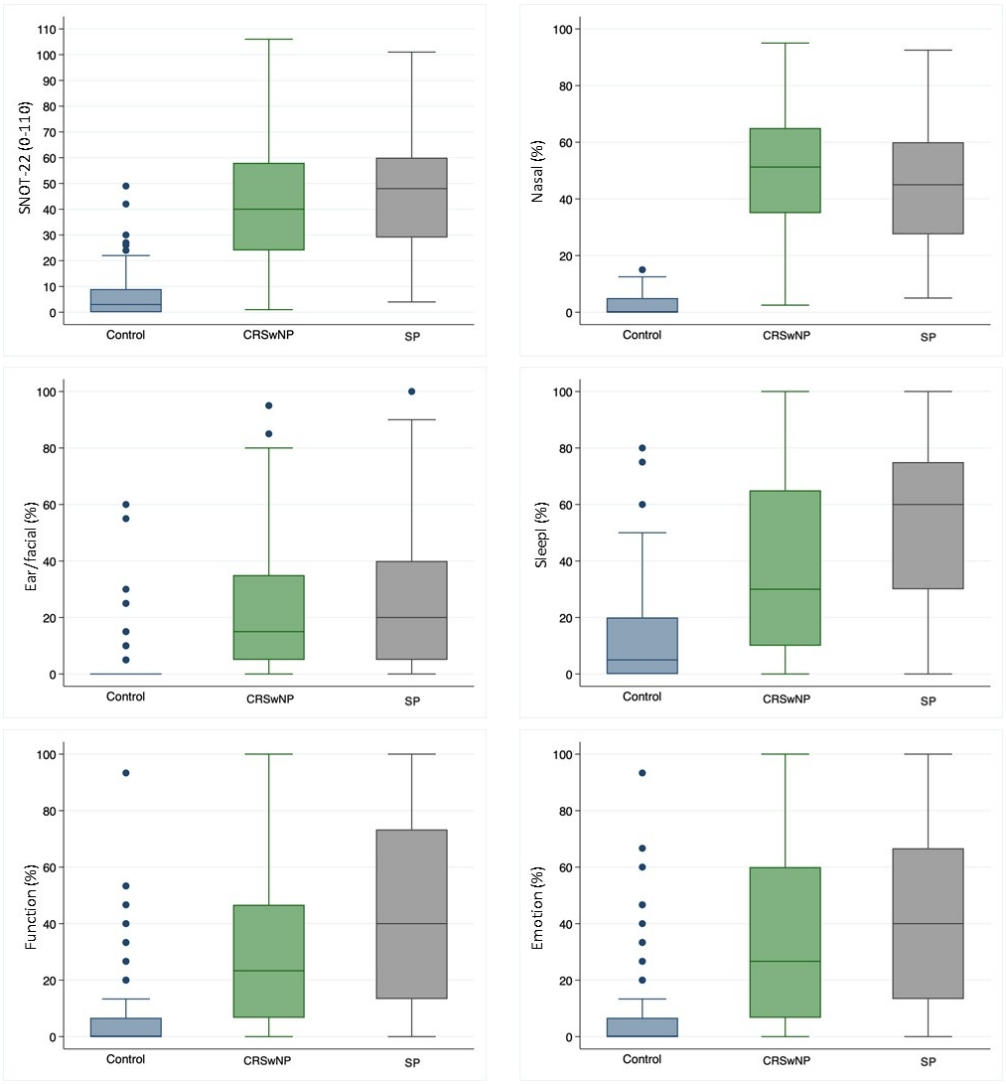

Figure 3. Box plots of the total score of the SNOT-22 and by domains expressed as a percentage of the three cohorts.
CRSwNP: chronic rhinosinusitis with nasal polyposis. SP: septal perforation.

170x183mm (150 x 150 DPI)