ORIGINAL CONTRIBUTION

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# Impact of chronic rhinosinusitis therapy on quality of life; A prospective randomized controlled trial*

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SUMMARY

***Objectives:*** *To conduct the first prospective randomized controlled trial, evaluating and comparing the effect of medical and surgical treatment of chronic rhinosinusitis (CRS) on quality of life.*

***Materials and Methods:*** *Ninety patients with CRS, who remained symptomatic after initial medical treatment with Dexarhinaspray duo and nasal douche, were randomized either to medical or surgical therapy. All patients underwent pre- and post-treatment assessments of the Sinonasal Outcome Test-20 (SNOT-20), and the Short Form 36 Health Survey (SF-36). Each patient had three assessments: before starting the randomized treatment, after six months and finally after one year.*

***Results:*** *Both the medical and surgical treatment of CRS significantly improved almost all the parameters of SNOT and SF-36 ($p < 0.05$), with no significant difference being found between the medical and surgical groups ($p > 0.05$).*

***Conclusion:*** *Both maximal medical and surgical therapy of CRS improves the quality of life of CRS patients, providing further evidence that chronic rhinosinusitis should be targeted with maximal medical therapy in the first instance, with surgical treatment being reserved for cases refractory to medical therapy. The presence of nasal polyps does not imply any negative effect on the quality of life after CRS therapy, either medical or surgical.*

*Key words: chronic rhinosinusitis, nasal polyposis, randomized, medical treatment, surgical treatment, endoscopic sinus surgery, SNOT-20, SF-36.*

## INTRODUCTION

Chronic rhinosinusitis (CRS) has been reported to affect 5-15% of urban populations in Europe [(1)]. In the United States, approximately 12 % of the Americans below the age of 45 years have been described as suffering symptoms of chronic rhinosinusitis [(2)]. CRS has been shown to have a significant impact on patients and their families, not only physically, but also psychologically affecting the overall emotional well-being. Because of the physical and psychological consequences of CRS, a great emphasis is placed on its meticulous treatment. A wide range of medical and surgical therapies has been used to treat CRS. Medical therapy of CRS includes antimicrobials, corticosteroids, decongestants, antihistamines, mast cell stabilizers, antileukotrienes, nasal douching, immunotherapy and reduction of irritant environmental factors. On the other hand, sinus surgery is broadly classified into conventional and endoscopic sinus surgery, with endoscopic sinus surgery largely replacing conventional sinus procedures [(3,4)].

Health-related quality-of-life questionnaires are increasingly used to measure disease severity and management outcomes. Quality-of-life instruments have been used to evaluate the impact of various situations such as cystic fibrosis [(5)], otitis media [(6)], obstructive sleep apnea [(7)] and rhinosinusitis [(8)]. Some studies documented the improvement of quality of life in patients with CRS after sinus surgery [(9)]. On the other hand, few trials have explored the effect of medical treatment of CRS on quality of life. This lack of documentation of medical therapy, has led to the suggestion that sinus surgery has a better impact on the quality of life than medical therapy in the absence of a well-performed, prospective, randomized, controlled trial that fulfils level I/II evidence. Therefore, the present investigation was designed as a prospective randomized

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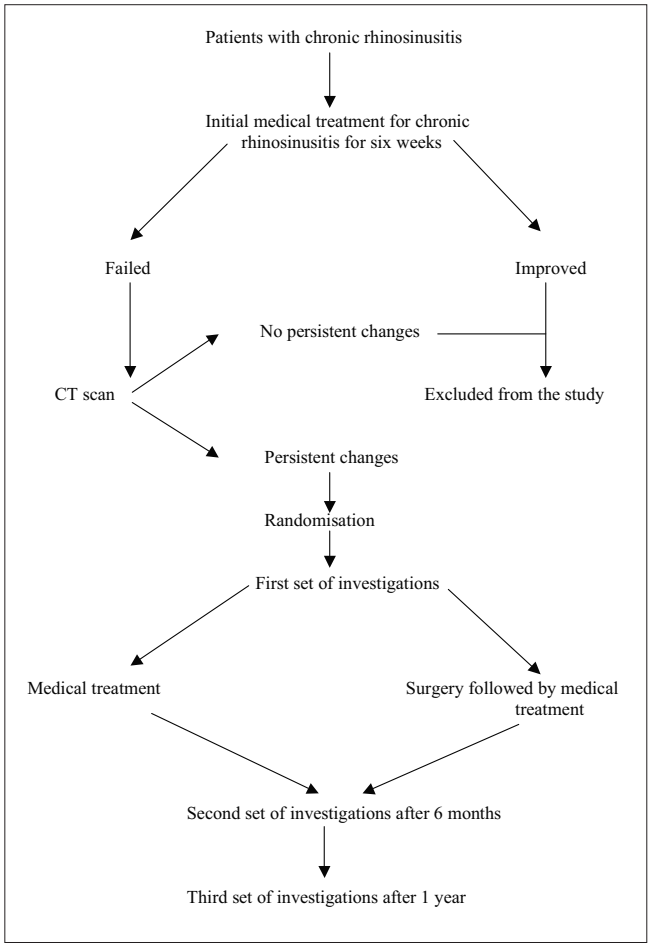


Figure 1. Study design.

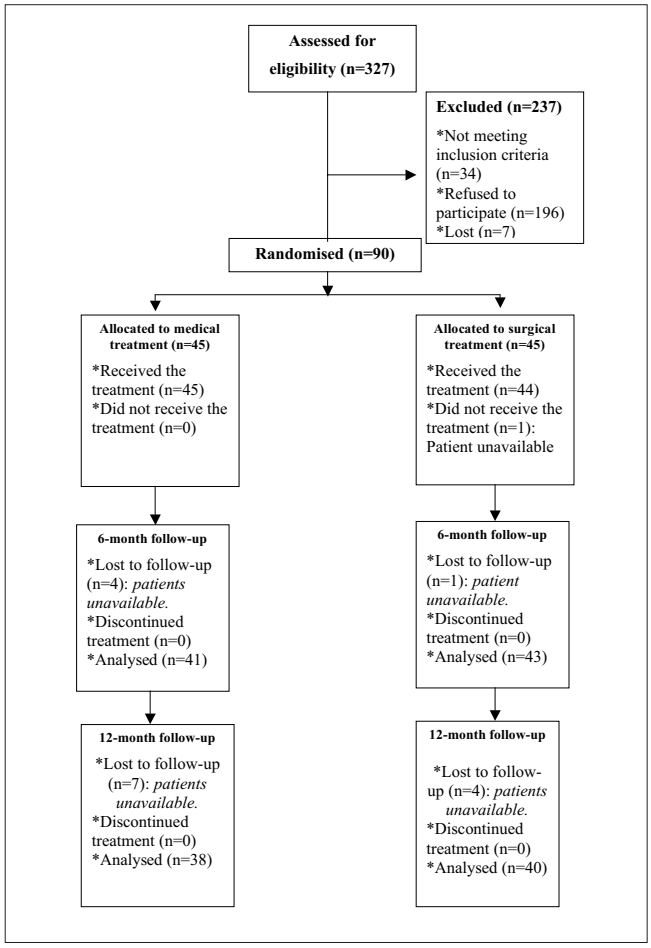


Figure 2. Flow chart of the study.

controlled trial to investigate and compare the effect of the medical and surgical treatment of CRS on quality-of-life as well as on symptoms and signs in upper and lower airways [10].

## METHODS

Ninety CRS patients (with and without polyps) were recruited over two years to be included in the study. The protocol of the study and the methods of consent had been approved by the Royal Free Hospital and Medical School Ethics Committee. The diagnosis of chronic rhinosinusitis was primarily based on the criteria described by the Staging and Therapy Group [11]. The patients were equally randomized to a medical and a surgical group. The design and flow chart of the study are shown in Figures 1 and 2 respectively. The exclusion criteria included pregnancy, lactation, significant psychological problems, inability to comply with the study protocol, children under 18 years of age, systemic diseases affecting the nose, acute upper or lower respiratory tract infections within two weeks prior to the inclusion visit, use of systemic corticosteroids within four weeks prior to the inclusion visit, systemic diseases preventing participation in the study and medical and/or surgical treatments influencing the study. The study comprised 45 males and 45 females, with a mean age ± [SD] of 43 ± [13], 35 CRS with polyposis (19 surgical and 16 medical), 43 asthmatics (23 surgical and 20 medical), 3 aspirin sensitive (2 surgical and 1 medical) and 49 with positive skin prick test (25 surgical and 24 medical). Patients were assessed subjectively using a visual analogue scale [11] and objectively using nasal endoscopy, acoustic rhinometry, nasal nitric oxide and saccharine clearance measurements. These results have been previously published [10]. Computed tomography was performed for every patient [10] prior to inclusion. Patients had to have evidence of inflammatory disease as defined by a Lund-Mackay score of $> 6$ [12] [Surgical group: mean 14 ± 0.8, medical group: mean 12 ± 0.7].

*The quality of life instruments*

a. The Sinonasal Outcome Test-20 (SNOT-20) (13)

The patients were asked to score a list of 20 symptoms, social and emotional consequences, grading them 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 the need to blow the nose, sneezing, runny nose, cough, postnasal discharge, thick nasal discharge, ear fullness, dizziness, ear pain, facial pain/pressure, difficulty falling asleep, waking up at night, lack of a good night's sleep, waking up tired, fatigue, reduced productivity, reduced concen-

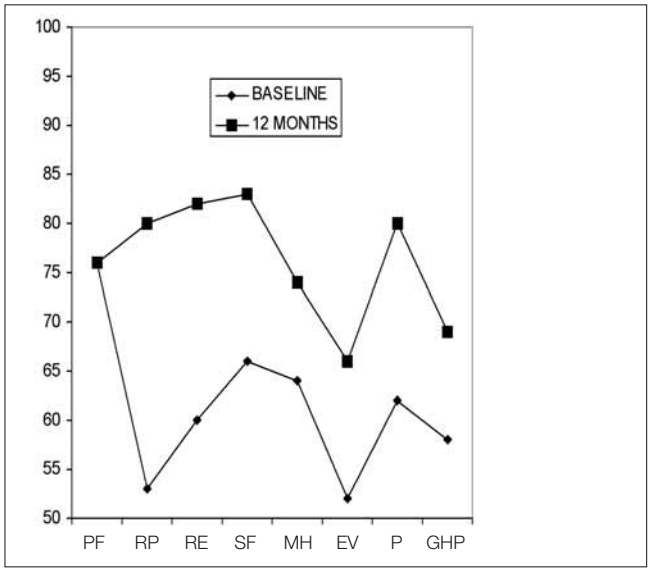


Figure 3A. Baseline and 12 month SF-36 of the surgical group.

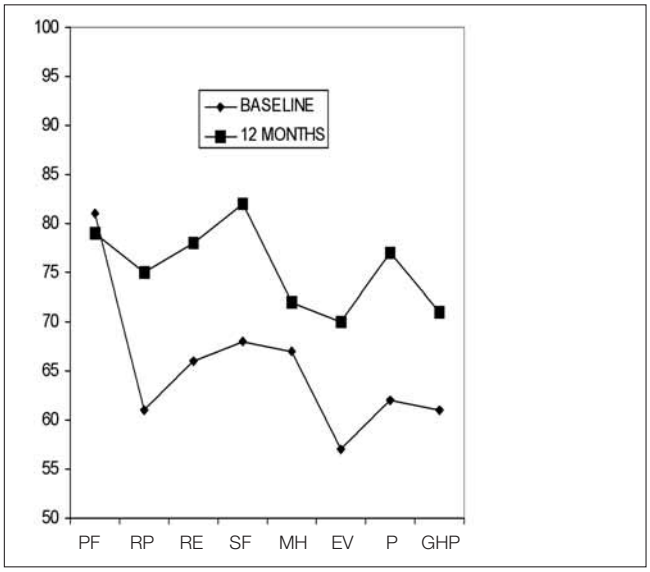


Figure 3B. Baseline and 12 month SF-36 of the medical group.

tration, frustrated/restless/irritable, sad and embarrassed. They were then requested to mark the most important 5 items, though these are not directly included in the scoring of SNOT-20. The average scores were used to compare patient data [13] (Permission from J. Piccirillo) (oto2.wustl.edu/clinepi/Forms/inst_snot20.doc).

b. The Short Form 36 Health Survey (SF-36) [14]

Patients were asked to score a set of eight domains. The eight domains were physical functioning (PF), role limitation due to physical problems (RP), role limitation due to emotional problems (RE), social functioning (SF), mental health (MH), energy/vitality (EV), pain (P) and general health perception (GHP). The number of items involved in the eight domains was ten, four, three, two, five, four, two and five respectively. Change in health was another subscale in the questionnaire but it was not presented in terms of means and standard deviations. Data were collected and scored according to the SF-36 analysis and interpretation manual. Permission to use this measure was obtained from the Medical Outcome Trust (Boston, United States of America). The interpretation of the SF-36 scores is described in Table 1.

*Medical treatment*

The initial medical treatment

The initial medical treatment included a six-week regimen of Dexarhinaspray duo (DRS) and an alkaline nasal douche (20 mls 0.75% sodium chloride and 0.75% sodium bicarbonate

Table 1. The interpretation of the SF-36 scores. Modified from Ware et al. [14].

| Domain | Score interpretation | |
|---|---|---|
| | Lowest possible score | Highest possible score |
| Physical functioning | All physical activities including bathing or dressing were limited a lot due to the patient's health. | All types of physical activities including the most vigorous were not limited at all. |
| Role limitation due to physical problems | During the previous 4 weeks, the patient had problems with work or other daily activities as a result of physical health. | During the previous 4 weeks, the patient had no problems with work or other daily activities as a result of physical health. |
| Role limitation due to emotional problems | During the previous 4 weeks, the patient had problems with work or other daily activities due to emotional problems. | During the previous 4 weeks, the patient had no problems with work or other daily activities due to emotional problems. |
| Social functioning | During the previous 4 weeks, the patient's physical health or emotional problems severely interfered with his normal social activities. | During the previous 4 weeks, the patient's physical health or emotional problems did not interfere with his normal social activities. |
| Mental health | During the previous 4 weeks, the patient felt nervous and depressed all the time. | During the previous 4 weeks, the patient felt happy, calm and peaceful all the time. |
| Energy/vitality | During the previous 4 weeks, the patient felt tired and worn out all the time. | During the previous 4 weeks, the patient felt full of pep and energy all the time. |
| Pain | During the previous 4 weeks, pain was very severe and seriously interfered with the patient' s normal work. | The patient did not have any pain or interference with his work due to pain in the previous 4 weeks. |
| General health perception | The patient believed that his personal health was poor and likely to get worse. | The patient believed that his health was excellent. |

solution). DRS was delivered as two puffs into each nostril twice daily, with each metered dose containing 20 micrograms of dexamethasone-21-isonicotinate and 120 micrograms of tramazoline hydrochloride. The alkaline nasal douche powder was prepared in a 1:1 mixture of sodium chloride and sodium bicarbonate. The douche was also used twice daily. Patients with positive SPT were also given allergen avoidance advice.

The medical treatment for the medically randomized group

All patients received a 12-week course of erythromycin, alkaline nasal douche and intranasal corticosteroid preparations. Erythromycin was prescribed orally as 500 mg twice daily for two weeks, followed by 250 mg twice daily for 10 weeks. Alkaline nasal douche was prepared and used as instructed above. Intranasal corticosteroid preparations, in patients of CRS without polyposis, were given as DRS, two puffs into each nostril, twice daily, for two weeks, followed by a twice daily dose of 100 micrograms (2 sprays) of fluticasone propionate spray into each nostril for 10 weeks. On the other hand, patients suffering CRS with polyposis received a 12-week course of twice daily use of 200 micrograms (6 drops) of fluticasone propionate drops into each nostril. In addition, 3 patients of CRS with polyposis were prescribed a 9-day course of oral prednisolone tablets, 30 mg for 3 days, 20 mg for 3 days and 10 mg for 3 days after failure of the above regimen to control their manifestations. After this, the use of intranasal corticosteroid preparations was tailored to the patient's clinical course.

The medical treatment after surgery

Following endoscopic sinus surgery, all patients were prescribed a two-week course of twice-daily use of 500 mg erythromycin, DRS and alkaline nasal douche. This was followed by a three-month course of twice-daily use of 100 micrograms (2 sprays) of fluticasone propionate intranasal spray, into each nostril and alkaline nasal douche. After this, the use of intranasal corticosteroid preparations was tailored to the patient's clinical course.

*Surgical treatment*

Endoscopic sinus surgery was performed in all patients following the Messerklinger/Stammberger technique [15]. All cases were done under general anesthesia. The extent of the procedure was tailored to the extent of sinus disease as documented by nasal endoscopy and CT scan findings. At the end of the procedure, a piece of Telfa was inserted into the ethmoidal cavity and taken out on the following day. Operative findings and complications were recorded in every case. Surgical steps were scored according to Lund and Mackay scoring system [12].

*Statistical methods*

To maintain exactly equal treatment numbers in both groups, randomization was done using random blocks. At the time of randomization, both the patient and the investigator were not aware of the group assignment. A sample size of 66 patients was calculated using Wilcoxon two-sample test, two-sided, at the 5% level of significance to give the study a statistical power of 80%. The primary end point was determined to be the visual analogue scale for chronic rhinosinusitis. However, the number of the patients intended to be recruited was 90 to raise the power of the study as well as to compensate for any loss, which might occur during the follow-up period. The analysis was done using SPSS for Windows version 9 statistics software package. Data were expressed as mean ± standard deviation (SD). P-values $< 0.05$ were considered signifi-

Table 2. Baseline and 12-month Total SNOT and most important 5 items in the surgical groups of CRS.

| Parameter | Group | baseline | | 12 months | | |
|---|---|---|---|---|---|---|
| | | *Mean* | *SD* | *Mean* | *SD* | *p value* |
| Total SNOT | *CRS* | 2.2 | 1 | 1.1 | 0.98 | $< 0.01$ |
| | *CRS without polyposis* | 2.3 | 0.9 | 1.2 | 0.8 | $< 0.01$ |
| | *CRS with polyposis* | 2 | 1 | 0.8 | 1 | $< 0.01$ |
| Most important 5 items | *CRS* | 3.8 | 0.8 | 1.7 | 1.2 | $< 0.01$ |
| | *CRS without polyposis* | 3.9 | 0.9 | 1.9 | 1.3 | $< 0.01$ |
| | *CRS with polyposis* | 3.6 | 0.8 | 1.5 | 1.3 | $< 0.01$ |

Table 3. Baseline and 12-month Total SNOT and most important 5 items in the medical groups of CRS.

| Parameter | Group | baseline | | 12 months | | |
|---|---|---|---|---|---|---|
| | | *Mean* | *SD* | *Mean* | *SD* | *p value* |
| Total SNOT | *CRS* | 2 | 0.9 | 1.1 | 1 | $< 0.01$ |
| | *CRS without polyposis* | 2.1 | 1 | 1.4 | 1.2 | $< 0.01$ |
| | *CRS with polyposis* | 1.6 | 0.6 | 0.7 | 0.4 | $< 0.01$ |
| Most important 5 items | *CRS* | 3.7 | 0.8 | 1.9 | 1.4 | $< 0.01$ |
| | *CRS without polyposis* | 3.8 | 0.9 | 2.1 | 1.5 | $< 0.01$ |
| | *CRS with polyposis* | 3.5 | 0.7 | 1.5 | 0.8 | $< 0.01$ |

Table 4. Baseline and 12-month SF-36 of the surgical groups of CRS.

| SF-36 domain | Group | baseline | | 12 months | | |
|---|---|---|---|---|---|---|
| | | *Mean* | *SD* | *Mean* | *SD* | *p value* |
| PF | *CRS* | 76 | 27 | 76 | 26 | $> 0.05$ |
| | *CRS without polyposis* | 73 | 30 | 70 | 28 | $> 0.05$ |
| | *CRS with polyposis* | 81 | 21 | 81 | 23 | $> 0.05$ |
| RP | *CRS* | 53 | 38 | 80 | 34 | $< 0.01$ |
| | *CRS without polyposis* | 42 | 37 | 71 | 37 | $< 0.01$ |
| | *CRS with polyposis* | 68 | 35 | 89 | 28 | $< 0.01$ |
| RE | *CRS* | 60 | 42 | 82 | 35 | $< 0.01$ |
| | *CRS without polyposis* | 45 | 41 | 71 | 41 | $< 0.01$ |
| | *CRS with polyposis* | 79 | 36 | 94 | 22 | $< 0.01$ |
| SF | *CRS* | 66 | 27 | 83 | 25 | $< 0.01$ |
| | *CRS without polyposis* | 60 | 26 | 77 | 25 | $< 0.01$ |
| | *CRS with polyposis* | 74 | 28 | 91 | 23 | $< 0.01$ |
| MH | *CRS* | 64 | 22 | 74 | 19 | $< 0.01$ |
| | *CRS without polyposis* | 59 | 24 | 69 | 20 | $< 0.01$ |
| | *CRS with polyposis* | 70 | 16 | 79 | 16 | $< 0.01$ |
| EV | *CRS* | 52 | 20 | 66 | 20 | $< 0.01$ |
| | *CRS without polyposis* | 50 | 18 | 62 | 20 | $< 0.01$ |
| | *CRS with polyposis* | 55 | 22 | 69 | 16 | $< 0.01$ |
| P | *CRS* | 62 | 29 | 80 | 21 | $< 0.01$ |
| | *CRS without polyposis* | 56 | 27 | 74 | 21 | $< 0.01$ |
| | *CRS with polyposis* | 70 | 30 | 87 | 20 | $< 0.01$ |
| GHP | *CRS* | 58 | 20 | 69 | 19 | $< 0.01$ |
| | *CRS without polyposis* | 60 | 18 | 69 | 18 | $< 0.01$ |
| | *CRS with polyposis* | 55 | 23 | 69 | 20 | $< 0.01$ |

Table 5. Baseline and 12-month SF-36 of the medical groups of CRS.

| SF-36 domain | Group | baseline | | 12 months | | |
|---|---|---|---|---|---|---|
| | | *Mean* | *SD* | *Mean* | *SD* | *p value* |
| PF | *CRS* | 81 | 21 | 79 | 21 | $> 0.05$ |
| | *CRS without polyposis* | 81 | 21 | 79 | 21 | $> 0.05$ |
| | *CRS with polyposis* | 81 | 22 | 77 | 21 | $> 0.05$ |
| RP | *CRS* | 61 | 39 | 75 | 33 | $< 0.01$ |
| | *CRS without polyposis* | 57 | 42 | 68 | 37 | $< 0.01$ |
| | *CRS with polyposis* | 67 | 33 | 90 | 16 | $< 0.01$ |
| RE | *CRS* | 66 | 39 | 78 | 35 | $< 0.01$ |
| | *CRS without polyposis* | 56 | 42 | 70 | 40 | $< 0.01$ |
| | *CRS with polyposis* | 83 | 26 | 92 | 19 | $< 0.01$ |
| SF | *CRS* | 68 | 27 | 82 | 22 | $< 0.01$ |
| | *CRS without polyposis* | 67 | 28 | 79 | 25 | $< 0.01$ |
| | *CRS with polyposis* | 69 | 25 | 87 | 16 | $< 0.01$ |
| MH | *CRS* | 67 | 21 | 72 | 20 | $< 0.01$ |
| | *CRS without polyposis* | 67 | 22 | 70 | 20 | $< 0.01$ |
| | *CRS with polyposis* | 68 | 18 | 77 | 18 | $< 0.01$ |
| EV | *CRS* | 57 | 19 | 70 | 17 | $< 0.01$ |
| | *CRS without polyposis* | 56 | 18 | 67 | 17 | $< 0.01$ |
| | *CRS with polyposis* | 60 | 20 | 76 | 16 | $< 0.01$ |
| P | *CRS* | 62 | 22 | 77 | 21 | $< 0.01$ |
| | *CRS without polyposis* | 56 | 21 | 71 | 20 | $< 0.01$ |
| | *CRS with polyposis* | 74 | 19 | 90 | 15 | $< 0.01$ |
| GHP | *CRS* | 61 | 21 | 71 | 16 | $< 0.01$ |
| | *CRS without polyposis* | 60 | 23 | 69 | 16 | $< 0.01$ |
| | *CRS with polyposis* | 63 | 16 | 73 | 16 | $< 0.01$ |

cant. Parametric tests such as paired t test, two-sample t test and analysis of variance were applied for data that followed or were transformed to a normal distribution. Either logarithmic or square transformation was tried to normalize the distribution so as to allow the use of parametric tests. Non-parametric tests such as Mann-Whitney U test, Wilcoxon signed ranks test, Sign test, Chi-squared test and Kruskal-Wallis test were applied for data that did not follow a normal distribution.

## RESULTS

### *a. SNOT*

In the 6- and 12-month follow-up settings, the Total SNOT and the most important 5 item scores showed a significant improvement in all groups ($p < 0.01$, Wilcoxon test), whereas there was no statistical evidence for differences between the medical and surgical groups ($p > 0.05$, Mann-Whitney test). The differences between the 6- and 12-month scores were statistically insignificant in all groups ($p > 0.05$, Wilcoxon test)

except for the total SNOT of the medical group of CRS with polyposis where there was a further improvement ($p < 0.05$, Wilcoxon test). Tables 2 and 3 show the baseline and 12-month Total SNOT and Most important 5 items in the surgical and medical groups of CRS.

*b. SF-36*

In the 6- and 12 month follow-up setting, PF did not change significantly from the baseline in all groups ($p > 0.05$, Wilcoxon test), whereas the other 7 domains showed a significant improvement ($p < 0.01$, Wilcoxon test). The differences between the medical and surgical groups were statistically insignificant ($p > 0.05$, Mann-Whitney test). The differences between the 6- and 12-month EV scores were statistically significant ($p < 0.05$, Wilcoxon test), whereas the other 7 domains were not ($p > 0.05$, Wilcoxon test). Tables 4 and 5 show the baseline and12-month SF-36 of the surgical and medical groups of CRS.

## DISCUSSION

There is a growing interest in the use of generic health status questionnaires to provide broad measures of health which can be used either to provide normative population data, to compare the impact of different diseases and conditions on health and/or to monitor the health of individuals and groups over time. CRS affects large numbers of the worldwide population and has a big impact on quality of life [16]. To date there have been no randomized trials studying the effect of the medical and surgical treatment of CRS in improving the quality of life. In the current study we tested and compared the change in quality of life after medical and surgical treatment of CRS using two quality of life instruments: The Sinonasal Outcome Test-20 (SNOT-20) [13] and The Short Form 36 Health Survey (SF-36) [14]. SNOT-20 is a validated rhinosinusitis specific health-related quality of life instrument that measures both sinusitis specific and general health items. In this study, the total SNOT and the most important 5 item scores showed a significant improvement in CRS overall, both for CRS without polyposis and CRS with polyposis. No statistical evidence for differences between the medical and surgical groups was shown. On the other hand, SF-36 is a general health-status quality of life instrument that translates symptoms into an important broader concern to the patients. In our trial, the medical and surgical treatment improved 7 of the 8 domains of the SF-36 quality of life instrument, with no difference between the surgical and medical groups.

This study has documented that both maximal medical and surgical therapy of CRS improve quality of life in CRS patients. Litvack et al. [16] in an observational study showed that both primary and revision endoscopic sinus surgery equally improved quality of life using instruments: the Rhinosinusitis Disability Index (RSDI) and Chronic Sinusitis Survey (CSS). Videler et al., in a prospective questionnaire based study, stated that radical sinus surgery also improved quality of life in a cohort of 23 patients [17]. Other studies have described a similar improvement in quality of life in patients of CRS after sinus surgery [8,18-21].

This overall study considered many other objective outcome measures, which also showed significant improvement in both the surgical and medical arms. The effect of treatment on the lower respiratory tract was considered and showed benefit in both medical and surgical arms in those patients with pre-existing asthma [22]. This might also have had an influence on quality of life though no statistical difference was shown in this respect between the asthmatics and non-asthmatics. The use of expired nitric oxide was also explored in both the upper and lower respiratory tract [23].

Nasal polyposis has been suggested as a poor prognostic factor for the efficacy of surgical therapy to control CRS manifestations and hence is thought to have a negative effect on quality of life [24-26]. The present study does not support this since almost all the parameters of SNOT and SF-36 quality of life questionnaires improved significantly in the surgical and medical groups of CRS with polyposis, with no significant difference between the corresponding surgical and medical groups.

In an earlier study, Uri et al. showed endoscopic surgery improved symptoms and quality of life in asthmatic patients with massive polyposis [27]. A recent prospective audit conducted by the Royal College of Surgeons of England on 3128 patients undergoing surgery for chronic rhinosinusitis with and without nasal polyps also showed significant improvement over a 36-month follow-up using a SNOT questionnaire as a primary outcome measure [28]. However, it was not possible with this outcome measure to show advantage of extended sinus clearance over 'simple' polypectomy even when the latter was conducted endoscopically. This aspect was not considered in the present study where disease extent determined extent of surgery.
Interestingly there was no statistical difference in those lost to follow-up in the respective arms and in both groups; improvement was maintained with topical medical treatment during the one-year follow-up period [10]. However, it would be interesting to know over a much longer period how the two groups fared.

## CONCLUSION

Both maximal medical and surgical therapy of CRS improve the quality of life of CRS patients, providing further evidence that chronic rhinosinusitis should be targeted with maximal medical therapy in the first instance, with surgical treatment being reserved for cases refractory to medical therapy. The presence of nasal polyps is not associated with any negative effect on the quality of life after CRS therapy, either medical or surgical.

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