Change in nasal congestion index after treatment in patients with chronic rhinosinusitis with nasal polyposis

Serap Sahin-Onder, M.D.,[1] Asli Sahin-Yilmaz, M.D.,[2] Cagatay Oysu, M.D.,[2] Ildem Deveci, M.D.,[2] Samil Sahin, M.D.,[2] and Betul Aktas, M.D.[2]

ABSTRACT

Background: *The management of chronic rhinosinusitis with nasal polyposis (CRSwNP) involves both surgical and medical approaches, and remains a controversial subject.*

Objective*: The objective of this prospective, randomized, controlled trial was to compare the medical and surgical treatments of CRSwNP in terms of their effect on the nasal congestion index (NCI).*

Methods: *Forty-eight patients with CRSwNP were randomized either to medical or surgical therapy. Pretreatment and 3- and 6-month posttreatment assessments of the visual analog scale score, the 20-Item Sino-Nasal Outcome Test, saccharine clearance time, nasal endoscopy, and NCI measurement with acoustic rhinometry were performed. Forty-one subjects were included in the analysis.*

Results: *Both the medical and surgical interventions for CRSwNP resulted in significant improvement in the visual analog scale score, 20-Item Sino-Nasal Outcome Test, saccharine clearance time, and nasal endoscopic examination scores. There was no difference between the two groups in terms of the percentage change from baseline for any of the parameters at the 6-month posttreatment assessment. NCI showed no significant difference from baseline. Similarly, no significant difference was found between the medical and surgical groups in terms of their effect on the NCI ($p > 0.05$).*

Conclusion: *Because NCI does not correlate with standard subjective measures in outcomes for this group of patients, it cannot be used as an outcome measurement of treatment of subjects with CRSwNP. Results of this prospective randomized study did not find any additional benefit of surgical therapy over medical therapy in subjects with CRSwNP.*

(Allergy Rhinol 7:e193–e199, 2016; doi: 10.2500/ar.2016.7.0177)

Nasal polyposis is a benign inflammatory disease of the nasal cavity and paranasal sinuses. This condition is considered a subgroup of chronic rhinosinusitis. The symptoms include nasal obstruction, poor sinus drainage, loss of smell, runny nose, and nasal congestion. Chronic rhinosinusitis with nasal polyposis (CRSwNP) affects 4% of the population.[1] A diagnosis of CRSwNP is based on a history, anterior rhinoscopy, endoscopic examination, radiology, and histopathology. The management of CRSwP involves both surgical and medical approaches, and remains a controversial subject.[2] The aims of both modalities are to relieve nasal obstruction, restore olfaction, improve sinus drainage, and treat any accompanying rhinitic symptoms.[3] Medical therapy includes antimicrobials, nasal and oral corticosteroids, decongestants, antihistamines, mast cell stabilizers, antileukotrienes, nasal douching, immunotherapy, and reduction of environmental factors. Corticosteroids are the only medical therapy to have a proven effect on the symptoms and signs of CRSwP, and can be used topically or systemically.[4] The initial surgical management of CRSwP is endoscopic sinus surgery.

A recent Cochrane database review on the surgical versus medical interventions for CRSwP concluded that the evidence that related the effectiveness of different types of surgery versus medical treatment is of very low quality. It is unclear whether one treatment is better than the other in terms of patient-reported symptom scores and quality of life measurements.[2] A measurement for quantification of mucosal congestion has been defined by several investigators.[5–7] The nasal congestion index (NCI), as designated by Kjeargaad *et al.*[7] in 2009, indirectly assesses the amount of reversible mucosal congestion in the anterior and middle parts of the nasal cavities. NCI has been proven to be useful for evaluating patients with symptoms of nasal obstruction. Subjects with severe nasal obstruction have been shown to have significantly higher NCI than subjects with mild or moderate symptoms.[6,7] We believe that the NCI in subjects with CRSwNP may influence their postoperative quality of life. Therefore, we conducted a randomized prospective controlled study that evaluated the subjective and objective outcomes for the

From the [1]Otolaryngology Clinic, Amasya Suluova Government Hospital, Amasya, Turkey, and [2]Otolaryngology Clinic, Umraniye Education and Research Hospital, Istanbul, Turkey
No external funding sources reported
The authors have no conflicts of interest to declare pertaining to this article
Oral presentation at The Turkish Otolaryngology Society annual meeting, Antalya, Turkey, October 28–31, 2015
Address correspondence to Asli Sahin-Yilmaz, M.D., Otolaryngology Clinic, Umraniye Education and Research Hospital, Istanbul, Turkey
E-mail address: aslisahin@hotmail.com
Copyright © 2016, OceanSide Publications, Inc., U.S.A.

Delivered by Ingenta to: Guest User IP: 78.13.202.106 On: Sun, 05 Mar 2017 13:58:29
Copyright (c) Oceanside Publications, Inc. All rights reserved.
For permission to copy go to https://www.oceansidepubl.com/permission.htm

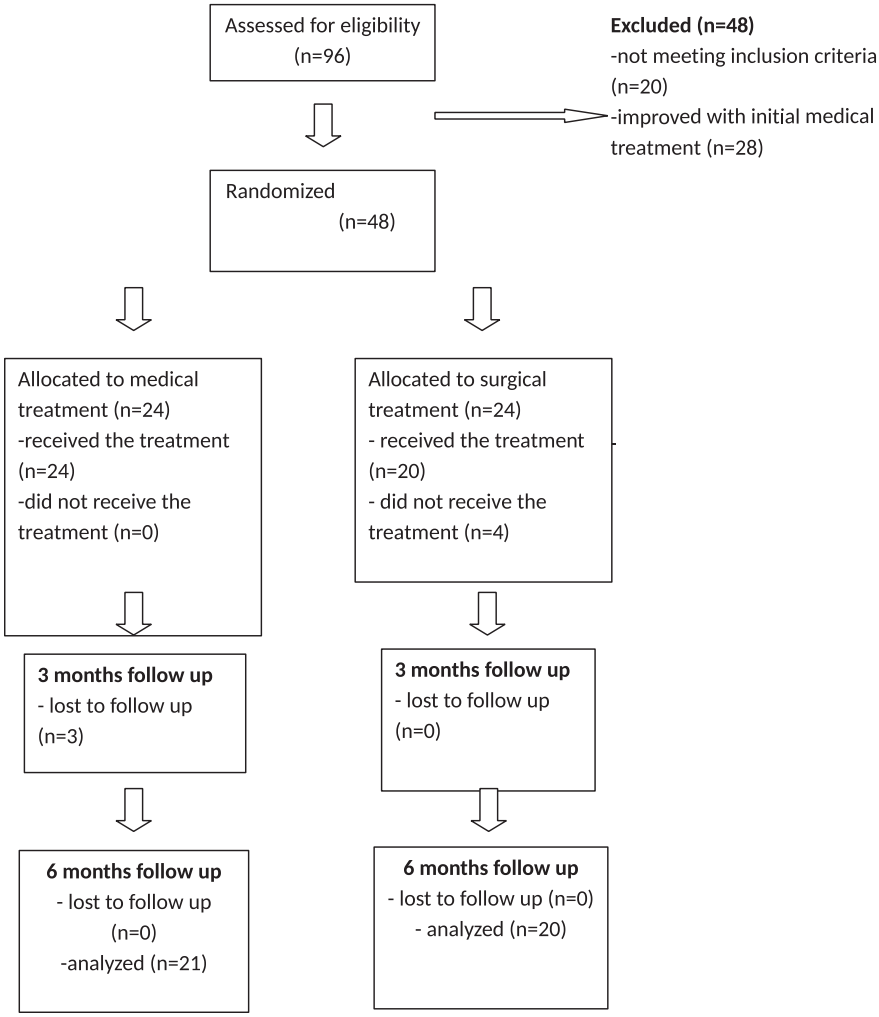

Figure 1. *The study design.*

surgical versus medical treatment of CRSwNP and added the NCI as an objective outcome measurement. As far as we know, our study was the first randomized controlled, prospective study that used this parameter as an outcome measurement in subjects with CRSwNP.

METHODS

Patients were recruited from the Otorhinolaryngology Clinics, Umraniye Research and Education Hospital. The protocol of the study and the methods of consent had been approved by Umraniye Research and Education Hospital Ethics Committee. The process of recruitment took place over 1 year. The flow chart and design of the study were planned similar to the exceptional study by Ragab *et al.*[8] and is shown in Fig. 1. The study was discussed with 96 consecutive patients with a primary diagnosis of CRSwNP. Forty-eight of the patients were excluded (20 of them did not meet the study criteria, 28 of them responded to initial medical treatment). Allocation was concealed from both the study participants and investigators before randomization. Forty-eight patients were randomized for inclusion in the study by using computer-generated random numbers.

The diagnosis of CRSwNP was primarily based on the criteria described by the European Position Paper on Rhinosinusitis and Nasal Polyps,[9] which defines these conditions clinically as "inflammation of the nose and paranasal sinuses, associated with two or more of the following symptoms for a duration of ≥12 weeks:

- blockage/congestion; discharge (anterior or postnasal drip); facial pain/pressure; reduction of smell; and
- either endoscopic evidence of polyps; mucopurulent discharge from the middle meatus or edema/mucosal obstruction primarily in the middle meatus; and/or mucosal changes within the osteomeatal complex or sinuses on computed tomography (CT) imaging."

The exclusion criteria were children <18 years of age, pregnancy, psychological problems, systemic diseases that affect the nose, acute upper or lower respi-

Delivered by Ingenta to: Guest User IP: 78.13.202.106 On: Sun, 05 Mar 2017 13:58:29
Copyright (c) Oceanside Publications, Inc. All rights reserved.
For permission to copy go to https://www.oceansidepubl.com/permission.htm

ratory tract infections within 2 weeks, use of systemic corticosteroids within 4 weeks before the inclusion visit, and other medical or surgical treatments that may influence the study.

Subjective Assessment

Subjective assessment of patients was made by using a visual analog scale (VAS) of 0 to 10 cm. Nasal blockage or congestion, nasal discharge, olfactory disturbance, facial pain or pressure, headache, and overall discomfort were used as the scoring criteria. A total score was calculated. The 20-Item Sino-Nasal Outcome Test (SNOT-20) was also used in this study. Assessment included 20 symptoms and social and emotional consequences.

Examination of the Nose. Nasal endoscopy was performed in all the subjects. The scoring system by Mackay was used, which evaluated the following: nasal polyps size (0, none; 1, limited to the middle meatus; 2, filling the nasal cavity), the presence of pus (0, no; 1, thin purulent; 2, mucoid), edema, crusting, and scar.[10] When present during the endoscopic examination, edema, crusting, and scar were scored as "1" point for each.

Objective Measurements

Acoustic Rhinometry. Measurements were taken with the use of acoustic rhinometry (Interacoustics, Assens, Denmark). During the measurements, the subjects sat erect in the chair and kept the head perpendicular to the horizontal plane. They were instructed to hold their breath during the measurement. The test was repeated three times, and estimates of the minimum cross-sectional area and volume of the nasal cavity were calculated from the mean of the three sets of five measurements. Measurements from both nostrils were averaged to get an overall mean value to represent both nasal cavities and to account for variations between nostrils due to the nasal cycle.[7] The measurements were repeated 10 minutes after application of a topical nasal decongestant (0.1% xylometazoline hydrochloride nasal spray) to both nostrils. The parameters used for the calculation of NCI included the total minimal cross-sectional area (MCA3) and the volume of the nasal cavity between 0 and 5 cm from the tip of the nosepiece (VOL3). The NCI was calculated for the total MCA3 (NCI-MCA3) and the total VOL3 (NCI-VOL3) by using the following formula by Kjaergaard[7]:

$$\text{NCI} = (\text{postdecongestant value} - \text{baseline predecongestant value})/(\text{baseline predecongestant value} \times 100)$$

SCT. One saccharine tablet was placed 1 cm behind the anterior end of the inferior turbinate of the subjects' nasal cavity while the subjects were in a sitting position. The subjects were asked to breathe through the nose normally but not to sniff, sneeze, eat, or drink. When the subject perceived a sweet taste, then the SCT was recorded in minutes and seconds by using chronometer.

Medical Treatment

Initial Medical Treatment. The initial medical treatment included a 6-week regimen of a nasal douche and fluticasone furoate (FF) intranasal spray. The nasal douche powder was a preservative- and iodine-free, pH balanced, sodium chloride, sodium bicarbonate mixture. The subjects were instructed to use the douche twice daily 15 minutes before taking FF, delivered as two puffs into each nostril twice daily. The subjects who remained symptomatic after this treatment were randomized into the study.

Medical Treatment for the Medically Randomized Group. All the patients received a 12-week course of clarithromycin, nasal douche, intranasal fluticasone propionate nasal drops, and oral steroids. Clarithromycin was prescribed orally as 500 mg twice daily for 2 weeks, followed by 250 mg twice daily for 10 weeks. Nasal douche was prepared and used as described elsewhere in the text. All the patients received a 12-week course of twice daily use of 400 μg of fluticasone propionate nasal drops into each nostril, and 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.

Surgical Treatment

In all the patients, endoscopic sinus surgery with the patient under general anesthesia was performed by two surgeons (S.O., A.S.Y.). The extent of the procedure was tailored to the extent of sinus disease as documented by nasal endoscopy and computed tomography findings. A microdebrider was used in all the cases. At the end of the procedure, a portion of a Merocel (Jacksonville, MN) sinus pack was inserted into the ethmoidal cavity on each side and was removed on the following day. Operative findings and complications were documented for all the subjects.

Medical Treatment after Surgery. After endoscopic sinus surgery, all the patients were prescribed a 2-week course of twice daily use of 500 mg of clarithromycin, FF, and nasal douche, which was followed by a 3-month course of twice daily use of 100 μg (2 sprays) of FF intranasal spray into each nostril and nasal douche. After that, the medical treatment was tailored to the patient's manifestations, which usually included topical FF. None of the subjects received oral steroids after surgery.

Delivered by Ingenta to: Guest User IP: 78.13.202.106 On: Sun, 05 Mar 2017 13:58:29
Copyright (c) Oceanside Publications, Inc. All rights reserved.
For permission to copy go to https://www.oceansidepubl.com/permission.htm

Table 1 **A comparison of the medical and surgical groups in terms of baseline parameters**

Baseline Parameters	Surgical Group	Medical Group	*p*
Age, mean ± SD, y	40.8 ± 11.9	45.19 ± 15.1	NS
Men/women, %	65/35	66/34	NS
VAS score, mean ± SD	30.9 ± 10.33	28.19 ± 8.21	NS
SNOT-20 score, mean ± SD	37.9 ± 23.77	35.86 ± 17.59	NS
Examination of the nose, mean ± SD	3.25 ± 1.37	3.95 ± 1.6	NS
NCI-MCA3, mean ± SD	0.38 ± 0.35	0.21 ± 0.23	NS
NCI-VOL3, mean ± SD	0.15 ± 0.15	0.21 ± 0.23	NS
SCT, mean ± SD	13.5 ± 9	14.4 ± 8.9	NS
Other medical conditions, mean ± SD	none	none	NS

SD = Standard deviation; NS = nonsignificant; VAS = visual analog scale; SNOT-20 = 20-Item Sino-Nasal Outcome Test; NCI-MCA3 = nasal congestion index for minimal total cross-sectional area; NCI-VOL3 = nasal congestion index for total volume; SCT = saccharine clearance time.

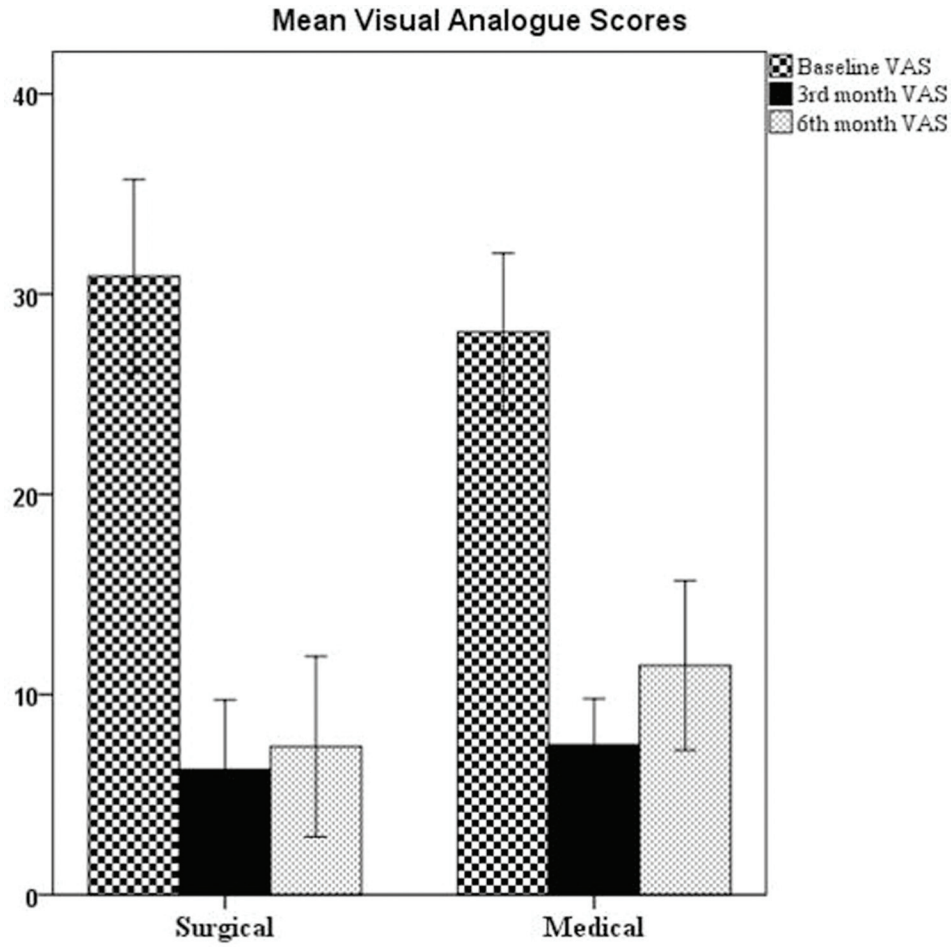

Figure 2. *The change in the visual analog scale score (VAS) of the medical and surgical groups.*

Statistical Methods

The analysis was performed by using SPSS for Windows (IBM SPSS, Istanbul, Turkey). Parametric tests, such as the paired *t*-test and analysis of variance, were used for the parameters that showed a normal distribution. For the data that did not follow a normal distribution, the Mann-Whitney *U* test was used. A *p* value of <0.05 was considered significant.

RESULTS

The final analysis included 41 patients in total (27 men and 14 women), with a mean age of 43 years.

Baseline Data

There was no statistically significant difference between the medical and surgical groups in the baseline

Delivered by Ingenta to: Guest User IP: 78.13.202.106 On: Sun, 05 Mar 2017 13:58:29
Copyright (c) Oceanside Publications, Inc. All rights reserved.
For permission to copy go to https://www.oceansidepubl.com/permission.htm

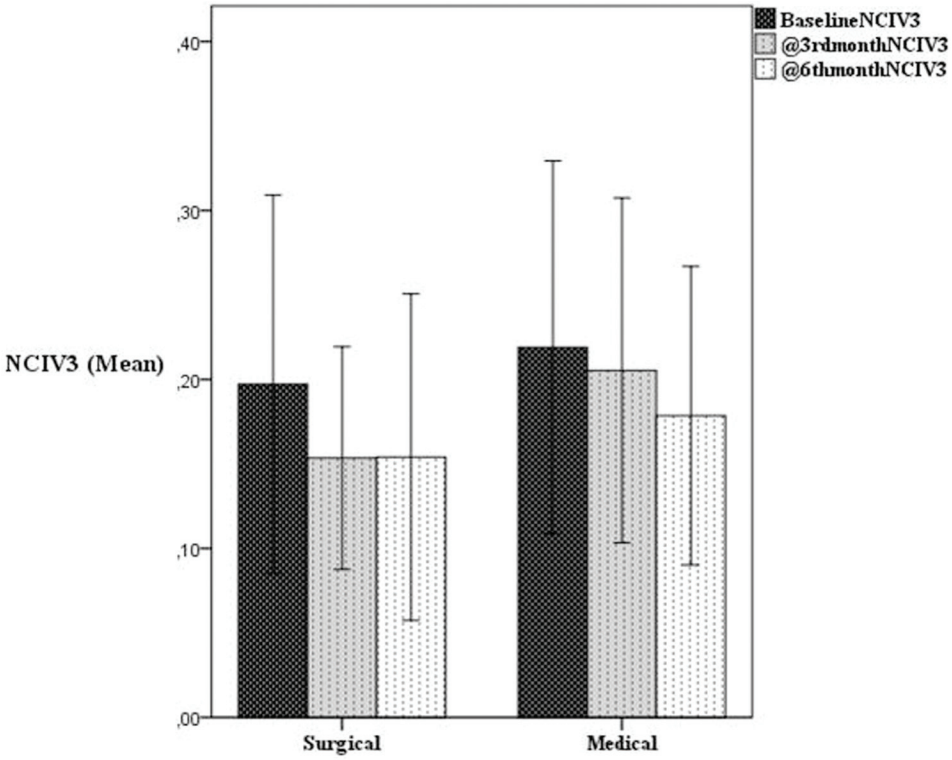

Figure 3. *Baseline, and 3- and 6-month measurements of the nasal congestion index for the total nasal cavity volume (NCI-VOL3) of both groups.*

data of any of the following parameters: demographic characteristics, VAS, SNOT-20, saccharine clearance time (SCT), NCI-MCA3, NCI-VOL3, and the endoscopic score (Table 1).

Subjective Assessment

VAS. In the 3- and 6-month follow-up data, we saw that all the groups experienced a significant improvement in the total VAS scores ($p < 0.01$) (Fig. 2). There was no statistical difference between the medical and surgical groups ($p > 0.05$). The difference between the two groups for the 3- and 6-month percentage change in VAS from baseline was statistically insignificant ($p > 0.05$). Changes and significance tests of VAS in the medical and surgical groups are illustrated in Table 1.

SNOT-20. In the 3- and 6-month follow-up settings, the total SNOT-20 scores showed a significant improvement in all the groups ($p < 0.01$), whereas there was no statistical difference between the medical and surgical groups ($p > 0.05$). The comparison of the percentage change in SNOT-20 scores from baseline for the 3- and 6-month for the two groups revealed no statistical significance ($p > 0.05$).

Examination of the Nose. In the 3- and 6-month settings, endoscopic scores increased significantly when compared with the baseline levels ($p < 0.05$). For the 3-month examination, the surgical group had a significantly higher change in the endoscopic scores ($p < 0.05$). No statistical evidence for significant difference was detected among the surgical and medical groups for the 6-month scores ($p > 0.05$).The differences between the 3- and 6-month scores were statistically insignificant as well ($p > 0.05$).

Objective Measurements

SCT. In the 3- and 6-month follow-up settings, SCT improved significantly ($p < 0.05$), whereas there was no statistical evidence for the percentage change from baseline between the medical and surgical groups ($p > 0.05$).

Acoustic Rhinometry

NCI-MCA3. There was no statistically significant difference between the baseline measurements of the two groups for NCI-MCA3. The 3- and 6-month NCI-MCA3 of the medical and surgical groups did not show any significant changes from the baseline measurements. The difference between the surgical and medical groups in terms of the percentage change from baseline for MCA3 was not significant in terms of NCI on postoperative months 3 and 6 ($p > 0.05$).

NCI-VOL3. There was no statistically significant difference between the baseline measurements of the two groups for NCI-VOL3. The 3- and 6-month NCI-VOL3 of the medical and surgical groups did not show any significant changes from the baseline measurements (Fig. 3). The difference between the surgical and medical groups in terms of the percentage change from

Delivered by Ingenta to: Guest User IP: 78.13.202.106 On: Sun, 05 Mar 2017 13:58:29
Copyright (c) Oceanside Publications, Inc. All rights reserved.
For permission to copy go to https://www.oceansidepubl.com/permission.htm

baseline for VOL3 was not significant in terms of NCI on postoperative months 3 and 6 ($p > 0.05$).

Adverse Events. One patient in the medical group developed arrhythmia. He had to stop medical treatment and was excluded from the study.

DISCUSSION

In our study, the medical treatment of CRSwNP (which consists of 12 weeks of clarithromycin, nasal douche, prednisolone, fluticasone propionate) resulted in a significant improvement in total VAS, SNOT-20, and endoscopic examination scores, and in the mucociliary clearance rate. Similarly, the surgical treatment of CRSwNP with endoscopic sinus surgery had a similar outcome, *i.e.,* a significant improvement in total VAS, SNOT-20, and endoscopic examination scores, and in the mucociliary clearance rate. When both groups were compared in terms of the percentage change in subjective and objective outcomes from the baseline, we did not find a significant difference between the two treatment modalities. There are few direct comparisons of medical and surgical treatment of CRSwNP in the literature. The 2012 European Position Paper on Rhinosinusitis and Nasal Polyp indicated that the efficacy of endoscopic sinus surgery is equivalent to that of medical therapy in CRSwNP.[9]

However, a recent article[2] by the Cochrane collaboration assessed the effectiveness of endonasal and/or endoscopic surgery versus medical treatment in subjects with CRSwNP. A meta-analysis was not possible due to the heterogeneity of the studies and incomplete outcome reporting by the studies.[2] A recent study showed that extensive endoscopic sinus surgery (*i.e.,* including middle turbinate and superior turbinate resection with total ethmoidectomy) for patients with CRSwNP and with asthma may better improve the subjective olfaction and endoscopic appearance compared with conventional endoscopic sinus surgery[11]Apparently, at this time, the evidence is not enough to show that one treatment is better than another in terms of patient-reported symptom scores and quality of life measurements.

As a new outcome parameter, we evaluated the NCI of our study population before and after both treatment modalities. It is well known that nasal congestion is a major concern in subjects with CRSwNP. The NCI has been indicated to have the potential to become an important measurement for the evaluation of patients with nasal symptoms.[7] The NCI indirectly assesses the amount of reversible mucosal congestion in the anterior and middle parts of the nasal cavities, which enables a quantification of nasal congestion and its effect on nasal flow. It has been indicated that NCIs are significantly higher in subjects with severe symptoms of nasal obstruction compared with subjects with lesser symptoms. NCI-VOL3, in particular, has been shown to reflect changes in nasal cavity volume after decongestion, including both flow limiting and nonflow limiting areas of the nasal cavities.[7]

Therefore, in our study, we assumed that an improvement in NCI, especially in NCI-VOL3, would be observed in both groups because it is well known that both medical and surgical treatment of CRSwNP results in a subjective improvement of nasal airflow. Although there was a trend toward a decrease in both study groups, no statistically significant change was observed in NCI in both groups after treatment. Similarly, the percentage change in NCI from baseline in both groups was not significantly different. We suggest that NCI, in subjects with CRSwNP, cannot be used as an outcome measurement for assessing the success of treatment. There may be several reasons for this. In subjects with nasal polyposis, it is likely that the application of nasal decongestants does not result in reduction in the volume of the nasal polyps or that the presence of polyps in the nasal cavity may reduce the decongestive ability of the nasal mucosa. The degree of mucosal decongestion may be under- or overvalued due to the presence of chronic inflammation, mucosal fibrosis, and hyperplasia.[7] The presence of an immunoglobulin E mediated type allergy was not evaluated in our study population, and allergic rhinitis, in addition to nasal polyposis, could be a confounder for the lack of a significant change in NCI after medical or surgical treatment.

Rimmer *et al.*,[2] in their Cochrane database review for the management of patients with CRSwNP, implied that they had low confidence in the estimates of the reviewed studies and that further research is necessary to change these estimates. To do so, we tried to run a similar study to the study by Ragab *et al.*[8] in terms of methodology and the medical treatment regimen; however, one limitation of our study was that the number of participants involved was smaller and the statistical power was inevitably low. One advantage of our study was that our study group was homogenous, *i.e.,* we included only patients with CRSwNP. In addition, other than these investigators' outcome measurements, we used the NCI. Our results were similar for the outcome measurements in common.

Ragab *et al.*[8] reported no significant differences between the 6- and 12-month measurements for the subjective and objective outcomes. Therefore, we believed that our 6-month measurements could be interpreted as long-term outcomes of treatment. Similar to their study, we did not find any additional benefit of endoscopic sinus surgery instead of medical therapy on our study population. The only significant positive effect of surgery was observed on endoscopic nasal examination on postoperative month 3. However, no significant

Delivered by Ingenta to: Guest User IP: 78.13.202.106 On: Sun, 05 Mar 2017 13:58:29
Copyright (c) Oceanside Publications, Inc. All rights reserved.
For permission to copy go to https://www.oceansidepubl.com/permission.htm

difference was available for postoperative month 6. As pointed out by Rimmer *et al.*,[2] it has not been possible to blind either the participants or the investigators to the medical versus surgical interventions. Because evidence of surgery may be apparent on endoscopic examination, the significantly positive effect of surgery on postoperative month 3 has a serious risk of bias.

CONCLUSION

In our study, we tried to determine which intervention would lead to improvements in patient-related symptom scores and some objective measurements, including the NCI, to increase the quality of evidence to allow a robust conclusion regarding the method of therapy to be chosen for CRSwNP. According to our results, the surgical and medical treatments for this condition seem to be similar in outcome, and the risks of each must be considered as the treatment is planned. The NCI has been indicated to have the potential to become an important measurement for the evaluation of patients with nasal symptoms.[7] However, we did not find a significant change in NCI in both groups after treatment. Similarly, the percentage change in NCI from baseline in both groups were not significantly different. NCI does not correlate with standard subjective measurements in outcomes for this patient group. We indicated that NCI in subjects with CRSwNP could not be used as an outcome measurement for assessing the success of treatment.

REFERENCES

1. Hedman J, Kaprio J, Poussa T, and Nieminen MM. Prevalence of asthma, aspirin intolerance, nasal polyposis and chronic obstructive pulmonary disease in a population-based study. Int J Epidemiol 28:717–722, 1999.
2. Rimmer J, Fokkens W, Chong LY, and Hopkins C. Surgical versus medical interventions for chronic rhinosinusitis with nasal polyps. Cochrane Database Syst Rev (12):CD006991, 2014.
3. Scadding GK. Comparison of medical and surgical treatment of nasal polyposis. Curr Allergy Asthma Rep 2:494–499, 2002.
4. Mygind N, and Lildholdt T. Nasal polyps treatment: Medical management. Allergy Asthma Proc 17:275–282, 1996.
5. Corey JP, Kemker BJ, Nelson R, and Gungor A. Evaluation of the nasal cavity by acoustic rhinometry in normal and allergic subjects. Otolaryngol Head Neck Surg 117;22–28, 1997.
6. Mamikoglu B, Houser SM, and Corey JP. An interpretation method for objective assessment of nasal congestion with acoustic rhinometry. Laryngoscope 112:926–929, 2002.
7. Kjaergaard T, Cvancarova M, and Steinsvåg SK. Nasal congestion index: A measure for nasal obstruction. Laryngoscope 119: 1628–1632, 2009.
8. Ragab SM, Lund VJ, and Scadding G. Evaluation of the medical and surgical treatment of chronic rhinosinusitis: A prospective, randomised, controlled trial. Laryngoscope 114: 923–930, 2004.
9. Fokkens WJ, Lund VJ, Mullol J, et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2012. Rhinol Suppl (23):3 p preceding table of contents, 1–298, 2012.
10. Mackay IS, and Lund VJ. Imaging and staging. In: Mygind N, and Lildholdt T, eds. Nasal Polyposis. An Inflammatory Disease and Its Treatment. Copenhagen: Munksgaard, 137–144, 1997.
11. Chen FH, Deng J, Hong HY, et al. Extensive versus functional endoscopic sinus surgery for chronic rhinosinusitis with nasal polyps and asthma: A 1-year study. Am J Rhinol Allergy 30: 143–148, 2016. □

Delivered by Ingenta to: Guest User IP: 78.13.202.106 On: Sun, 05 Mar 2017 13:58:29
Copyright (c) Oceanside Publications, Inc. All rights reserved.
For permission to copy go to https://www.oceansidepubl.com/permission.htm