ORIGINAL STUDY

Do we need aggressive surgery in recurrent chronic rhinosinusitis with nasal polyposis? A point of view

Codrut Sarafoleanu[1], Raluca Enache[2]

[1]"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

[2]"Sarafoleanu" ENT Medical Clinic, Bucharest, Romania

ABSTRACT

Chronic rhinosinusitis with nasal polyposis (CRSwNP) represents one of the most common pathology, being an inflammatory process involving the sinonasal mucosa characterized by nasal obstruction, rhinorrhea, with/without facial pain or pressure and smell disorders. The most important key point of the treatment is still surgery (especially aggressive procedures) reserved for severe forms of the disease that failed to respond to maximal medical therapy.

Various treatment protocols are described in the literature so the authors tried to emphasize the most important aspects of surgery in patients with chronic rhinosinusitis with nasal polyposis.

KEYWORDS: chronic rhinosinusitis, nasal polyposis, endoscopic sinus surgery, nasalisation, corticosteroids

INTRODUCTION

Chronic rhinosinusitis (CRS) represents one of the most common pathology found in otorhinolaryngology practice, an increasing health problem with large financial implications[1-3]. Rhinosinusitis is an inflammatory process involving the sinonasal mucosa characterized by nasal obstruction, rhinorrhea, with/without facial pain or pressure and smell disorders.

Chronic rhinosinusitis can be classified (according to European Rhinologic Society papers 2007 and 2012) in two clinical entities – CRS with nasal polyposis (CRSwNP) and without nasal polyps (CRSsNP). Along with the clinical aspect, there is a histological difference between these two forms. CRSwNP is defined by the existence of an eosinophilic inflammation and CRSsNP by a neutrophilic one[4-7].

Histologically, nasal polyps represent the nasal manifestation of an unstable respiratory mucosa. There have been described different types of nasal polyposis[8]:

- Eosinophil-dominated nasal polyposis (allergic rhinitis, fungal allergic rhinosinusitis, non-allergic rhinitis, etc.) – the most frequent (63-95%)[8-10];
- Neutrophil-dominated nasal polyposis (bacteria, cystic fibrosis, foreign body, etc.);
- Other (virusis, granulomatous disease, vasculitis, etc.).

Studies have shown that there can be a bigger concentration of eosinophils, neutrophils and plasma cells in polyps structures than in nasal mucosa in both infectious or non-infectious inflammation[11,12].

Eosinophilic inflammation is the key point in CRSwNP, with an increase in eosinophil cationic protein and a wide release of cytokines, factors responsible for inflammation and oedema[3,13]. The presence of a high concentration of eosinophils within the stroma associated with pseudocyst formation and albumin deposition contributes to the growth of nasal polyps, by activating some growth factors (insulin-like growth factor, transforming growth factor – TGF, platelet-derived growth factor – PDGF or vascular endothelial growth factor – VEGF)[13-17]. Also elevated levels of IL-5 and eotaxin in association with chemokines are responsible for the recruitment and activation of eosinohils[18,19]. Eosinophils accumulations determine the release of cytokines responsible for inflammation and oedema. Both eosinophils and cytokines deter-

Corresponding author: Codrut Sarafoleanu, MD, Professor
email: csarafoleanu@gmail.com

mine epithelial damage which can be repaired via increased cell proliferation. Due to this circle the inflammatory reaction is upregulated, existing a "self perpetuating" inflammatory reaction[20,21]. So, the goal of the treatment should be to minimize the accumulation of the eosinophils in the sinus mucosa in order to eradicate the "local eosinophil pool" and to reduce the recurrences. These should be achieved and can be a rationale for extensive surgery in diffuse polyposis.

PREDICTORS IN CRSwNP

In eosinophil-dominated CRSwNP IgE proved to be an important severity predictor, some studies demonstrating a correlation between serum total IgE levels and mucosal disease on CT scans[22,23]. But, there also have been related cases with no significant changes in IgE one year after surgery in patients reporting an improvement in symptoms evolution[24].

Various authors discovered a positive correlation between CT images and peripheral eosinophilia, but not with total IgE, as well as with the degree of nasal polyps[25,26]. For surgical patients an elevated mucosal eosinophil level (>5 cells per high-power fields) might indicate a more severe disease[27].

These theories are also sustained by van Zele and Gevaert[28] in their in course study. They perform a 3-month double-blind, randomized, placebo-controlled trial on 32 patients with nasal polyposis who underwent a 20 days methylprednisolon treatment. The intermediary results show a non significant difference between placebo and oral steroid groups, sustaining the idea that oral steroids have a mild local anti-inflammatory effect.

Mostafa et al. presented in their retrospective study performed on 100 patients with nasal polyposis that maxillary involvement and positive bacterial cultures may be the most predictive criteria of recurrence in nasal polyposis. They analyzed various parameters like radiologic images, intraoperative and bacteriologic data[29].

SURGERY IN CRSwNP

When talking about nasal polyposis and its high recurrence rate we have to keep in mind the following aspects:

1. Is it possible to identify preoperatively risk factors for polyp recurrence by screening?[30]
2. Can the identification, of certain clinical patterns of recurrence, provide clues for successful treatment?
3. What constitutes appropriate follow up of surgically treated nasal polyposis when recurrence is anticipated?

There always have been many controversies regarding the origin of nasal polyps. In 1991, Larsen and Tos sustained the idea that polyps arise within the middle or superior meatus[31], while Stammberger described in his study an anterior (in 30% of the patients) and posterior (27%) ethmoidal cells origin[32,33]. In 1997 Krajina and Markov suggested that nasal polyps develop in regions where the thinner sinus mucosa turns into thicker nasal mucosa[33,34]. Later on Masaki and Tanaka emitted a new hypothesis according to which polyps arise from olfactory cleft mucosa[35]. But no matter the origin, the conclusion is that the higher the polyps

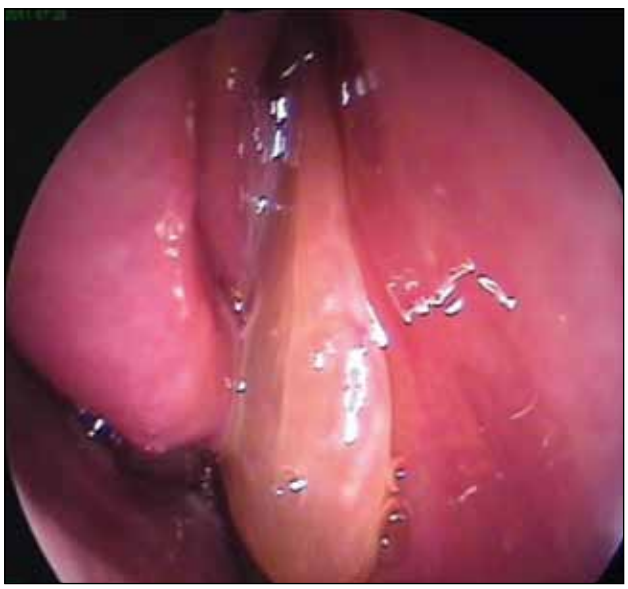

Figure 1 Nasal polyps with ethmoidal cells origin

Figure 2 Nasal polyps developed from the left maxillary sinus mucosa

grade, the greater the number of patients with polyps at each site and the greater the number of anatomical sites involved (Figure 1, Figure 2).

Before considering surgery in patients with nasal polyposis the rhinologist should follow some surgical principles:

- If polyposis affects the entire ethmoid than limited surgery is useless
- Classic ethmoidectomy is less effective than nasalisation
- Unnecessary surgery should be avoid (e.g. inferior turbinectomy)
- Limited recurrence needs limited approach
- Widespread recurrence needs nasalization

The most important key point in managing a CRSwNP case is that surgery is reserved for severe forms of the disease that failed to respond to maximal medical therapy. Though it is not a substitute for medical management, endoscopic sinus surgery (ESS) represents, during the last years, the main technique indicated for the surgical treatment of NP. Even if ESS yields poorer results in cases of massive polyposis and in comorbidities (e.g. asthma, non-steroids anti-inflammatory drugs intolerance, etc.) it can afford improvements in subjective and objective assessment of this conditions. According to the European Position Paper on Rhinosinusitis and Nasal Polyposis 2012 a prolonged postoperative medical treatment with topical corticosteroids sprays appear to improve outcomes post ESS for CRSwNP[36].

Regarding the extent surgery that can be required to optimize the outcomes in patients with CRSwNP there have not been established any limits, even if there are reports suggesting that outcomes may be improved after such interventions[36-38].

So, when do we need aggressive surgery?

Although there are many studies supporting the effectiveness of medical treatment and endoscopic sinus surgery in managing nasal polyposis, we have to consider the high recurrence rate of this disease due to different factors (e.g. non-steroid responsive patients, contraindications for steroid medication, immunodeficiency, etc.). One of the best predictors for recurrence is the initial disease severity. Watelet concluded in his prospective study performed on 36 patients with chronic rhinosinusitis and nasal polyposis that initial disease and its severity were the best predictors for the objective outcome at 6 months after sinus surgery[39].

Another recurrence predictor is the CT score before treatment. The most widely used system is represented by the Lund-Mackay CT staging system, due to its simplicity and effective evaluation of the cranio-facial imaging[40]. Also, subjective olfactory changes can be considered an early marker for recurrent disease[41].

So, aggressive surgery should be the choice in all cases of recurrent disease.

Unusual sites of polyps' origin (nasal septum, olfactory cleft, turbinate, etc.) require an extensive surgery procedure.

There are also special situations in which aggressive endoscopic sinus surgery is needed. Cystic fibrosis is a neutrophil-dominated CRSwNP found especially in children. Because of the persistent nature of the disease, aggressive surgery opening of the sinus cavities may be the only one which can provide long-lasting benefit though polyps will regrow in most patients[42,43]. The same management is taken in consideration in patients with humoral immunodeficiencies[36,44,45]. Patients with granulomatous disease such as Wegener's granulomatosis, appear to suffer from a symptom burden that is equivalent to the broader population of chronic rhinosinusitis patients.

Fungi represent an increasingly recognized factor in CRSwNP pathology. The recommended therapies for both chronic indolent and fulminant fungal rhinosinusitis are aggressive surgical removal of the fungal material and intravenous anti-fungal therapy[46,47].

A controversy raised the number of regions included in the aggressive surgery. It is well known that polypectomy alone is associated with high recurrence rates[48,49]. Despite this aspect, in case of polyps with nasal origin there should be made a limited approach with mucosal preservation.

In those cases with ethmoid origin of polyps endoscopic sinus surgery must be extensive and exhaustive. Studies comparing classic ethmoidectomy and nasalisation (radical ethmoidectomy) reported an overall functional benefit for the second technique[37,38]. Jankowski[36,37] performed a prospective study on patients with severe nasal polyposis – 39 underwent radical ethmoidectomy and 37 functional ethmoidectomy. His results showed a significant lower recurrence rate of 22.7% versus 58.3% in the functional ethmoidectomy group, with a significant improvement in symptoms score and a decrease in postoperatory steroids use.

Another question that is taken into consideration when talking about CRSwNP is whether the treatment has to depend on histological features. In noneosinophil-dominated forms surgery is indicated only after corticosteroid therapy, in those cases where medical therapy was ineffective. It is important to identify the origin of the polyps and to totally remove them.

In diffuse polyposis with eosinophil-dominated CRSwNP on the other hand, the repeated polyp formation is not a true recurrence, but the result of an ongoing immunological inflammation response, most of this patients having a history of asthma, airway hyper-responsiveness or aspirin hypersensitiveness. In these cases, the destruction of the bone and elevation of the dura, possibly due to eosinophilic cation pro-

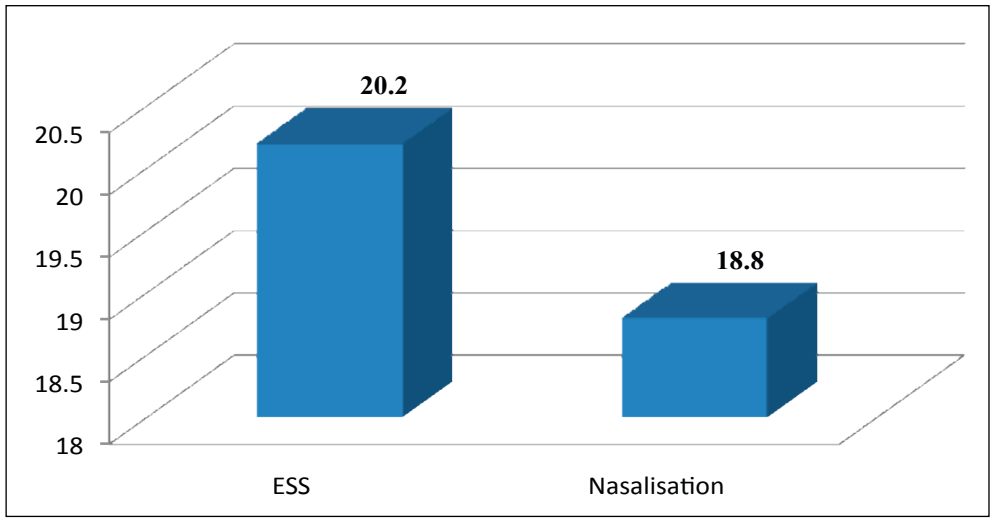

Chart 2 Revision surgery cases at 12 months after ESS

tein and other inflammatory mediators, illustrate the need for aggressive surgery[50].

OUR EXPERIENCE

We performed a 36 months prospective study on 138 patients with chronic rhinosinusitis with nasal polyposis (21.7% of the patients were diagnosed with NSAID intolerance and 36.2% with allergic asthma). All patients received previous surgery after failure of the medical therapy.

Patients were distributed into two equal groups – 69 underwent endoscopic sinus surgery and 69 nasalisation. Each type of pathology was equally represented in both groups. Postoperatory each patient received intranasal corticotherapy for 3 months.

For evaluation the sino-nasal outcome test – SNOT20 – was used before surgery and then at 3, 6 and 12 months after.

At 12 months after surgery, of the patients who had originally received ESS 20.2% had undergone revision surgery compared to 18.8% of patients who had nasalisation (Chart 1). The difference in unadjusted revision surgery rates was not statistically significant between the two study groups (chi(2)=0.22; p-value = 0.64).

From the quality of life (QoL) point of view, SNOT scores showed a significant improvement of this parameter at 3 and 6 months after surgery (Chart 2), but with an important decrease after 12 months, when revision surgery was taken into consideration.

From our own experience we can conclude that aggressive surgery does not necessarily mean better

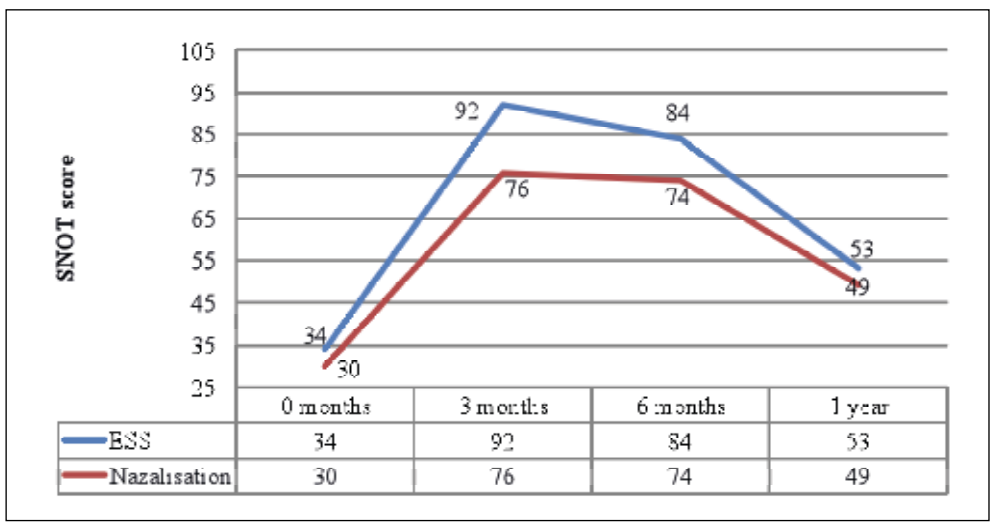

Chart 2 SNOT score evolution

results in terms of QoL. We consider that radical endoscopic sinus surgery is indicated in those cases of diffuse polyposis, with multiple recurrences and when nasal polyposis is associated with asthma or NSAID intolerance.

We sustain the idea that in some cases, the greater the number of surgical procedures the quicker the recurrences. For this cases with multiple recurrences even after aggressive surgery, Catalano et al. consider "permeabilisation" of the nasal cavities with special drug elution techniques (corticosteroid placement with special devices on the remnant nasal polyps or diseased mucosa)[51].

CONCLUSIONS

Even if it is a wide spread disease and a lot of studies have been made upon this topic, there is currently no way to predict which patients with CRSwNP will benefit from corticotherapy. Not all patients respond to topical or even systemic corticosteroids, therefore there are cases which require frequent and aggressive surgery. So, consider aggressive surgery only in extensive forms refractory to vigorous medical treatment.

In treating chronic rhinosinusitis with nasal polyposis the inflammatory infiltrate on the histopathologic specimens can be helpful as predictor for the aggressiveness of surgery.

In the end all rhinologists conclude that diffuse polyposis with multiple recurrences require aggressive surgery despite the fact that there are no significant statistic differences comparative with simple endoscopic sinus surgery.

REFERENCES

1. Goetzel R.Z., Hawkins K., Ozminkowski R.J., Wang S. – The health and productivity cost burden on the "top 10" physical and mental health conditions affecting six large U.S. employers in 1999. J Occup Environ Med., 2003;45:5-14.
2. Durr D.G., Desrasiers M.Y., Dassa C. – Impact of rhinosinusitis in health care delivery: the Quebec experience. J Otolaryngol., 2001;30:93-97.
3. Huvenn W., van Bruaene N., Zhang N., van Zele T., Patou J., Gevaert P., Claeys S., van Cauwenberge P., Bachert C. – Chronic rhinosinusitis with and without nasal polyps: what is the difference? Current Allergy and Asthma Reports, 2009;9(3):213-20.
4. Fokkens W., Lund V., Bachert C., et al. - EAACI position paper on rhinosinusitis and nasal polyps executive summary. Allergy., 2005;60:583-601.
5. Meltzer E.O., Hamilos D.L., Hadley J.A., Lanza D.C., Marple B.F., Nicklas R.A. et al. - Rhinosinusitis: Establishing definitions for clinical research and patient care. Otolaryngol Head Neck Surg., 2004;131(6 Suppl):S1-62.
6. Fokkens W., Lund V., Mullol J.; European Position Paper on Rhinosinusitis and Nasal Polyps Group. - EP3OS 2007: European position paper on rhinosinusitis and nasal polyps 2007. A summary for otorhinolaryngologists. Rhinology., 2007;45(2): 97-101.
7. Stammberger H. - Surgical treatment of nasal polyps: past, present, and future. Allergy., 1999;54(Suppl 53):7-11.
8. Kirtsreesakul V. - Update on Nasal Polyps: Etiopathogenesis. J Med Assoc Thai, 2005;88(12):1966-72.
9. Vento S.I., Ertama L.O., Hytonen M.L., Wolff C.H., Malmberg C.H. - Nasal polyposis: clinical course during 20 years. Ann Allergy Asthma Immunol, 2000;85:209-14.
10. Kirtsreesakul V. - Nasal polyps: the relationship to allergy, sinonasal infection and histopathological type. J Med Assoc Thai, 2004;87:277-82.
11. Norlander T., Bronnegard M., Stierna P. - The relationship of nasal polyps, infection, and inflammation. Am J Rhinol, 1999;13:349–535.
12. Morinaka S., Nakamura H. - Inflammatory cells in nasal mucosa and nasal polyps. Auris Nasus Larynx, 2000;27:59–64.
13. Bachert C., Gevaert P., Holtappels G., et al. - Nasal polyposis: from cytokines to growth. Am J Rhinol., 2000;14:279– 290.
14. Fruth K., Zhu C., Schramek E., Angermair J., Kassem W., Haxel B.R., Schneider A., Mann W.J., Brieger J. - Vascular endothelial growth factor expression in nasal polyps of aspirin-intolerant patients. Arch Otolaryngol Head Neck Surg., 2012 Mar;138(3):286-93.
15. Coste A., Brugel L., MaõÃtre B., Boussat S, Papon J.F., Wingerstmann L., PeyneÁgre R., Escudier E. Inflammatory cells as well as epithelial cells in nasal polyps express vascular endothelial growth factor. Eur Respir J., 2000;15:367±372.
16. Zaravinos A., Soufla G., Bizakis J., Spandidos D.A. - Expression analysis of VEGFA, FGF2, TGFß1, EGF and IGF1 in human nasal polyposis. Oncology Reports, 2008;19:385-391.
17. Kouzaki H., Seno S., Fukui J., Owaki S., Shimizu T. - Role of platelet-derived growth factor in airway remodeling in rhinosinusitis. Am J Rhinol Allergy., 2009 May-Jun;23(3):273-80.
18. Lee C.H., Lee K.S., Rhee C.S., et al. - Distribution of RANTES and interleukin-5 in allergic nasal mucosa and nasal polyps. Ann Otol Rhinol Laryngol, 1999;108:594–598.
19. Nonaka M., Pawankar R., Saji F., et al. - Eotaxin synthesis by nasal polyp fibroblasts. Acta Otolaryngol., 1999;119:816–820.
20. Denburg J. - Cytokines and inflammatory cells. In: Mygind N., Lildholdt T. - Nasal Polyposis: An Inflammatory Disease and Its Treatment.. Copenhagen: Munksgaard, 1997;p.78–87.
21. Assanasen P., Naclerio R.M. - Medical and surgical management of nasal polyps. Curr Opin Otolaryngol Head Neck Surg., 2001;9:27-36.
22. Baroody F.M., Se-Hoon, S., Naclerio R.M. - Total IgE serum levels correlate with sinus mucosal thickness on computerized tomography scans. J Allergy Clin Immunol., 1997;100:563-568.
23. Mehta V., Campeau N.G., Kita H., Hagan J.B. - Blood and Sputum Eosinophil Levels in Asthma and Their Relationship to Sinus Computed Tomographic Findings. Mayo Clin Proc., 2008 June;83(6):671–678.
24. Lal D., Baroody F.M., Weitzel E.K., deTineo M., Naclerio R.M. – Total IgE levels do not change 1 year after endoscopic sinus surgery in patients with chronic rhinosinusitis. Int Arch Allergy Immunol., 2006;139:146-148.
25. Staikuniene J., Vaitkus S., Japertiene L.M., Ryškiene S. - Association of chronic rhinosinusitis with nasal polyps and asthma: clinical and radiological features, allergy and inflammation markers. Medicina (Kaunas), 2008;44(4).
26. Poznanovic S.A., Kingdom T.T. - Total IgE level and peripheral eosinophilia: correlation with mucosal disease based on computed tomographic imaging of the paranasal sinus. Arch Otolaryngol Head Neck Surg., 2007;133:701-4.
27. Kountakis S.E., Arango P., Bradley D., Wade Z.K., Borish L. – Molecular and cellular staging for the severity of chronic rhinosinusitis. Laryngoscope, 2004;114:1895-1905.
28. Van Zele T., Gevaert P. et al. – Oral steroids in nasal polyposis: a 3-month double blind, randomized, placebo-controlled trial. In preparation.
29. Mostafa B.E., El Fiky L., Sallam F.A. - Simple clinical system for the prediction of recurrence of nasal polyps. Auris Nasus Larynx, 1999;26:165–168.

30. Rouvier P., Peynegre R. – Recurrence of polyposis: risk factors, prevention, treatment and follow-up. In: Stamm A., Draf W. ed. – Micro-endoscopic surgery of the paranasal sinuses and the skull base. Springer – Verlag Berlin Heidelberg, 2000;p.287-308.
31. Larsen P.L., Tos M. – Origin of nasal polyps. Laryngoscope, 1991;101:305-312.
32. Stammberger H. – Functional endoscopic sinus surgery. The Messerklinger technique. Philadelphia: DC Decker; 1991.
33. Andrews A.E., Bryson J.M., Rowe-Jones J.M. - Site of origin of nasal polyps: relevance to pathogenesis and management. Rhinology, 2005;43:180-184.
34. Krajina Z., Markov D. - A contribution to the etiopathogenesis of nasal polyps. Acta Med Croatica, 1997;51:167-170.
35. Masaki M., Tanaka Y. - Nasal polyps in the Olfactory Cleft. Laryngoscope, 1998;108:1243-1246.
36. Fokkens W.J., Lund V.J., Mullol J., Bachert C. Et al. – European Position Paper on Rhinosinusitis and Nasal Polyps 2012. Rhinology, 2012;Suppl23:1-298.
37. Jankowski R., Pigret D., Decroocq F., Blum A., Gillet P. - Comparison of radical (nasalisation) and functional ethmoidectomy in patients with severe sinonasal polyposis. A retrospective study. Rev Laryngol Otol Rhinol (Bord), 2006;127(3):131-40.
38. Masterson L., Tanweer F., Bueser T., Leong P. - Extensive endoscopic sinus surgery: does this reduce the revision rate for nasal polyposis? European archives of oto-rhino-laryngology : official journal of the European Federation of Oto- Rhino-Laryngological Societies (EUFOS): affiliated with the German Society for Oto-Rhino - Laryngology - Head and Neck Surgery, 2010 Oct;267(10):1557-61.
39. Watelet J.B., Annicq B., van Cauwenberge P., Bachert C. - Objective outcome after functional endoscopic sinus surgery: prediction factors. Laryngoscope, 2004;114:1092-7.
40. Lund V.J., Mackay I.S. - Staging in rhinosinusitus. Rhinology., 1993;31:183-184.
41. Senior B.A., Kennedy D.W., Tanabodee J., Kroger H., Hassab M., Lanza D. - Long-term results of functional endoscopic sinus surgery. Laryngoscope, 1998;108:151-7.
42. Gysin C., Alothman G.A., Papsin B.C. - Sinonasal disease in cystic fi brosis: clinical characteristics, diagnosis, and management. Pediatr Pulmonol., 2000;30:481– 489.
43. Coste A., Idrissi F., Beautru R., et al. - Endoscopic endonasal ethmoidectomy in severe sinusitis of cystic fi brosis. Mid-term results in 12 patients. Ann Otolaryngol Chir Cervicofac, 1997;114:99– 104.
44. Lusk R.P., Polmar S.H., Muntz H.R. - Endoscopic ethmoidectomy and maxillary antrostomy in immunodeficient patients. Archives of otolaryngology--head & neck surgery, 1991;117(1):60-3.
45. Buehring I., Friedrich B., Schaaf J., Schmidt H., Ahrens P., Zielen S. - Chronic s inus i t i s ref ra c tor y to s tandar d management in patients with humoral immunodeficiencies. Clin Exp Immunol., 1997;109(3):468-72.
46. Uffredi M.L., Mangiapan G., Cadranel J., Kac G. - Signifi - cance of Aspergillus fumigatus isolation from respiratory specimens of non-granulocytopenic patients. Eur J Clin Microbiol Infect Dis, 2003;22:457– 462.
47. Lund V.J. – What is the place of endonasal surgery in fungal sinusitis? In: Stamm A., Draf W. ed. – Micro-endoscopic surgery of the paranasal sinuses and the skull base. Springer – Verlag Berlin Heidelberg, 2000;p.309-314.
48. Wynn R., Har-El G. - Recurrence rates after endoscopic sinus surgery for massive sinus polyposis. The Laryngoscope., 2004 May;114(5):811-3.
49. Schapowal A.G., Simon H.U., Schmitz-Schumann M. - Phenomenology, pathogenesis, diagnosis and treatment of aspirin-sensitive rhinosinusitis. Acta Otorhinolaryngol Belg., 1995;49(3):235-50.
50. Stammberger H. - Rhinoscopic surgery. In: Settipane G.A., Lund V.J., Bemstein J.M., Tos M., editor. - Nasal polyps: epidemiology, pathogenesis and treatment. Providence, RI Oceanside Publications, 1997;p.165-176.
51. Catalano P.J., Payne S.C. - Balloon dilation of the frontal recess in patients with chronic frontal sinusitis and advanced sinus disease: an initial report. Annals of Otology, Rhinology and Laryngology, 2009;118(2):107–12.