

Nasal polyposis: microsurgical ethmoidectomy and interruption of autonomic innervation vs conventional surgery

La chirurgia della poliposi nasale: tecnica convenzionale vs tecnica microchirurgica associata a resezione dell'innervazione parasimpatica

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Parole chiave

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Summary

Nasal polyposis is an invalidating disease which develops through chronic inflammation which leads to tissue oedema and eventually polyps. Treatment is aimed at eliminating polyps, resolving rhinitis symptoms, re-establishing nasal breathing and olfaction and preventing recurrence. The pathogenesis can be explained, in part, by degranulation of mast cells and release of mediators attracting eosinophils which, in turn, can cause tissue damage and oedema. Neurovascular reflexes and factors related to the complex anatomy of ethmoidal labyrinth may be responsible for the onset and persistence of oedema. This would offer a rationale to treatments modifying ethmoid anatomy and blocking neurovascular reflexes in the management of nasal polyposis. The advent of microsurgery and of diagnostic and operative endoscopy has led, over the last twenty years, to earlier detection and to less traumatic and more precise surgical treatment of nasal polyps. With these techniques resection of parasympathetic innervation is also possible, which is in keeping with the proposed rationale and cannot be easily achieved by conventional surgery. To evaluate the impact of this resection on the management of nasal polyposis a review of data has been made in a series of patients with diagnosis of nasal polyposis established by clinical examination, resistant to pharmacological therapy and treated between 1983 and 1998 at the Oto-Neuro-Ophthalmology Department of Florence University (Italy). Patients were treated by conventional surgery (386 cases), by microsurgery without resection of the parasympathetic component of the vidian nerve (97 cases), or by microsurgery with resection of this latter component (94 cases). The rate of recurrence and of major post-operative complications, respectively, were: 39.9% and 4.4% for patients treated by conventional surgery; 37.1% and 6.2% with microsurgery without resection of parasympathetic innervation; and 25.5% and 2.1% with resection of this innervation. The difference in recurrence rate between the three groups was significant ($p < 0.05$). The average disease-free interval was 45.7 months with conventional surgery and 53.5 months with microsurgery (regardless of resection of innervation). Results show that microsurgery for nasal polyposis together with resection of parasympathetic innervation improves results compared to those with conventional surgery and does not cause an increase in post-operative complications.

Riassunto

La patogenesi dei polipi nasali avviene attraverso stadi che coinvolgono i fattori della flogosi e lo sviluppo di sintomi legati a queste reazioni. L'origine dell'edema tessutale è spiegato a livello cellulare con la degranolazione mastocitaria, la liberazione dei fattori della flogosi, e il richiamo di granulociti eosinofili che a loro volta provocano un danno tessutale e quindi la formazione dell'edema. I riflessi neurovascolari ed il complesso anatomico del labirinto etmoidale possono determinare la persistenza dell'edema. Gli obiettivi del trattamento della poliposi nasale è quello di eliminare i polipi, mitigare i sintomi della rinite, ristabilire la respirazione nasale e la funzione olfattoria ed infine di prevenire e ritardare la recidiva della poliposi nasale. Negli ultimi venti anni l'approccio chirurgico della poliposi nasale è radicalmente cambiato. L'avvento della microchirurgia e dell'endoscopia ha permesso non solo una diagnosi più precoce, ma anche un trattamento chirurgico meno traumatico più preciso e finalizzato. Il nostro studio è stato condotto in 678 pazienti con poliposi nasale diagnosticata con esame clinico e resistente a terapia farmacologica. I polipi nasali sono stati trattati con tecnica chirurgica convenzionale o con microchirurgia associata in certi casi e resezione della componente parasimpatica del nervo vidiano tra il 1983 e il 1998 presso la Sezione di Otorinolaringoiatria del Dipartimento di Scienze Chirurgiche Oto-Neuro-Oftalmologiche di Firenze. La percentuale totale di recidive è stata del 39,9% nei pazienti trattati con microchirurgia (media dell'intervallo libero da malattia: 53,5 mesi). La differenza dei due gruppi era ai limiti della significatività statistica ($p=0,077$). L'analisi dei risultati mostra che il trattamento chirurgico della poliposi etmoidale con svuotamento etmoido-sinusale in microscopia, associato eventualmente alla soppressione della componente autonoma, risulta più efficace rispetto all'intervento convenzionale.

Introduction

Nasal polyposis is the final result of a chronic ethmoido-sinusal inflammation, the aetiology of which is multifactorial and the pathogenesis is still unclear. The disease may present with single, monolateral lesions or with bilateral, massive lesions; it may be isolated or associated with marked deformities of nasal bones or with other diseases.

The incidence of nasal polyposis is difficult to estimate. The incidence has been estimated to be 0.3% in the entire population of the United States of America¹ and 0.2-3% in adults in Great Britain². The frequency of nasal polyps increases with age, reaching its peak around fifty years of age, and is higher in males; nasal polyposis can be a frequent complication of other diseases (Table I)³⁻¹⁰.

The limited knowledge of nasal physiology and physiopathology, the anatomic characteristics of the ethmoido-sinusal area, and the high rate of relapse after surgery have led to nasal polyposis becoming a controversial nosological and therapeutic entity.

Despite the increased number of studies, progress in pharmacology, and improvement in surgical techniques, no single therapeutic protocol is available for this disease. The therapeutic choice, whether medical or surgical, as well as the choice of the surgical procedure, have given rise to discussion and controversy. The aims of surgical treatment are to resolve the nasal obstruction and to prevent recurrence with the least risk possible of complications. The failure rate is high, with 7 to 50% patients experiencing recurrence. The aims of medical treatment are to reduce polyp size and symptoms, to delay as long as possi-

ble or, even avoid, surgery, and to prevent recurrence upon surgery.

The pathophysiological mechanisms responsible for the growth of nasal polyps are difficult to define. Polyps are now considered the end-result of an inflammatory process of multifactorial aetiology including familiar¹¹ and hereditary factors¹², activation of local immune responses and hyperactivity of parasympathetic innervation.

Many Authors have suggested a correlation between nasal allergy and specific HLA antigens¹³. Drake-Lee and McLaughan¹⁴ showed that all classes of immunoglobulins are present in polyps, although IgE levels tend to be higher than in serum or tonsils. The levels of IgG, IgA and IgM are variable, elevated levels probably representing the result of a recent upper respiratory tract infection. Several chemical mediators of inflammation have been studied in nasal polyps; histamine is the most abundant, with a concentration, in polyp stroma, 100 to 1000 times that in serum¹⁴. It has also been demonstrated that nasal polyps contain levels of interleukin (IL-8)¹⁵, IL-3, IL-5 and Granulocyte-Macrophage Colony Stimulating Factor (GM-CSF) which are much higher than those in normal mucosa¹⁶. Other chemical mediators involved in the pathogenesis of nasal polyps are gamma interferon (IFN- γ) and tumour-growth factor β (TFG- β). IFN- γ is greatly increased in nasal polyps and the increase is directly correlated with the severity of the clinical picture, and, therefore, the increase in this cytokine has been suggested to be predictive of recurrence¹⁷. It has been hypothesized IFN- γ act by recruiting and activating eosinophils "in situ" which, in turn, release toxic mediators responsible

Table I. Prevalence of polyposis in various diseases.

Disease	Nasal polyposis (%)	First Author, year, ref.
Allergic rhinitis	1.5-4	Settipane 1977 ³ Caplin 1971 ⁴
Allergic asthma	20-42	Blumstein 1966 ⁵
Non-allergic asthma	13	Settipane 1997 ⁶
Aspirin intolerance	35-96	Settipane 1997 ⁶ Ezman 1983 ⁷
Widal syndrome	8	Widal 1922 ⁸
Churg-Strauss syndrome	50	Olsen 1992 ⁹
Cystic fibrosis	20	Settipane 1997 ⁶
AIDS and congenital immunodeficiency syndrome	Occasional	Drake-Lee 1997 ¹⁰

for epithelial damage^{18 19} and for the synthesis of collagen by fibroblasts. Transforming TFG- β , which is not generally detected in the normal mucosa, is the most powerful factor responsible for attracting fibroblasts and stimulating the synthesis of the extracellular matrix²⁰. The rhino-sinusal mucosa, when damaged by any chemical, exhibits a higher permeability to sodium ions than normal, resulting in the development of submucosal oedema which, in turn, causes polyps¹¹.

These studies demonstrate that different chemical mediators released locally are responsible for a local inflammatory response with recruitment and activation of eosinophils and mast cells and eventual onset of polyps, due to epithelial damage and accumulation of extracellular matrix in the connective tissue.

Autonomic innervation may also play an important role in the pathogenesis of nasal polyposis. Stimulation of the parasympathetic system in man^{22 23} causes an increase in glandular secretion, especially in serous secretion, mast cell degranulation and vasodilatation. The use of sympatholytic drugs, like atropine, inhibit secretion without affecting vasodilatation²⁴; this demonstrates that the secretory response depends on cholinergic pathways while vasomotion is controlled by other pathways. Local chemical mediators, like neuropeptides VIP, P substance and cGRP, may be responsible for mast cell degranulation and vasodilatation²⁵. However, it has been demonstrated that cholinergic stimulation can induce histamine secretion²⁶. The importance of the histamine-induced vasodilatation in the pathogenesis of polyposis is confirmed by the fact that the concentration of mast cells is higher in patients with nasal polyps than in control subjects and that mast cells within polyps are in various stages of degranulation²⁷.

Nasal polyposis can, therefore, be considered a response to chronic inflammatory processes in which parasympathetic pathways play an important role, both by release of VIP²⁸ and acetylcholine from nerve endings and by acetylcholine-induced release of histamine from mast cells. It is also well known that the complex anatomy of ethmoidal labyrinth concurs to the onset and persistence of polyps. These considerations offer a rationale to treatments modifying ethmoid anatomy and blocking neurovascular reflexes in the management of nasal polyposis. One such treatment is based on ethmoid emptying enhanced by interruption of parasympathetic innervation and of part of the arterial influx to nasal pits, an operation which can be performed using microsurgery.

The present research was aimed at evaluating short- and long-term results of this treatment, which have then been compared with the results not only of microsurgical ethmoid emptying alone but also of conventional surgery for nasal polyposis.

Patients and methods

The study population consisted of 678 consecutive patients with a clinical diagnosis of nasal polyposis not responsive to topical medical therapy and operated upon between 1983-1998 at the Oto-Neuro-Ophthalmology Department, Section of Ear-Nose-Throat Surgery of the University of Florence, Italy. Median age of the patients was 47.2 years (range: 10-83), with a male/female ratio of 5.4 (573/105).

Diagnosis was achieved by clinical examination followed by endoscopy with optics of 0°, 30° and 70° and by computerised tomography (CT) scan of paranasal sinuses. This scan was also used to evaluate the width or dehiscence of the ethmoid roof, the relationship of polyps to papiraceous lamina, the insertion region of the inferior turbinate, the intrasphenoid projection of the optic canal and the internal carotid artery.

In this study population, 94 patients (13.8%) presented recurrence following previous surgical treatment elsewhere, 126 (18.6%) had nasal polyposis associated with allergic rhinitis as ascertained by prick-test (showing intense positivity to graminaceae, parietaria, or dermatophagoides), 72 (10.6%) were intolerant to aspirin, 61 (9.0%) presented nasal polyps and asthma, 20 (2.9%) nasal polyps, asthma and aspirin intolerance and two (0.3%) Churg-Strauss syndrome as revealed by pathological and immunohistochemical studies. A total of 264 (38.9%) patients were smokers or past smokers. Indication to surgery was based on the entity of nasal obstruction or of subjective symptoms resistant to steroid therapy.

Three different surgical procedures were adopted and the patients were accordingly classified into three groups for retrospective analysis, as follows:

Group I: 456 (67.2%) patients were submitted to ethmoid emptying by conventional surgery according to Yankauer²⁹: 198 patients were treated by ethmoid and/or trans-antral maxillary sinus emptying, bilaterally (50 cases) or monolaterally (148 cases). In addition, septal resection according to Killian was performed in 57 patients and trimming of the inferior turbinate was performed in 92 patients, to emendate nasal stenosis.

Group II: 114 (16.8%) patients were submitted to functional microsurgical ethmoidectomy according to Wigand and Hoseman³⁰ associated with retrograde emptying and, in some cases, to fenestration of the maxillary sinus through the middle meatus³¹. This procedure was performed bilaterally, in all cases, and was associated with septal dislocation and/or septoplasty according to Cottle in 53 (16.5%) cases.

Group III: 108 (16%) patients were treated as group II patients plus section of the sphenopalatine artery and nasal nerves, bilaterally (42 cases) or monolaterally (66 cases). Septoplasty according to Cottle was performed in 45 (41.7%) of these patients.

In group II and III patients, surgery was performed under microscopic control; endoscopy was also used, when needed, to complete the operation.

Of the 678 patients, 101 (14.9%) were not included in the statistical analysis as they were lost at follow up. Therefore, the results concern 577 patients, 389 treated by conventional surgery, 97 by microsurgical ethmoidectomy and 94 by microsurgical ethmoidectomy plus section of the sphenopalatine artery and nasal nerves. Follow-up lasted at least to 16 years, median 82.5 months.

Differences in recurrence rate were analysed with non-parametrical chi-square test; a level of $p < 0.05$ being assumed as significant³².

Results

The disease-free interval was 48.2 months (45.7 and 53.5 in the patients submitted to conventional and microsurgery, respectively).

Recurrence of disease, as ascertained by clinical examination, was observed in 214 out of 577 patients (37%); namely, in 154 (39.9%) of the 386 patients in group I, i.e., those submitted to conventional surgery; in 36 of the 97 patients (37.1%) in group II, i.e., those who underwent microsurgery without section of the sphenopalatine artery and nasal nerves; and in 24 of

the 94 patients (25.5%) in group III, i.e., those who underwent microsurgery with sphenopalatine artery and nasal nerve resection. Differences between the groups of patients were significant ($p < 0.05$).

Of the patients in group I who experienced recurrence, 61 received additional surgery, as follows: 49 underwent conventional surgery, 10 of whom in day-hospital; 6 were treated with endoscopic surgery; 4 with microsurgery; and 2 with Nd-YAG laser surgery. Of the patients treated by microsurgery (second and third group together) who experienced recurrence, 23 underwent additional surgery. Of these, 16 had been treated without section of the sphenopalatine artery and nasal nerves and 7 with resection. Of these 23 patients, 12 underwent conventional surgery, 3 of whom in day-hospital; 8 were submitted to microsurgery; and 3, originally submitted to unilateral ethmoidectomy and interruption of sympathetic innervation, were treated by the section of the contralateral sphenopalatine artery and nasal nerves.

Figure 1 shows the results (in terms of recurrence) of the two surgical techniques in the patients with allergy, aspirin intolerance, asthma and Widal's syndrome. The patients submitted to microsurgery were considered together for this analysis, to prevent excessive reduction of the sample size. Differences between groups were minor and not significant.

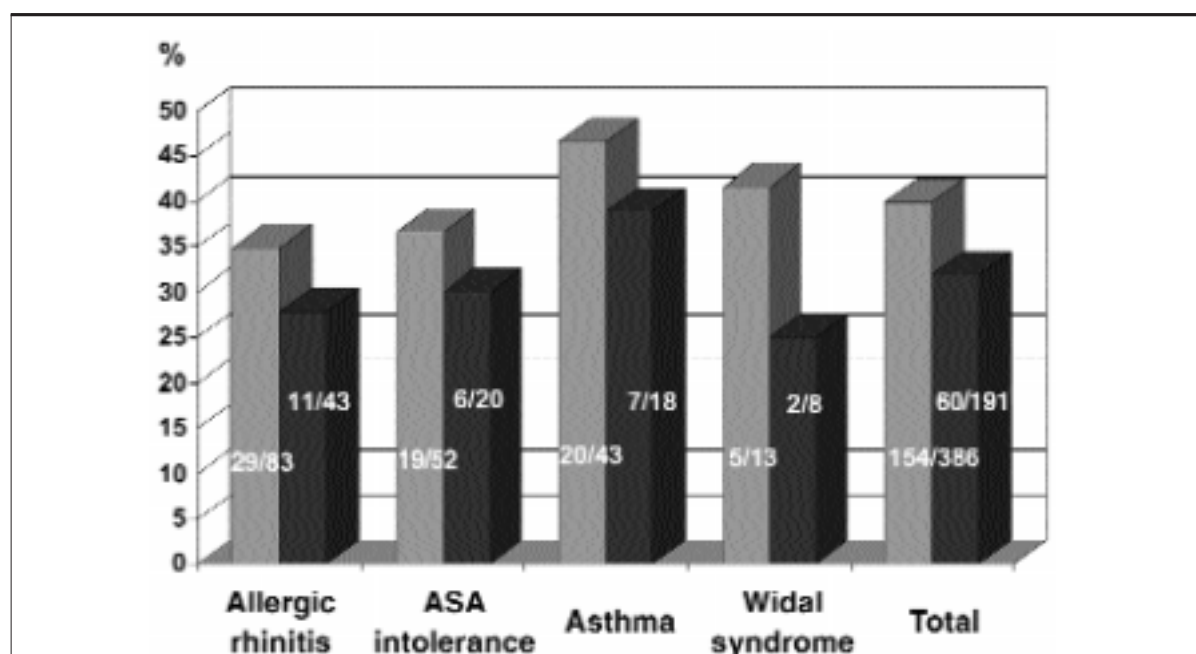


Fig. 1. Recurrence rate (%) in selected groups of patients with nasal polyposis related to surgical technique adopted. Light gray: conventional surgery; dark gray: microsurgical ethmoidectomy (independent of interruption of parasympathetic innervation).

Nasal packing was maintained for 3-4 days, with 3-4 gauzes per nasal pit, upon conventional surgery; it was maintained for 1-2 days, with 1-2 gauzes per nasal pit, upon microsurgery, independently of resection of the sphenopalatine artery and nasal nerves.

Major surgical complications were as follows. In the group I patients: three cases of liquorrhoea which resolved spontaneously without sequelae, two of these cases also developed transient pneumocephalus; two cases of periorbital oedema due to infraction of the ethmoid papiraceous lamina, which resolved spontaneously; one case of transient monolateral temporal hemianopsia (probably due to vasospasm); eight cases of epistaxis, one of which (from an anterior ethmoidal artery) required repeat surgery a few hours after the original procedure; two attacks of hypertension; and one case of angina pectoris in a cardiopathic patient. Within the second group of patients: one case of emphysema of the lower eyelid due to infraction of the ethmoid papiraceous lamina, which resolved spontaneously; three cases of epistaxis; and two asthmatic attacks. Within the third group of patients: two cases of epistaxis, one of which (from a sphenopalatine artery) required further surgery.

No patient suffered complications to the internal carotid artery, meningitis, cerebral abscess or secondary encephalocele.

Minor complications (all groups together) included hypo-anosmia (10 cases) and septal perforation (3 cases). Fever occurred in 39.2% patients in group I, in 37.5% patients in group II and in 36.8% patients in group III. The median hospitalisation time was 4.9 days (range 1-37), 3.5 days (range 1-6) and 2.95 days (range 1-7) in the three groups, respectively.

Discussion

The results of this study show that microsurgery is more effective than conventional surgery for the treatment of nasal polyposis and that combination of microsurgery with interruption of parasympathetic innervation, as achieved by resection of sphenopalatine artery and nasal nerves, further reduces the incidence of relapse without increasing the risk of major or minor complications. Indeed, addition of the interruption of parasympathetic innervation to microsurgery offers advantage with regard to fever, hospitalization time, major complications and relapse.

The efficiency and safety of microsurgery presumably depend on the advantage offered by the use of the operative microscope to define, in each case, the anatomy of the sphenothmoidal region, leading to more radical and, at the same time, more selective ethmoidectomy. This has a major impact on the prevention of the "operated maxillary sinus syndrome", including neurological sequelae due to possible

stretching of the infraorbital nerve during conventional surgery³³. Furthermore, microsurgery allows the procedure to be extended to the section of nasal nerves, thus removing, at least in part, a cause of the disease.

Indeed, this procedure leads to a significant modification in vasomotion and gland secretion and can thus correct the impaired local reactivity involved in the pathogenesis of nasal polyposis.

Histological examination two years after resection of the nasal nerves showed constriction of the vessels in the deep venous plexus and a reduction in mast cell degranulation, although fibrosis, mucosal metaplasia of the epithelium and gland atrophy persisted^{22 34}. Moreover, several veins of the deep plexus were obliterated by fibrosis. The effects of the section of nasal nerves may depend on the interruption of the parasympathetic nerve fibres which are the main component of these nerves. These fibres possess acetylcholine and probably VIP as mediators and their activation causes, or at least enhances, inflammation.

There are few comparable data on the efficiency of microsurgery with interruption of parasympathetic innervation in the treatment of nasal polyposis^{35 36}. The latter reports refer to a total of 38 patients and do not compare the results with those of other techniques in the same hospitals. However, they do not contradict the present results showing that this type of surgery is effective and at low risk of major and minor complications. Despite the fundamental role of operative microscopy to achieve good results in our patients, as pointed out above, it is worthwhile stressing the importance of preoperative CT scans in order to define the extent of disease and rule out anatomical peculiarities which may lead to risk of complications. Post-operative CT scans are justified in patients with persistent discomfort, especially localised headache, or in the case of relapse before reintervention.

In our experience, the best outcome of microsurgery occurred in patients with circumscribed, primary nasosinus pathology and the worst in patients with massive polyposis, in those who had previously been operated on and in those who also suffered from asthma, acetylcolicylic acid (ASA) sensitivity or Widal's syndrome. These findings coincide with those of other Authors in patients submitted to microsurgery without interruption of parasympathetic innervation^{37 38}.

It should be stressed that the interruption of parasympathetic innervation makes microsurgery more effective with no increase in post-surgery complications. However, this can be achieved only after extensive training on autopsy specimens and the need for this training before addressing patients cannot be overemphasised. A minor drawback of microsurgery

(with or without section of sphenopalatine artery and nasal nerves) is that it requires longer operation times than conventional surgery, with consequently a greater load on the operating room schedule.

Conclusions

An analysis of the results of microsurgical ethmoido-sinusal emptying shows that this treatment is more effective than, and as well tolerated as, conventional surgery. The efficiency of microsurgical treatment is enhanced by completing the operation with the inter-

ruption of parasympathetic innervation which leads to reducing relapses and post-surgery complications. Nasal polyposis depends on impaired reactivity of the nasal mucosa due to various causes and, therefore, persists after conventional and microsurgery, despite the progress in surgical techniques and in pharmacological agents. The invalidating load of nasal and sinusal inflammation can be reduced by well planned microsurgery in the early stages of the disease, extended to include interruption of the autonomic innervation and combined with pharmacological treatment.

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