# Endoscopic *versus* open surgical interventions for inverted nasal papilloma: a systematic review

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## Keypoints

- Inverted nasal papilloma is a unique neoplasm characterised by a tendency to recur following excision, an association with malignancy and an ability to destroy bone.
- The coexistence with nasal polyps (not always sent for histology), the lack of a universally accepted staging system and the fact that most data on Inverted papilloma come from tertiary centres (selected cases probably the most aggressive) account for the difficulty in determining its true incidence.
- Treatment is surgical. The gold standard approach was an open radical procedure. The introduction of endoscopic surgery for primary or recurrent lesions has shown potential advantages. Lack of complications of open surgery together with improved access to specific nasal areas suggests that the endoscopic techniques in experienced hands and for selected lesions may be a good alternative.
- The aim of this review was to assess the effectiveness of the endoscopic *versus* open techniques for management of inverted papilloma.
- There is not enough evidence in the literature to support one or the other treatment option for management of inverted papilloma. There is a trend though towards endoscopic approach.
- Ideal management should aim at complete removal of all diseased mucosa with creation of wide cavities and long term follow-up to detect subsequent recurrence or malignant transformation.

Inverted papilloma is a benign sinonasal tumour with variable biological behaviour. It is an epithelial neoplasm arising from the Schneiderian membrane that lines the nose and paranasal sinuses.

The impact on patients' health most often relates to: (i) reduced quality of life because of compromised nasal function (ii) extension to the orbit (1–8%)[1–3] or the brain (in the absence of concurrent malignancy), which can very rarely lead to death[4,5] and (iii) the association with neoplasia.

Inverted papilloma's overall risk of malignancy varies from <2% to >56% but probably is ≈9%.[6] Differences in referral patterns and difficulties in accurate histological diagnosis may account for this variation.[7] Malignancy can either coexist with Inverted papilloma at the time of diagnosis (synchronous) or develop later at the site of resection of this benign tumour (metachronous). The risk of the latter has been overestimated in the past as a result of different pathological criteria being employed by studies[8] and has led to overtreatment.[1] True transformation to invasive carcinoma is proved in a minority of cases and it is estimated at <2%.[9] Particularly for unselected populations, if concurrent malignancy has been carefully excluded, the risk of subsequent malignancy is very small.[10]

Treatment of inverted papilloma is surgical. The gold standard approach was an open radical procedure in the form of a lateral rhinotomy with medial maxillectomy.[2,11–13] The midfacial degloving approach appears to be a good alternative. These approaches may entail functional or cosmetic complications (atrophic rhinitis, scar). Limited lesions can be managed effectively with conservative intranasal (simple polypectomy) or extranasal procedures.[14]

Recurrence rate, the main outcome measure when comparing 'radical' with 'conservative' procedures, is directly linked to the extent of the definitive procedure and it is estimated at 58% for limited procedures and 14% for radical procedures.[15] However, this may not be the case according to two studies, which found no correlation between recurrence rates and aggressiveness of sur-

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gery.[10,16] In general, most recurrences develop within 2 years after initial treatment at the site of the previous resection (suggesting incomplete removal) although it can take 10–24 years.[1] There are no robust clinical or histological prognostic factors to determine who is at high risk of recurrence.

The introduction of endoscopic techniques in the management of primary or recurrent lesions has shown potential advantages. Lack of complications of open surgery, improved access to specific nasal areas and shorter hospital stay with acceptable recurrence rates suggest that the endoscopic techniques in experienced hands and for selected, limited lesions may offer a good alternative to open techniques.[6,17–20]

Overall, management aims at providing the best chance of controlling disease (complete removal and adequate access for post-operative examination). The role of radiotherapy as a primary therapy for benign inverted papilloma is not clearly defined yet.[21] The aim of this systematic review is to assess the effectiveness of endoscopic *versus* open procedures for management of Inverted papilloma.

## Materials and methods

### *Literature search*

Studies were located using systematic searches in Medline, Embase, Cinahl and the Cochrane Library electronic databases, together with hand searching of key texts, references and reviews relevant to the field. Medical Subject heading used included the terms: 'Inverted', 'inverting', 'papilloma', 'nose', 'sinuses' 'sinonasal' and 'paranasal'. The additional keywords 'treatment', 'endoscopic', 'external' and 'open' were also used in Medline and in searching the remaining databases. References from the relevant articles were also searched.

### *Inclusion criteria and analysis*

All randomised and non-randomised controlled prospective and retrospective trials and case series of five or more (in total, for both approaches) patients of any age with Inverted papilloma of the nasal cavity and paranasal sinuses were included. Bilateral and recurrent lesions were also included. A literature search was performed between 1981 and 2006 (March).

Types of interventions included were endoscopic resections *versus* any surgical approach which involves an incision (lateral rhinotomy and modifications, midfacial degloving approach and modifications, Denker's procedure, craniofacial resection, Caldwel-Luc, external sphenoethmoidectomy and osteoplastic procedure of the frontal sinus). Main outcome measures included the recurrence rate and the length of follow-up (of at least 12 months).

### *Exclusion criteria*

Non-English language articles were excluded. Case reports and series of less than five patients (in total) and data involving non-endoscopic 'polypectomies' and studies using combined procedures such as endoscopic resection with the Caldwell-Luc approach were also excluded. Reviews featuring one of the two approaches only (i.e. endoscopic only or open only) were included in the table but not in the analysis, as this was not the aim of the present review. Studies with vaguely or not at all defined length of follow-up periods were excluded. Additionally, follow-ups of <24 months were also excluded, as there is some evidence that most recurrences develop within 2 years after initial treatment.

## Results

Selection bias in disease extent and length of follow-up, blinding of the results, lack of common outcome measures and uncontrolled studies were some of the problems preventing a formal meta-analysis. The literature review identified 52 articles published in the English literature of which 15 only met our strict inclusion criteria. Table 1 summarizes the studies, which were retrospective uncontrolled trials comparing endoscopic *versus* open approaches (same surgeons, same institutions, using both approaches) for management of inverted papilloma. Table 2 summarizes studies – from recognised authors/institutions – depicting only endoscopic treatment; these series were not included in the analysis.In total there were 292 endoscopic cases and 353 open cases. The mean recurrence rate for the endoscopic approach was 12% and for the open approach 17%. The mean follow-up was 46 months.

## Discussion

There is a lot of controversy in the literature regarding management of nasal Inverted papilloma. Open approaches have been the historical standard of care, but endoscopic techniques are favoured in recent years. All systematic reviews, including ours, are flawed by selection bias. Lack of a universally accepted staging system, different lengths of follow-ups, had difficulty in understanding the aetiopathology of these tumours and in determining the incidence of the disease are to blame.

**Table 1.** Studies (in chronological order) comparing endoscopic *versus* open approach for the management of inverted nasal papilloma

| First author and reference number | Year of publication | No. pts in EG | Recurrence in EG (%) | No. pts in OG | Recurrence in OG (%) | Mean fup (months) |
|---|---|---|---|---|---|---|
| Waitz[17] | 1992 | 35 | 17 | 16 | 19 | 46 |
| Mccary[28] | 1994 | 4 | 0 | 20 | 20 | 30 |
| Raveh[29] | 1996 | 9 | 22 | 39 | 36 | 26 |
| Peter[30] | 1997 | 18 | 31 | 7 | 29 | 52 |
| Klimek[31] | 2000 | 33 | 18 | 22 | 18 | 36 |
| Lund[15] | 2000 | 13 | 8 | 24 | 21 | 45 |
| Krouse[6] | 2001 | 7 | 14 | 5 | 0 | 40 |
| Schlosser[20] | 2001 | 20 | 20 | 1 | 0 | 42 |
| Han[32] | 2001 | 15 | 13 | 12 | 8 | 54 |
| Thorp[33] | 2001 | 2 | 0 | 41 | 27 | 32 |
| Sadeghi[34] | 2003 | 5 | 0 | 6 | 0 | 66 |
| Kraft[35] | 2003 | 26 | 8 | 8 | 37 | 62 |
| Lawson[3] | 2003 | 41 | 12 | 119 | 15 | 62 |
| Pasquini[36] | 2004 | 36 | 3 | 32 | 19 | 74 |
| Busquets[37] | 2006 | 28 | 11 | 1 | 0 | 22 |
| Total | | 292 | 12 | 353 | 17 | 46 |

Total follow-up and recurrence rates are expressed in means. Pts, patients; EG, Endoscopic group; OG, open group; fup, follow-up.

**Table 2.** These studies – although from recognised authors/institutions – depict only endoscopic cases and therefore did not meet the inclusion criteria of the present review

| First author and reference number | Year of publication | No. pts | Recurrence rate (%) | Mean f-up (months) |
|---|---|---|---|---|
| Stammberger[38] | 1981 | 16 | 19 | >24 |
| Stankiewicz[39] | 1993 | 15 | 33 | 36 |
| Buchald[16] | 1995 | 5 | 0 | 24 |
| Kamel[40] | 1995 | 12 | 0 | 35 |
| Xu[41] | 1996 | 14 | 7 | >24 |
| Sham[42] | 1998 | 22 | 27 | 53 |
| Chee[43] | 1999 | 18 | 5 | 33 |
| Tufano[44] | 1999 | 33 | 15 | 20 |
| Bertrand[45] | 2000 | 84 | 18 | 42 |
| Sukenik[46] | 2000 | 19 | 21 | 36 |
| Winter[47] | 2000 | 67 | 22 | >12 |
| Keles[48] | 2001 | 13 | 23 | 27 |
| Kunn[49] | 2001 | 28 | 7 | 22 |
| Baruah[50] | 2003 | 6 | 17 | 21 |
| Wormald[51] | 2003 | 17 | 6 | 39 |
| Kaza[52] | 2003 | 51 | 14 | 30 |
| Llorente[53] | 2003 | 26 | 8 | 60 |
| Lee[26] | 2004 | 43 | 9 | 25 |
| Tomenzoli[54] | 2004 | 47 | 0 | 55 |
| Total | | 536 | 13 | 35 |

The incidence of the disease has not been accurately defined yet. It is estimated at 0.52 per 100 000 per year and it increases to 0.74 per 100 000 per year if all histological types of sinonasal papillomas are taken into account.[16] However, these numbers reflect inverted papilloma's occurrence in a single European population. The rarity of the disease (4% of all nasal tumours), the underdiagnosis due to the long clinical course, the coexistence with simple nasal polyps, which are not routinely sent for histological examination and ultimately the fact that most data come from tertiary referral centres (selected cases probably the most aggressive) explain the difficulty in determining the true incidence of the disease. Increased awareness by general otolaryngologists and referrals to

dedicated rhinologists may lead to a higher numbers ofInverted papillomas being diagnosed[16] and a better estimation of the impact of the disease on Health Economics. The aetiology of these tumours is unclear. The human papilloma virus has been implicated but data are not conclusive.[22–24]

Inverted papilloma affects all ages, most commonly white males in their fifth to seventh decade. The most common presenting symptom is unilateral nasal obstruction followed by nasal discharge, epistaxis and facial pain/pressure. Duration of symptoms before definitive treatment ranges from months to several years. Several decades' duration has also been reported[1,11] but this probably reflects delayed diagnosis as patients often undergo several debulking polypectomies before the histological diagnosis of inverted papilloma is established.

Radiological diagnosis was traditionally based on computerised tomography, but it is often impossible to differentiate between polyps with entrapped debris and Inverted papilloma. Magnetic resonance imaging, especially T2-weighted images is perhaps a better tool in differentiating Inverted papilloma from other nasal lesions and is more recently advocated as the imaging of choice.[25]

Widespread use of endoscopic techniques and better training of surgeons in these approaches means that more and more nasal tumours can be managed endoscopically. Most rhinologists today will choose to tailor their approach based on the location and the extent of the tumour as determined preoperatively, but mainly intraoperatively. Tumours of the medial wall of the maxillary sinus are usually amenable to endoscopic medial maxillectomy whereas a Caldwell-Luc approach can be used when the lateral wall is involved. If the inferomedial wall of the frontal sinus is involved a modified Lothrop procedure can be performed, whereas for more superior involvement a combined approach with an osteoplastic flap maybe necessary.[26] Finally, lesions of the sphenoid sinus are uncommon and often impossible to manage in one sitting. Delay in diagnosis (lack of specific symptoms means that tumours are often advanced) and proximity of tumour to major structures (optic nerve, carotid artery and pituitary gland) means that staged resections and use of imaging–guidance techniques are often necessary for large sphenoid Inverted papilloma.[27] Whatever the chosen approach for treatment of inverted papilloma, there is no doubt although that endoscopic post-operative surveillance in the outpatient setting has allowed us to detect recurrences much sooner than before.

Management of Inverted papilloma remains controversial mainly due to the high-risk of recurrence and the association with malignancy. With increasing knowledge with regards to the aetiopathology of this benign tumour, we may be able to better understand its natural history and prevent or more efficiently manage both primary and recurrent disease.

## Conflict of interest

None declared.

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