

# Endoscopic management of sinus neoplasia: case series of image-guided surgery of inverted papillomata and recommended best practice for managing cases.

Gabi Klyvyte<sup>1</sup>, Jeremy Wong<sup>2</sup>, Shyam Gokani<sup>1</sup>, Louis Luke<sup>2</sup>, Lavandan Jegatheswaran<sup>2</sup>, and Carl Philpott<sup>1</sup>

<sup>1</sup>University of East Anglia Norwich Medical School

<sup>2</sup>James Paget University Hospitals NHS Foundation Trust

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## Abstract

**Key Points** Inverted papillomata are benign sinonasal tumours with high recurrence rates. Inverted papillomata recurrence is increased if operated on by a non-fellowship trained rhinologist. Inverted papillomata recurrence can be detected earlier in cases managed by specialist rhinology services. Inverted papillomata should be managed through a clear treatment pathway for sinonasal tumours. Other risk factors associated with increased recurrence include Krouse stage 3 and involvement of the frontal or maxillary sinuses.

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## Key Points

- Inverted papillomata are benign sinonasal tumours with high recurrence rates.
- Inverted papillomata recurrence is increased if operated on by a non-fellowship trained rhinologist.
- Inverted papillomata recurrence can be detected earlier in cases managed by specialist rhinology services.
- Inverted papillomata should be managed through a clear treatment pathway for sinonasal tumours.
- Other risk factors associated with increased recurrence include Krouse stage 3 and involvement of the frontal or maxillary sinuses.

## Introduction

Inverted papillomata (IP) are rare and benign sinonasal tumours that account for 0.4-7% of sinonasal tumours excised, with an estimated annual incidence of 0.2-1.5 cases per 100,000. In patients, the highest incidence is seen in the 5<sup>th</sup> and 6<sup>th</sup> decades of life, with a 2-5:1 male-to-female ratio (1,2). Despite being benign tumours, IPs are locally aggressive and have high recurrence rates of up to 78% (1). There is also a known association with malignancy, with a synchronous and metachronous carcinomatous rate estimated at 7.1% and 3.6% respectively (2). The aetiology of IP remains unknown, but evidence demonstrates an association with Human Papilloma Virus (HPV), p53 and p21 oncogenes in malignant transformation of IP (1).

Patients with IP can present with a variety of symptoms, including unilateral nasal obstruction, rhinorrhoea, epistaxis, facial pain, or hyposmia/anosmia (1,2). Conversely, IP can also present asymptotically in 4-23% of cases with the IPs being an incidental finding (1).

On endoscopy, IPs appear as a reddish-grey, friable lobulated mass that is firmer than an inflammatory polyp. IPs are predominantly unilateral, with bilateral lesions accounting for 1-9% of cases (2). Histopathological diagnosis is essential for diagnosis and to rule out associated malignancy. Characteristic features on microscopy include the invagination of the superficial IP epithelium into the underlying stroma, hence the ‘inverted’ descriptor. The epithelium may be of the stratified squamous, ciliated pseudostratified columnar epithelium or transitional types (1,3).

Radiological assessment is essential to determine the tumour location and extension for surgical planning. Computed Tomography (CT) of the sinuses is widely used to evaluate sinonasal masses and assess for underlying bony changes. Unlike malignant tumours that cause bony destruction, IP causes hyperostosis or sclerosis. (1,2) Magnetic resonance imaging (MRI) can be useful in addition to CT scans to determine the lesion’s exact location and decide upon the best surgical approach. (2)

The optimal management of IP involves the complete surgical excision of the diseased mucosa and mucoperiosteum. (2) Historically, gold-standard management techniques involved external approaches such as a lateral rhinotomy with medial maxillectomy. (1) With the progression of minimally invasive techniques and high-quality imaging, endoscopic management techniques have become the gold standard for IP resection. Compared to external approaches, they result in lower recurrence rates and reduce surgical morbidity. (1,4) Due to the high recurrence rates associated with IP, a minimum follow-up period of five years is recommended (4).

As many cases managed in our centre had already undergone a previous procedure, the objective of this retrospective case series was to evaluate the outcomes for primary and secondary cases of sinonasal IP including recurrence rates and complication rates.

## Materials and methods

### *Study design and setting*

We retrospectively reviewed clinical records for all patients with histologically confirmed inverted papilloma who received surgical management under the care of the senior author at a tertiary rhinology referral centre. Records were reviewed between 01/01/2011 - 31/12/2022.

This project was a local service evaluation and did not require ethical approval, following completion of the NHS Research Ethics Committee Tool, provided by the Medical Research Council. The STROBE guidelines were adhered to for reporting.

### *Participants*

Cases were identified from the operation logbooks of the Ears, Nose and Throat (ENT) Department operating theatres. The following cases were excluded:

- Pre-operative intracranial involvement – these were referred externally to the local neurosurgical unit.
- Features of alternative sinus neoplasia, such as squamous cell carcinoma, osteoma, or malignant melanoma.
- Conservative or palliative management as the sole treatment modality.

Practice at our centre is for primarily endoscopic resection of inverted papillomata with the use of intraoperative Medtronic computer-assisted navigation software.

### *Main outcome measures, variables, and data sources*

Anonymised data was collected from patients’ electronic clinic letters and operation notes for age, histological diagnosis, site of the tumour, date of operation, details of surgical management, postoperative complications, need for revision surgery and outcome at five years post-operatively (or most recent follow up if less than five years).

Surgical procedures were classified as primary if surgery was conducted at our centre for the first time and secondary if a prior attempted resection had been undertaken elsewhere.

Statistical analysis was done using a Chi-squared calculation with the significance level of  $p < 0.05$ .

## Results

### *Participant characteristics*

Between 2010 to 2022 there were 40 cases of inverted papilloma - 22 were primary and 18 were secondary. A consultant rhinologist did primary cases, whereas secondary cases were operated on by a general ENT surgeon at the first procedure. Our cohort included 26 males and 14 females. The average age at surgery was 62.8 ranging from 22.4 to 89. In addition to the endoscopic approach, 31% of our participants had a medial maxillectomy or Draf IIB/III as an adjunct.

### *Main results*

The most common area for IP in our cohort was the maxillary sinus (33%) which is displayed in Table 1. Recurrence was most common in the frontal and maxillary sinuses and the most common procedure performed was a medial maxillectomy (30%).

After 5 years of follow-up, there were a total of 21 recurrences in our cohort (figure 1) – these consisted of 6 recurrences in primary cases and 15 recurrences in secondary cases. When the number of recurrences between primary and secondary cases was compared, the difference was found to be statistically significant ( $X^2(1, n=40) = 19.1583, p = 0.000412$ ). A range of 1-2 episodes of recurrence were seen in each primary case, compared to 1-7 episodes in each secondary case.

On average, recurrence was detected within 20 and 39 months in primary and secondary cases respectively. Most recurrences were treated with local resection (50%) or topical intranasal mitomycin (20%). Regarding complications, there was 1 case of intra-operative CSF leak (repaired intra-operatively) and 1 case of temporary post-operative facial numbness.

### *Krouse staging*

Sinonasal IPs were staged using the Krouse system. Most patients (58.5%) in our cohort presented with Krouse stage 3 – this is when the tumour invades lateral, inferior, superior, anterior, or posterior walls of the maxillary sinus and/or frontal sinus. (1,2) Table 2 summarises the rate of recurrences according to different Krouse stages. The highest rates of recurrence were seen in stage 3, reflecting the more advanced presentation of the cases, especially in secondary cases. (Table 2)

## Discussion

### *Key results*

Our patient cohort demographics were similar to other studies, with an observed 2:1 male-to-female ratio and average age of presentation of 62.8 years. As in previous research, the maxillary sinus was the most common site for primary IPs. (5) In literature, primary and secondary cases have recurrence rates of 10% and 29% respectively (5,6), which is comparable to our cohort's recurrence rates of 15% (6/40) and 37.5% (15/40) for our primary and secondary cases.

The mean time of recurrence was 20 and 39 months for primary and secondary cases, which is different to what has been found in previous literature. (5) This difference could be explained by the faster detection rate and the significantly smaller number of recurrences in primary cases seen in our cohort (16% vs 84%), highlighting that outcomes and recurrence rates for IP are better when managed by a fellowship-trained rhinologist.

As in previous literature, patients with Krouse stage 3 cases and IPs located in the frontal and maxillary sinuses had the highest rates of recurrences. (5,6) This may be explained by the technical difficulty of accessing the frontal sinus, limited visualisation of the tumour via endoscopy, and the challenge of obtaining

a margin when up against critical structures. (8) Similarly, maxillary IPs are associated with increased recurrence rates in literature; (6) due to the challenging visualisation and access of the site (2,6), especially the floor of the antrum and medial maxillary wall.

The worse outcomes seen in secondary cases may be explained by the absence of landmarks due to previous dissections, scarring and distorted anatomy. (9) However, our cohort further highlights that IPs have a lower rate of recurrences when managed by a fellowship-trained rhinologist. Thus, figure 2 contains the suggested gold-standard treatment pathway for all sinonasal tumours.

### Limitations

Potential limitations of our study include the lack of information on patient characteristics such as smoking, HPV and inflammatory disease status since these were not well recorded in the electronic records. Our population sample size was small and from a single centre, reflecting the smaller regional population.

### Conclusions

This retrospective review suggests that recurrence rates of IPs may be higher in cases operated on initially by a non-specialist surgeon. We therefore recommend that all IP cases should be referred to a fellowship-trained rhinologist using the suggested management gold-standard flow chart (figure 2). Our study further demonstrates that endoscopic approaches remain a beneficial technique in managing IPs (2,5) by reducing morbidity, decreasing post-operative complications, and inpatient stays. (4,6)

Word count – 1433/1500

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**Tables and Figures:**

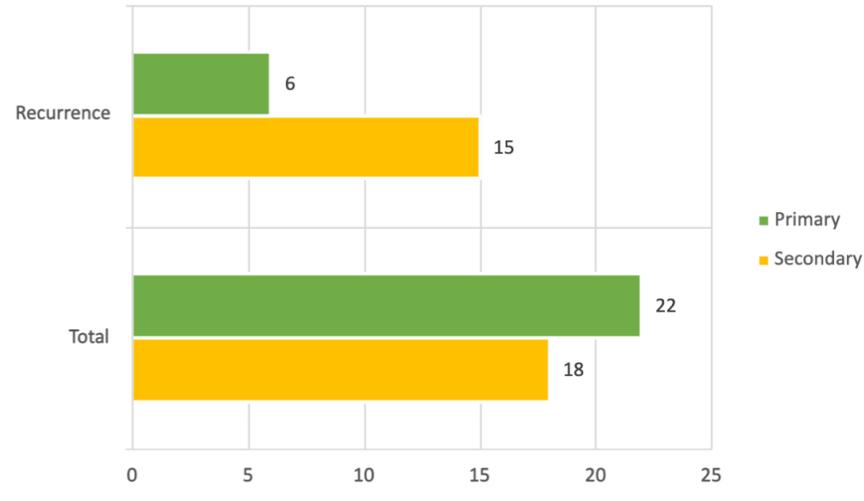
**Table 1: Location of Inverted Papilloma and Rate of Recurrence**

Area	Right	Left	Total	Percentage of total	Recurrence Rate (Percentage)
Nasal vestibule, septum	0	4	4	10	0
Frontal sinus	3	3	6	15	31
Maxillary sinus	5	8	13	33	31
Turbinates	3	3	6	15	5
Ethmoid sinus	5	5	10	24	26
Sphenoid sinus	1	0	1	2	5

**Table 2: The Rate of Recurrence according to Krouse stage**

Krouse Stage	Primary cases	Number of primary recurrences	Secondary cases	Number of secondary recurrences
T1	3	0	2	6
T2	8	3	3	8
T3	11	8	13	23
T4	0	0	0	0

**Figure 1: The Rate of Recurrence Between Primary and Secondary Lesions**



**Figure 2: A Recommended Patient Pathway for Sinonasal Tumours.**

