

Main Article

Prof D H Lee takes responsibility for the integrity of the content of the paper

Cite this article: Yeom S, Lee DH, Lim SC. Clinical outcomes of sinonasal inverted papilloma: a retrospective analysis of 139 cases. *J Laryngol Otol* 2023;**137**:1154–1157. <https://doi.org/10.1017/S0022215123000361>

Accepted: 16 February 2023
First published online: 6 March 2023

Keywords:

Papilloma, inverted; paranasal sinuses; paranasal sinus neoplasms; recurrence; malignancy; natural orifice endoscopic surgery

Corresponding author:

Prof Dong Hoon Lee;
Email: leen3L@hanmail.net

Clinical outcomes of sinonasal inverted papilloma: a retrospective analysis of 139 cases

S Yeom, D H Lee  and S C Lim

Department of Otolaryngology – Head and Neck Surgery, Chonnam National University Medical School and Hwasun Hospital, Hwasun, South Korea

Abstract

Objectives. Sinonasal inverted papilloma has a high tendency for recurrence, local bone destruction and risk of malignant transformation. Therefore, complete resection of the tumour is required, and close follow up is essential. This article describes the clinical outcomes, recurrence rate and malignant transformation rate of sinonasal inverted papilloma.

Methods. In this study, 139 patients diagnosed with sinonasal inverted papilloma in our hospital from December 2010 to May 2022 were retrospectively analysed. All patients underwent endoscopic surgery.

Results. Sinonasal inverted papilloma occurred more often in males than in females. The mean age of patients with sinonasal inverted papilloma was 67.3 ± 5.7 years at diagnosis. The most prevalent site of origin was the maxillary sinus (50.4 per cent). The recurrence rate was 5.75 per cent, and the malignant transformation rate was 6.5 per cent.

Conclusion. All patients in this study underwent endoscopic surgery. Meticulous resection and regular long-term follow ups are crucial to reducing sinonasal inverted papilloma recurrence after surgery.

Introduction

Sinonasal inverted papilloma is a rare but the most prevalent sinonasal tumour, accounting for 0.5–4 per cent of nasal sinus neoplasms.¹ Sinonasal inverted papilloma arises from the Schneiderian epithelium of the nasal cavity and paranasal sinus. There are three histologically unique papilloma types: exophytic, oncocytic and, the most common, inverted papilloma.^{2,3}

Sinonasal inverted papilloma has three key features distinguishing it from other sinonasal tumours: high potential for recurrence, local bone destruction and risk of malignant transformation. Sinonasal inverted papilloma tends to occur more commonly in males, with a ratio of 3:1. The mean age of sinonasal inverted papilloma patients is 55 years.^{2,4}

The aetiology of sinonasal inverted papilloma remains unclear. Smoking, viral infections, diabetes, allergies and chronic inflammation are possible causes. Human papillomavirus (HPV) is considered a significant cofactor in the pathogenesis, especially HPV types 6, 11, 16 and 18. Recent reports suggest that occupational exposure is a risk factor for sinonasal inverted papilloma.^{5–9}

This study aimed to analyse clinical outcomes, recurrence rate and malignant transformation rate of sinonasal inverted papilloma.

Materials and methods

We conducted a retrospective analysis of patients diagnosed with sinonasal inverted papilloma in our hospital from December 2010 to May 2022. A total of 139 patients were reviewed. Clinical characteristics included sex, age, symptoms, previous sinus surgery history, tumour location, alcoholism and smoking history. Twelve patients presented with sinonasal inverted papilloma recurrence.

Computed tomography (CT) or magnetic resonance imaging (MRI) was conducted on all patients to identify the characteristics, location and tumour extension before surgery. All patients who underwent endoscopic surgery were classified according to four staging systems: Krouse, Cannady, Hans and Dragonetti.^{10–14}

The patients visited the hospital a week after surgery for a post-operative check-up and then two weeks later. Subsequently, they attended follow-up appointments at three months, six months and finally once a year. An endoscopic examination was performed at each visit to evaluate recurrence.

Results

The demographics of the 139 patients are summarised in [Table 1](#) (100 males (71.9 per cent); 39 females (28.1 per cent)). The mean age was 67.3 years (standard deviation (SD) = 5.7) (age range: 17–79 years). Seventy-six patients (54.7 per cent) had a smoking history and 53 (38.1 per cent) had an alcohol drinking history. The tumour was located in

Table 1. Clinical demographics of 139 sinonasal inverted papilloma cases

Factor	Value
Sex (male:female) (n)	100:39
Age (mean ± SD (range); years)	67.3 ± 5.7 (17–79)
Smoking? (Yes:no) (n)	76:63
Alcoholism? (Yes:no) (n)	53:86
Location (right:left:both) (n)	74:59:6
Previous sinus surgery? (yes:no) (n)	47:92
Symptoms (% (n))	
– Nasal obstruction	81 (58.3)
– Incidental detection	25 (17.9)
– Rhinorrhoea	18 (12.9)
– Post-nasal drip	3 (2.2)
– Headache	3 (2.2)
– Foul odour	3 (2.2)
– Nasal bleeding	2 (1.4)
– Nasal discomfort	2 (1.4)
– Dysgeusia	1 (0.7)
– Snoring	1 (0.7)
Histological findings (% (n))	
– SNIP without dysplasia	125 (90)
– SNIP with low-grade dysplasia	4 (2.9)
– SNIP with high-grade dysplasia	2 (1.42)
Malignant transformation (% (n))	9 (6.5)
Recurrence (% (n))	8 (5.8)

SD = standard deviation; SNIP = sinonasal inverted papilloma

the right nasal cavity in 74 cases (53.2 per cent), the left nasal cavity in 59 cases (42.4 per cent) and both nasal cavities in 6 patients (4.3 per cent).

The most common chief complaint was nasal obstruction (*n* = 81, 58.3 per cent). Twenty-five cases (17.9 per cent) were incidentally detected on endoscopy or imaging. The third most common complaint was rhinorrhoea (*n* = 18, 12.9 per cent), followed by post-nasal drip (*n* = 3, 2.2 per cent), headache (*n* = 3, 2.2 per cent) and foul odour (*n* = 3, 2.2 per cent), nasal bleeding (*n* = 2, 1.4 per cent) and nasal discomfort (*n* = 2, 1.4 per cent), and dysgeusia (*n* = 1, 0.7 per cent) and snoring (*n* = 1, 0.7 per cent).

The maxillary sinus (*n* = 70, 50.4 per cent) was the most prevalent site of sinonasal inverted papilloma, followed by the ethmoid sinus (*n* = 33, 23.7 per cent), frontal sinus (*n* = 9, 6.5 per cent) and sphenoid sinus (*n* = 7, 5.0 per cent). The origin sites of sinonasal inverted papilloma in this study are summarised in Table 2.

We classified cases according to the Krouse, Cannady, Hans and Dragonetti staging systems (Table 3). According to the Krouse system, 11 patients had stage T₁ tumours (7.9 per cent), 37 were T₂ (26.6 per cent), 68 were T₃ (48.9 per cent) and 23 were T₄ (16 per cent). Regarding the Cannady system, 49 were staged as group A (35.2 per cent), 72 were group B (51.8 per cent) and 18 were group C (12.9 per cent). For the Hans system, 47 were staged as group I (33.8 per cent), 60 were group II (43.2 per cent), 16 were group III (11.5 per cent) and 16 were group IV (11.5 per cent). According to the Dragonetti system, 39 were staged as type I (28.0 per cent), 6 were type II (4.3 per cent),

Table 2. Origin site of sinonasal inverted papilloma

Location	n (%)
Maxillary sinus	70 (50.4)
Ethmoid sinus	33 (23.7)
Frontal sinus	9 (6.5)
Sphenoid sinus	7 (5.0)
Middle turbinate	5 (3.6)
Inferior turbinate	3 (2.2)
Septum	3 (2.2)
Uncinate process	3 (2.2)
Lamina papyracea	3 (2.2)
Origin site not clear	2 (1.4)
Superior turbinate	1 (0.71)

Table 3. Classification according to four sinonasal inverted papilloma staging systems

Staging	n (%)
Krouse	
– T ₁	11 (7.9)
– T ₂	37 (26.6)
– T ₃	68 (48.9)
– T ₄	23 (16)
Cannady	
– A	49 (35.2)
– B	72 (51.8)
– C	18 (12.9)
Hans	
– I	47 (33.8)
– II	60 (43.2)
– III	16 (11.5)
– IV	16 (11.5)
Dragonetti	
– Type I	39 (28.1)
– Type II	6 (4.3)
– Type III	10 (7.2)
– Type IVa	35 (25.2)
– Type IVb	20 (14.4)
– Type V	12 (8.6)
– Type VI	17 (12.2)

10 were type III (7.2 per cent), 35 were type IVa (25.2 per cent), 20 were type IVb (14.4 per cent), 12 were type V (8.6 per cent) and 17 were type VI (12.2 per cent).

Of the patients, 125 (90 per cent) received a pathological diagnosis of sinonasal inverted papilloma without dysplasia. Four patients (2.9 per cent) were diagnosed with sinonasal inverted papilloma with low-grade dysplasia (mild to focal dysplasia), two (1.42 per cent) were diagnosed with sinonasal inverted papilloma with high-grade dysplasia, while nine (6.5 per cent) were diagnosed with squamous cell carcinoma.

Table 4. Data of eight patients with recurrence

Pt no.	Sex	Age (years)	Sinonasal inverted papilloma staging				Smoking?	Alcoholism?
			Krouse	Cannady	Hans	Dragonetti		
1	M	61	T ₃	B	III	V	No	No
2	M	69	T ₄	C	IV	VI	Yes	Yes
3	F	62	T ₂	A	I	III	No	Yes
4	M	59	T ₄	C	IV	VI	No	No
5	M	46	T ₁	A	I	I	Yes	No
6	M	42	T ₃	B	II	IVa	Yes	No
7	M	53	T ₃	B	II	IVa	Yes	Yes
8	M	55	T ₄	C	IV	VI	Yes	No

Pt no. = patient number; M = male; F = female

Recurrence occurred in eight patients (5.75 per cent). Data for these patients are summarised in Table 4. Seven of the patients were male (87.5 per cent), with a mean age at recurrence of 55.8 years (SD = 8.82). Five of the patients had a smoking history (62.5 per cent), and three had an alcohol history (37.5 per cent). The mean time to recurrence was 81.4 ± 88.4 months, ranging from 3 to 288 months. According to the Krouse system, three of the patients were at stage T₄ (37.5 per cent), three were at stage T₃ (37.5 per cent) and one each at stage T₂ and T₁ (12.5 per cent). In the Cannady system, three patients each (37.5 per cent) were in group B and group C, and two patients (25 per cent) were in group A. In the Hans system, the most prevalent stage was IV, with three patients (37.5 per cent). Two patients each (25 per cent) were in stage I and II. Only one patient (12.5 per cent) was in stage III. In the Dragonetti system, the most common stage was stage VI, with three patients (37.5 per cent), followed by stage IVa with two patients (25 per cent). Stages I, III and V included one patient each (12.5 per cent).

After surgery, the mean follow-up period was 19.5 ± 34.9 months, ranging from 0.2 to 127 months.

Discussion

Sinonasal inverted papilloma is three times more prevalent in males than in females (mean age: 55 years).^{2,3} In this study, sinonasal inverted papilloma occurred more often in males than in females, with a ratio of 2.6:1 (mean age: 67.3 ± 5.7 years at diagnosis). The youngest patient was a 17-year-old female; the oldest was a 79-year-old female.

Patients with sinonasal inverted papilloma had symptoms such as rhinorrhoea, nasal obstruction, nasal bleeding, hyposmia or anosmia, headache, and facial pain.¹⁵ Nasal obstruction (58.3 per cent) was the most common symptom in this study. Of the cases, 17.9 per cent were incidentally detected. Rhinorrhoea (12.9 per cent) was the third most common symptom.

- Sinonasal inverted papilloma has a high tendency for recurrence, local bone destruction and risk of malignant transformation
- A total of 139 sinonasal inverted papilloma patients were reviewed; sex, age, symptoms, previous sinus surgery history, tumour location, alcoholism and smoking history were assessed
- The recurrence rate was 5.75 per cent and the malignant transformation rate was 6.5 per cent
- All study patients underwent endoscopic surgery and showed no significant difference in recurrence rate compared to the rates reported in current literature

Computed tomography and MRI are preferred for determining tumour site and extension. The key features of sinonasal inverted papilloma on CT are an isodense lobulated mass with or without calcification, prevalent bone erosion, and focal hyperostosis.^{16–18} On MRI, sinonasal inverted papilloma presents as an isodense to hypodense mass on T1-weighted images and as hyperdense on T2-weighted images. Convoluted cerebriform morphology is a frequent MRI presentation.^{17–19} We conducted CT or MRI on all our patients to evaluate tumour location, origin site and extension. After imaging, we determined sinonasal inverted papilloma staging and type of surgery.

The most common origin site was the maxillary sinus, accounting for 50.4 per cent. This finding is consistent with current literature, in which the maxillary sinus is the most prevalent site of inverted papilloma.²⁰ The second most common origin site was the ethmoid sinus, accounting for 23.7 per cent, followed by the frontal sinus and the sphenoid sinus.

The literature describes several sinonasal inverted papilloma classifications, with the Krouse system being the most widely used. We classified our patients according to the Krouse, Cannady, Hans and Dragonetti staging systems.^{10–14} Stage T₃ was most common (48.9 per cent) in the Krouse system, group B (51.8 per cent) was most common in the Cannady system, group II (43.2 per cent) was most common in the Hans system, and type I (28.1 per cent) was most common in the Dragonetti system.

The recurrence rate was 5.75 per cent, which is consistent with the rate reported in the literature, of 5–30 per cent (up to 78 per cent in another article).^{3,21–23} In the Krouse staging system, 12.5 per cent of recurrences occurred in both stage T₁ and stage T₂ and 37.5 per cent in both stage T₃ and stage T₄. According to the Cannady system, groups B and C had the same rate of 37.5 per cent. In the Hans system, stage IV was the most common at recurrence (37.5 per cent), and in the Dragonetti system stage VI was the most common (37.5 per cent).

The malignant transformation rate was 6.5 per cent. This finding is consistent with the current literature, in which the malignant transformation rate ranges from 7 per cent to 11 per cent.^{23–25}

Up to the mid-1990s, the 'gold standard' was external approach surgery. Since endoscopic surgery was first described, the endoscopic approach has become the new gold standard. According to current literature, there is little difference in efficacy between the external approach and endoscopic surgery.^{2,24–30} All patients in this study underwent endoscopic surgery.

Recurrence rates are significant, and recurrences have been reported several years after surgery.²³ Therefore, periodic follow up of at least three years is essential.²³

Conclusion

In this study, the recurrence rate was 5.75 per cent and the malignant transformation rate was 6.5 per cent. All patients in this study underwent endoscopic surgery, and showed no significant difference in recurrence rate compared with the rates reported in current literature. Meticulous resection and regular long-term follow-up sessions are important to reduce the incidence of sinonasal inverted papilloma recurrence after surgery.

Competing interests. None declared.

References

- 1 Wang MJ, Noel JE. Etiology of sinonasal inverted papilloma: a narrative review. *World J Otorhinolaryngol Head Neck Surg* 2017;**3**:54–8
- 2 Lisan Q, Laccourreye O, Bonfils P. Sinonasal inverted papilloma: from diagnosis to treatment. *Eur Ann Otorhinolaryngol Head Neck Dis* 2016;**133**:337–41
- 3 Barnes L. Schneiderian papillomas and nonsalivary glandular neoplasms of the head and neck. *Mod Pathol* 2002;**15**:279–97
- 4 Govindaraj S, Wang H. Does human papilloma virus play a role in sinonasal inverted papilloma? *Curr Opin Otolaryngol Head Neck Surg* 2014;**22**:47–51
- 5 Hong SL, Kim BH, Lee JH, Cho KS, Roh HJ. Smoking and malignancy in sinonasal inverted papilloma. *Laryngoscope* 2013;**123**:1087–91
- 6 Lawson W, Schlecht NF, Brandwein-Gensler M. The role of the human papillomavirus in the pathogenesis of Schneiderian inverted papillomas: an analytic overview of the evidence. *Head Neck Pathol* 2008;**2**:49–59
- 7 Gupta R, Rady PL, Sikora AG, Tying SK. The role of human papillomavirus in the pathogenesis of sinonasal inverted papilloma: a narrative review. *Rev Med Virol* 2021;**31**:e2178
- 8 Ungari C, Riccardi E, Reale G, Agrillo A, Rinna C, Mitro V *et al.* Management and treatment of sinonasal inverted papilloma. *Ann Stomatol (Roma)* 2015;**6**:87–90
- 9 d'Errico A, Zajacova J, Cacciatore A, Baratti A, Zanelli R, Alfonso S *et al.* Occupational risk factors for sinonasal inverted papilloma: a case-control study. *Occup Environ Med* 2013;**70**:703–8
- 10 Krouse JH. Development of a staging system for inverted papilloma. *Laryngoscope* 2000;**110**:965–8
- 11 Cannady SB, Batra PS, Sautter NB, Roh HJ, Citardi MJ. New staging system for sinonasal inverted papilloma in the endoscopic era. *Laryngoscope* 2007;**117**:1283–7
- 12 Gras-Cabrerizo JR, Montserrat-Gili JR, Masegur-Solench H, León-Vintró X, De Juan J, Fabra-Llopis JM. Management of sinonasal inverted papillomas and comparison of classification staging systems. *Am J Rhinol Allergy* 2010;**24**:66–9
- 13 Han JK, Smith TL, Loehr T, Toohill RJ, Smith MM. An evolution in the management of sinonasal inverting papilloma. *Laryngoscope* 2001;**111**:1395–400
- 14 Dragonetti A, Gera R, Sciuto A, Scotti A, Bigoni A, Barbaro E *et al.* Sinonasal inverted papilloma: 84 patients treated by endoscopy and proposal for a new classification. *Rhinology* 2011;**49**:207–13
- 15 Doddawad VG, Premalatha BR, Sreeshyla HS, Nitin P. Classification staging systems on clinical and radiographic features of inverted sinonasal papilloma: a case report. *Oral Oncol* 2022;**127**:105768
- 16 Momeni AK, Roberts CC, Chew FS. Imaging of chronic and exotic sinonasal disease: review. *AJR Am J Roentgenol* 2007;**189**:S35–45
- 17 Savy L, Lloyd G, Lund VJ, Howard D. Optimum imaging for inverted papilloma. *J Laryngol Otol* 2000;**114**:891–3
- 18 Chawla A, Shenoy J, Chokkappan K, Chung R. Imaging features of sinonasal inverted papilloma: a pictorial review. *Curr Probl Diagn Radiol* 2016;**45**:347–53
- 19 Ojiri H, Ujita M, Tada S, Fukuda K. Potentially distinctive features of sinonasal inverted papilloma on MR imaging. *AJR Am J Roentgenol* 2000;**175**:465–8
- 20 Lian F, Juan H. Different endoscopic strategies in the management of recurrent sinonasal inverted papilloma. *J Craniofac Surg* 2012;**23**:e44–8
- 21 Gu FM, Zhang LS. Clinical outcomes of endoscopic and open resection of recurrent sinonasal inverted papilloma. *J Craniofac Surg* 2014;**25**:1090–3
- 22 Peng P, Har-El G. Management of inverted papillomas of the nose and paranasal sinuses. *Am J Otolaryngol* 2006;**27**:233–7
- 23 Lund VJ, Stammberger H, Nicolai P, Castelnuovo P, Beal T, Beham A *et al.* European position paper on endoscopic management of tumours of the nose, paranasal sinuses and skull base. *Rhinol Suppl* 2010;**22**:1–143
- 24 Mirza S, Bradley PJ, Acharya A, Stacey M, Jones NS. Sinonasal inverted papillomas: recurrence, and synchronous and metachronous malignancy. *J Laryngol Otol* 2007;**121**:857–64
- 25 Nowosielska-Grygiel J, Pietkiewicz P, Owczarek K, Olszewski J, Miłoński J. Diagnosis and treatment of nasal and paranasal inverted papillomas - epidemiology and own experience. *Otolaryngol Pol* 2017;**7**:27–32
- 26 Peng R, Thamboo A, Choby G, Ma Y, Zhou B, Hwang PH. Outcomes of sinonasal inverted papilloma resection by surgical approach: an updated systematic review and meta-analysis. *Int Forum Allergy Rhinol* 2019;**9**:573–81
- 27 Minni A, Gera R, Bulgheroni C, Ralli M, Cialente F, Candelori F *et al.* Endoscopic resection of sinonasal inverted papilloma: a multivariate retrospective analysis of factors affecting recurrence and persistence. *Ear Nose Throat J* 2021;**100**:542–8S
- 28 Kamel RH. Conservative endoscopic surgery in inverted papilloma. Preliminary report. *Arch Otolaryngol Head Neck Surg* 1992;**118**:649–53
- 29 Waitz G, Wigand ME. Results of endoscopic sinus surgery for the treatment of inverted papillomas. *Laryngoscope* 1992;**102**:917–22
- 30 Jiang XD, Dong QZ, Li SL, Huang TQ, Zhang NK. Endoscopic surgery of a sinonasal inverted papilloma: surgical strategy, follow-up, and recurrence rate. *Am J Rhinol Allergy* 2017;**31**:51–5