

# Management of sinonasal inverted papillomas and comparison of classification staging systems

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## ABSTRACT

**Background:** The aim of this study was to describe treatment results in patients with sinonasal inverted papilloma and to compare recent classification staging systems.

**Methods:** We performed a retrospective study of 79 patients with primary paranasal sinus inverted papilloma from 1978 to 2008.

**Results:** The median age at diagnosis was 59 years. There were 68 men (86%) and 11 women (14%). Sixty inverted papilloma (76%) were located in the ethmoidal sinus complex, 16 (20%) were in the maxillary sinus, 2 were in the sphenoid sinus (3%), and 1 was in the septum (1%). Malignancy was simultaneously associated in four cases (5%). Intracranial extension was found in five patients (6%) and we did not find orbital content involvement. The external approach was used in 22 cases (28%) and 57 patients were treated with endoscopic nasal resection (72%). The overall recurrence rate in the total population was 21%. Recurrences were observed in 7 cases (32%) in the group of patients who received external approach and in 10 (17%) patients in the endoscopic group. Recurrences according to the Krouse system were 0% in T1 stage, 16% in T2 stage, 25% in T3 stage, and 60% in T4 stage ( $p = 0.05$ ). Recurrences for groups A, B, and C stages using the Cannady staging system were 12, 26, and 60%, respectively ( $p = 0.039$ ). Recurrences according to Han's system were 19% in both T1 and T2, 20% in T3, and 60% in T4 ( $p > 0.05$ ).

**Conclusion:** Our results support the endoscopic approach as the treatment of choice when feasible in patients with inverted papilloma, combined in selected cases with external approaches. The Krouse and Cannady systems provided a good distribution of patients according to local control.

(Am J Rhinol Allergy 24, 66–69, 2010; doi: 10.2500/ajra.2010.24.3421)

**Key words:** Cannady, endoscopic approach, Han, inverted, Krouse, papilloma, paranasal sinus, staging

Three histopathological types of papillomas of the nasal cavity have been described by the World Health Organization Classification<sup>1</sup>; inverted papilloma is the most frequent variant, representing almost 70% of all sinonasal papillomas and between 0.5 and 7% of all nasal tumors. It has an incidence of ~0.52–1.5 per 100,000 cases a year.<sup>2–4</sup>

This benign tumor of epithelial origin does not therefore have the capacity to invade the underlying bone on its own. However, the surface border between the inverted papilloma and bone is usually pathological and irregular with crevices and variable inflammatory changes. This may lead to mucosal tissue embedded within bony crevices, and such crevices in the deep plane could be potential areas for tumor recurrences.<sup>5</sup>

The etiology of inverted papilloma is unknown. A relationship with the human papillomavirus has been suggested in 33–42% of cases, mainly subtypes 6, 11, 16, and 18.<sup>6,7</sup> An association between inverted papilloma and malignancy is controversial. A synchronous carcinoma has been established at diagnosis in 7–8% of cases and the risk of metachronous carcinoma has shown to be <3%.<sup>4,6–8</sup> Several classifications have been proposed<sup>9</sup> since 1966 when Skolnick developed a classification staging system for inverted papilloma based on the TNM system. Of these, Krouse's classification system<sup>10</sup> is probably the most widely used.

The aim of this study was to analyze the main characteristics of these tumors, review the results of treatment of patients treated in our hospital, and compare three of the major staging systems proposed to date: those of Krouse,<sup>10</sup> Han *et al.*,<sup>11</sup> and Cannady *et al.*<sup>12</sup> Table 1.

## MATERIALS AND METHODS

The data used in this study were obtained retrospectively from a database that prospectively collects information concerning all patients with neoplasms of the head and neck. From 1978 to 2008, 86 patients with inverted papilloma of the paranasal sinus were treated in our center. The extension of papilloma was evaluated preoperatively by nasal endoscopy and CT in all cases to assess tumor extension. CT staging has been the traditional "gold standard" by staging inverted papillomas. However, CT changes represent inflammatory as well as neoplastic changes.<sup>13</sup> Since 1990 MR has been systematically used in addition to CT to help differentiate these changes.

## Treatment

From 1970 to 1989 most patients underwent a radical resection by means of the external approach. As of 1990 sinonasal papillomas in our center have mainly been treated using the endoscopic surgical approach. This procedure includes complete ethmoidectomy with endonasal medial maxillectomy and may be associated with fronto-sphenoidectomy depending on the origin of the tumor.

When the papilloma involved the anteromedial wall of the maxillary sinus (alveolar recess), we performed either a Caldwell-Luc procedure associated with the endoscopic approach or an endoscopic medial maxillectomy with the novelty of conserving the inferior turbinate. This conservative approach consists of cutting and medially displacing the two anterior thirds of the inferior turbinate. The turbinate is pediculated at the inferior turbinate artery and part of the frontal process of the maxilla is removing it until the anteromedial wall is reached. We then replaced the turbinate on the lateral nasal wall to maintain nasal resistance.

When the lesion involved the lateral and superior walls of the frontal sinus we combined the endoscopic approach with an external approach (osteoplastic frontal flap or subciliary incision). When the tumor affected the anterior skull base we completed the endonasal approach with a craniofacial resection. In all cases the resections were performed through a subperiosteal plane. When this was not an option because of the bone irregularities or because of incrustations of

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**Table 1 Classification staging system for inverted papilloma**

Krouse system	
T1	Confined to the nasal cavity
T2	Ostiomeatal complex region, ethmoid, or medial maxillary involvement (with and without nasal cavity involvement)
T3	Any wall of maxillary sinus but medial, frontal sinus, or sphenoid with or without T2 criteria
T4	Any extrasinus involvement or malignancy
Han system	
Group I	Limited to nasal cavity, lateral nasal wall, medial maxillary sinus, ethmoid sinus, and sphenoid sinus
Group II	Extension lateral to medial maxillary wall with or without group I criteria
Group III	Extension into frontal sinus
Group IV	Extension outside sinuses
Cannady system	
Group A	Inverted papilloma confined to the nasal cavity, ethmoid sinuses, or medial maxillary wall
Group B	Inverted papilloma with involvement of any maxillary wall (other than the medial wall), or frontal sinus, or sphenoid sinus
Group C	Inverted papilloma with extension beyond the paranasal sinuses

the underlying mucosa, diamond burrs were used to remove a portion of bone.

### Statistical Analysis and Follow-Up

Local control and survival analyses were calculated using the Kaplan-Meier method and curves were compared using the Mantel-Haenszel test (log rank). End points were calculated from the date of diagnosis until recurrence. Chi-square or Fisher's exact test was used to analyze local recurrences. The minimum follow-up was 1 year.

## RESULTS

### Patients and Tumor Characteristics

Seventy-nine patients had primary lesions and seven patients had been previously treated. These 79 primary inverted papillomas made up the study group. Median age at diagnosis was 59 years with a range between 16 and 84 years. There were 68 men (86%) and 11 women (14%). Fifty-eight percent of patients (46/79) were nonsmokers and nondrinkers. Nasal obstruction was the most frequent symptom, occurring in 87% of patients and epistaxis, rhinorrhea, and facial pain were observed in 5, 4, and 1% of patients, respectively. Two patients (3%) were asymptomatic.

**Localization.** Sixty inverted papillomas (76%) were located in the ethmoidal sinus complex, 16 (20%) were in the maxillary sinus, 2 were in the sphenoid sinus (3%), and 1 was in the septum (1%), a very rare location.

There was no evidence of primary frontal inverted papillomas, although the frontal sinus was involved in 10.1% of patients (8/79) in the expansive tumor growth. The sphenoid sinus was involved in eight patients (10%); two papillomas originated in this sinus and six cases presented with involvement secondary to tumor extension. One patient had a bilateral inverted papilloma.

Intracranial extension was found in five patients (6%), four of whom were the patients with associated carcinoma. Malignancy was associated with inverted papilloma in four cases (5%). We did not find orbital content involvement in any case.

**Treatment.** An external approach was used in 28% of cases (20 lateral rhinotomy, 1 Caldwell-Luc, and 1 craniofacial resection). Four patients with cranial invasion and associated malignancy were treated with lateral rhinotomy and complementary radiotherapy. These tumors were diagnosed in older patients and surgery was performed in 1980s. There were five patients with intracranial invasion. Four of them had associated malignancy and one without it. This patient was treated with craniofacial resection. Fifty-seven patients were treated with endoscopic nasal resection (72%), complemented with a Caldwell-Luc procedure in nine cases.

We performed a medial maxillectomy conserving the inferior turbinate in five patients who underwent the endoscopic procedure. Frontal recess/sinuses occupied by papilloma were treated by endoscopic approach (two Draf IIa and one Draf IIb) in three cases and the external approach in three cases. Postoperative epistaxis was observed in three cases and epiphora was observed in one case.

**Classification Staging System.** According to Krouse's staging system the patients were classified as T1 in 8 cases (10%), T2 in 31 cases (39%), T3 in 35 cases (44%), and T4 in 5 cases (7%). Table 2 shows the total distribution and distribution over the decades. According to Han *et al.*'s system, patients were classified as T1 in 43 cases (54%), T2 in 26 cases (34%), T3 in 5 cases (6%), and T4 (6%) in 5 cases. Using Cannady *et al.*'s system 39 patients (49%) were distributed as A stage, 35 patients (44%) were classified as B stage, and 5 patients (7%) were C stage.

**Recurrences.** The overall recurrence rate in the sample was 21% (17/79). When patients with malignancy were excluded the rate was 18% (14/75). Recurrences were observed in 7 patients (32%) who underwent the external approach and in 10 patients (17%) who received endoscopic treatment. Recurrences according to Krouse's system were 0% in T1 stage, 16% (5/31) in T2 stage, 25% (9/35) in T3 stage, and 60% (3/5) in T4 stage ( $p = 0.05$ ). Distribution of recurrences in 1970s/1980s, 1990s, and 2000s were 45% (9/20), 16% (4/24), and 11% (4/35), respectively.

Recurrences according to Cannady were 12% for group A, 26% for group B, and 60% for group C stages ( $p = 0.039$ ). With Han's system, recurrences were 19% in both T1 and T2, 20% in T3, and 60% in T4 ( $p > 0.05$ ). Local recurrence free survival according to stages in the three classification system is shown in Fig. 1. Six of our 17 recurrences presented a second recurrence (35%).

## DISCUSSION

Inverted papilloma is a prevalent pathology in our center and is steadily increasing. In the past 10 years, we have treated 35 sinonasal inverted papilloma, accounting for 45% of cases treated in the last 30 years.

This tumor is a locally benign nasal lesion with a tendency to recur after incomplete removal. For several decades, traditional management was the external approach, lateral rhinotomy, or sublabial degloving. Endonasal endoscopic surgery results are successful and comparable with external techniques but have the added advantage of no facial incision and a decrease in morbidity, crusting, postoperative pain, bleeding, and health care costs. In our institution, today, sinonasal inverted papilloma are mainly treated with endoscopic surgical resection. We associate the endoscopic approach with a sub-

**Table 2 Distribution of patients using Krouse's staging system according to decade distribution**

Krouse System	1980s	1990s	2000s	Total
I	0	2	6	8
II	3	12	16	31
III	14	8	13	35
IV	3	2	0	5
Total	20	24	35	79

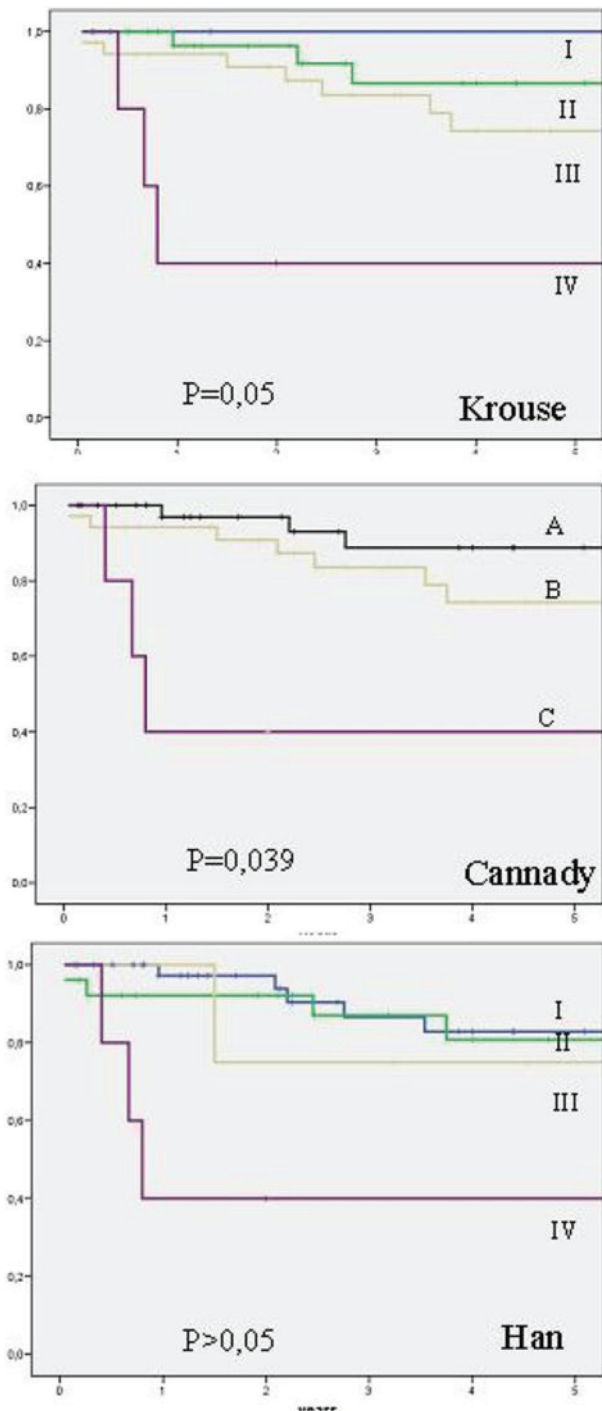


Figure 1. Local recurrence-free survival according to stages in the three classification systems.

labial procedure when the papilloma involves the anteromedial wall of the maxillary sinus or alveolar recess. Because it is difficult to reach this localization exclusively by endoscope because of the acute angle, we complement this approach with the Caldwell-Luc procedure. In the last few years, to avoid this sublabial incision, we perform a medial maxillectomy conserving the inferior turbinate. The technique has been used successfully without recurrence and has the advantage that the inferior turbinate function is preserved.

Extensive inverted papilloma with attachment to the frontal sinus

drainage pathway is infrequent, representing <15% of inverted papillomas, and its management is controversial.<sup>14,15</sup> In our department, when the lesion involves the lateral and superior walls of the frontal sinus, we combine the endoscopic approach with an external approach (osteoplastic frontal flap or through a subciliary incision).

In recent studies, local recurrence ranges from 0 to 24%.<sup>16-25</sup> In the present study our overall recurrence rate was 21% (17/79) and it was higher in the group of patients who received the external approach (32%) than in the endoscopic group (17%). It is surprising that the recurrence rate in the external group is twice as high as in the endoscopic group. However, several factors likely play a role here. In 1970s and 1980s recurrences were higher (45%) than in later decades (16 and 11%), and at that time most patients were treated with the external approach. Furthermore, there is no doubt we now have better knowledge concerning radical treatment of disease and, in addition, with the notable improvements in diagnostics procedures, these inverted papillomas are diagnosed in earlier stages than some years ago. Obviously, the higher the T category the greater the number of recurrences. According to Krouse's classification system most tumors in our series treated in the 1970s and 1980s were in advanced stages III-IV (87%), whereas no papilloma was diagnosed in the initial stage (stage I). As of the 1990s, the T distribution was more balanced and in 2000, 49% of patients were diagnosed in earlier stages and we did not treat any extrasinonasal inverted papilloma (T4). This improvement in T distribution would explain the better results in later decades and consistently in the endoscopic group.

Intracranial presentation is unusual. It is mostly associated with recurrent disease, and the site of extension in most such cases is the cribriform plate-ethmoid roof area.<sup>26</sup> We found five patients with intracranial extension and four had synchronous carcinoma. The orbit may be displaced laterally but it is infrequent that orbital contents are involved.<sup>27</sup> We agree with these findings because we did not find orbital content involvement in any patient.

Efforts to group patients with inverted papilloma began in the 1960s when several classification systems similar to the universal TNM system appeared. The purpose of these classifications was to build systems that were simple and easy to manage.

In 2000, Krouse<sup>10</sup> elaborated on a classification system using extension of the tumor beyond the medial maxillary wall and involvement of the frontal or sphenoid sinuses as important prognostic factors. He included extrasinonasal extension and malignancy in the last stage (T4). In 2001, Han *et al.*<sup>11</sup> and cols. developed a new staging system based on modifications of Krouse's classification. They joined Krouse's stages I and II and also included sphenoid sinus disease in this first stage (T1). Extension lateral to the medial maxillary wall was included in stage II. Frontal sinus disease was considered stage III, and stage IV was the same as the Krouse's system, but excluded malignancy. In 2007, Cannady *et al.*<sup>12</sup> elaborated on a more simple classification, grouping stages I and II together as stage A; the other stages remained unchanged.

We compared these three major systems in our population based on recurrences. Krouse's system<sup>10</sup> showed a progressive increase in recurrences in accordance with stages. Recurrences were 0% in T1 stage, 16% in T2 stage, 25% in T3 stage, and 60% in T4 stage. The Cannady system<sup>12</sup> showed also a good heterogeneity of recurrence in the three stages: 12% in stage A, 26% in stage B, and 60% in stage C. However, we did not find the minimum differences between Krouse's stages I and II (0% versus 16%) that Cannady proposed in his report. This could perhaps be caused by the small number of patients with respect to Cannady's meta-analysis and to our "historical group," which consists of patients classified as stage II and treated in 1970-1980. When we analyzed recurrences according to Han's system<sup>11</sup> we did not observe differences between stages; recurrences were ~20% in the first three stages and local recurrence-free survival curves overlapped. This similarity between the first three stages was probably because sphenoid sinus involvement was included in the best prog-

nosis group and because the few patients with frontal sinus invasion were included in a single stage.

In summary, in our population, Krouse and Cannady's systems showed a good distribution of patients according to recurrence, whereas Han's system was less accurate. The main drawback with Krouse's system was the inclusion of carcinoma patients in stage IV.

## CONCLUSIONS

Our experience confirms that the endoscopic approach is the treatment of choice in patients with inverted sinonasal papilloma, combined with external approaches in selected cases. It showed better results than external techniques and morbidity was lower. Distribution of patients according to recurrence was better with Krouse and Cannady's systems than with Han's system.

## REFERENCES

1. Barnes L, Eveson JW, Reichart P, and Sidransky D. WHO Classification of Tumours, Pathology and Genetics Head and Neck Tumours. IARC Press: Lyon, France, 2005.
2. Buchwald C, Franzmann MB, and Tos M. Sinonasal papillomas: A report of 82 cases in Copenhagen County, including a longitudinal epidemiological and clinical study. *Laryngoscope* 105:72–79, 1995.
3. Outzen KE, Grøntved A, Jørgensen K, et al. Inverted papilloma: Incidence and late results of surgical treatment. *Rhinology* 34:114–118, 1996.
4. Sauter A, Matharu R, Hörmann K, and Naim R. Current advances in the basic research and clinical management of sinonasal inverted papilloma (review). *Oncol Rep* 17:495–504, 2007.
5. Chiu AG, Jackman AH, Antunes MB, et al. Radiographic and histologic analysis of the bone underlying inverted papillomas. *Laryngoscope* 116:1617–1620, 2006.
6. Syrjänen KJ. HPV infections in benign and malignant sinonasal lesions. *J Clin Pathol* 56:174–181, 2003.
7. Katori H, Nozawa A, and Tsukuda M. Markers of malignant transformation of sinonasal inverted papilloma. *Eur J Surg Oncol* 31:905–911, 2005.
8. Mirza S, Bradley PJ, Acharya A, et al. Sinonasal inverted papillomas: Recurrence, and synchronous and metachronous malignancy. *J Laryngol Otol* 121:857–864, 2007.
9. Skolnik EM, Loewy A, and Friedman JE. Inverted papilloma of the nasal cavity. *Arch Otolaryngol* 84:61–67, 1966.
10. Krouse JH. Development of a staging system for inverted papilloma. *Laryngoscope* 110:965–968, 2000.
11. Han JK, Smith TL, Loehrl T, et al. An evolution in the management of sinonasal inverting papilloma. *Laryngoscope* 111:1395–1400, 2001.
12. Cannady SB, Batra PS, Sautter NB, et al. New staging system for sinonasal inverted papilloma in the endoscopic era. *Laryngoscope* 117:1283–1287, 2007.
13. Sham CL, King AD, van Hasselt A, and Tong MC. The roles and limitations of computed tomography in the preoperative assessment of sinonasal inverted papillomas. *Am J Rhinol* 22:144–150, 2008.
14. Shohet JA, and Duncavage JA. Management of the frontal sinus with inverted papilloma. *Otolaryngol Head Neck Surg* 114:649–652, 1996.
15. Zhang L, Han D, Wang C, et al. Endoscopic management of the inverted papilloma with attachment to the frontal sinus drainage pathway. *Acta Otolaryngol* 128:561–568, 2008.
16. Lawson W, Kaufman MR, and Biller HF. Treatment outcomes in the management of inverted papilloma: An analysis of 160 cases. *Laryngoscope* 113:1548–1556, 2003.
17. Lane AP, and Bolger WE. Endoscopic management of inverted papilloma. *Curr Opin Otolaryngol Head Neck Surg* 14:14–18, 2006.
18. Pasquini E, Sciarretta V, Farneti G, et al. Inverted papilloma: Report of 89 cases. *Am J Otolaryngol* 25:178–185, 2004.
19. Banhiran W, and Casiano RR. Endoscopic sinus surgery for benign and malignant nasal and sinus neoplasm. *Curr Opin Otolaryngol Head Neck Surg* 13:50–54, 2005.
20. Llorente JL, Deleyiannis F, Rodrigo JP, et al. Minimally invasive treatment of the nasal inverted papilloma. *Am J Rhinol* 17:335–341, 2003.
21. Kraft M, Simmen D, Kaufmann T, and Holzmann D. Long-term results of endonasal sinus surgery in sinonasal papillomas. *Laryngoscope* 113:1541–1547, 2003.
22. Tomenzoli D, Castelnuovo P, Pagella F, et al. Different endoscopic surgical strategies in the management of inverted papilloma of the sinonasal tract: Experience with 47 patients. *Laryngoscope* 114:193–200, 2004.
23. Von Buchwald C, and Larsen AS. Endoscopic surgery of inverted papillomas under image guidance—A prospective study of 42 consecutive cases at a Danish university clinic. *Otolaryngol Head Neck Surg* 132:602–607, 2005.
24. Busquets JM, and Hwang PH. Endoscopic resection of sinonasal inverted papilloma: A meta-analysis. *Otolaryngol Head Neck Surg* 134:476–482, 2006.
25. Woodworth BA, Bhargava GA, Palmer JN, et al. Clinical outcomes of endoscopic and endoscopic-assisted resection of inverted papillomas: A 15-year experience. *Am J Rhinol*. 21:591–600, 2007; Erratum, *Am J Rhinol* 22:97, 2008.
26. Vural E, Suen JY, and Hanna E. Intracranial extension of inverted papilloma: An unusual and potentially fatal complication. *Head Neck* 21:703–706, 1999.
27. Bajaj MS, and Pushker N. Inverted papilloma invading the orbit. *Orbit* 21:155–159, 2002. □