What Are the Surveillance Recommendations Following Resection of Sinonasal Inverted Papilloma?

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BACKGROUND

Inverted papilloma (IP) is a benign tumor of the nasal cavity and paranasal sinuses first described by Ward in 1854.1 IP is remarkable due to a high propensity for tumor recurrence with incomplete resection, potential for invasion of local structures, and an association with malignant transformation to squamous cell carcinoma.1,2 Surgery is the mainstay of treatment for sinonasal IP, and the initial controversy over the best approach for tumor removal has been replaced by the widespread use of endoscopic techniques when feasible.2 What remains unclear is the best practice for surveillance following surgery for a tumor that carries low but well-known potential for malignant transformation.

LITERATURE REVIEW

Sinonasal inverted papilloma generates significant interest because of the risk of malignant transformation from a benign tumor to a carcinoma. Postoperative surveillance for IP is unique because earlier detection of recurrences might also identify a metachronous carcinoma (carcinoma at a site that was previously a benign IP). The most common malignancy associated with IP is squamous cell carcinoma, but others such as mucoepidermoid carcinoma and adenocarcinoma have been described.1 The reported incidence of malignancy in IP varies greatly in the literature, and has been reported to be as high as 27%, but most commonly is thought to be between 5% and 10%.2,3 In a meta-analysis of 63 case series representing over 2,000 patients with IP, Mirza et al.3 reported that the rate of synchronous carcinoma (cancer found at the initial tumor resection) with IP was 7.1% and that of metachronous carcinoma was 3.6%.

Surgery is the recommended treatment for sinonasal inverted papilloma.2 A number of approaches are utilized, including open approaches, endoscopic approaches, or endoscopic-assisted approaches. The indications and limitations of each approach can be found in more detail elsewhere in the literature,1–5 but in general, a variety of factors such as tumor size, location, and surgeon comfort will ultimately determine which approach is best for a given patient. Incomplete resection of IP almost invariably leads to tumor recurrence. A recent systematic review by Busquets and Hwang2 of endoscopically excised IPs noted a tumor recurrence rate of just 12%, compared to 20% for open (nonendoscopic) surgery.

Rationale and Recommendations for Surveillance After Surgery

Currently, there are no consensus guidelines for tumor surveillance specific to IP or other benign sinonasal tumors. The primary benefit of earlier detection of recurrent tumor is that it allows for earlier and simpler re-resection. Regular endoscopic examinations and contrast-enhanced magnetic resonance imaging (MRI) are the best methods to evaluate for tumor recurrence. Prompt identification of recurrent IP compared to other benign sinus tumors is especially important due to the additional risk of malignant transformation. Early detection is important not only to identify recurrences that might harbor carcinoma, but also to reduce the time that recurrent IP has to develop into a carcinoma.

Due to a risk of malignant transformation in IP, it is reasonable to suggest that recommendations for surveillance can be based on guidelines for head and neck cancer surveillance. In the case of head and neck squamous cell carcinoma (HNSCC) and other malignancies, routine follow-up is essential to detect locoregional recurrences and to detect and manage complications, metastases, and second primary tumors at the earliest opportunity.4 A survey conducted among members of the American Society of Head and Neck Surgeons reported 73% agreement among respondents for offering monthly follow-up in the first year after surgery, 2- to 3-month follow-up in the second year, and 4- to 6-month follow-up in years 3 to 5 after surgery.4 It seems reasonable to base guidelines for surveillance of IP on those for
HNSCC; however, it can also be argued that such frequent and rigid surveillance schedules might be unnecessary for all IPs, as the risk of malignant transformation is generally low. Optimally, treating surgeons would know which patients are at the highest risk for recurrence and malignant transformation after surgery and follow those patients more closely.

The literature suggests that a majority of recurrences of IP occur within the first 2 years after definitive surgery.1–3 Regular surveillance in the first year, especially for higher-stage IPs, should detect >50% of recurrent tumors. However, long-term (>2 years after surgery) and potentially lifelong follow-up is required to detect late tumor recurrences and metachronous carcinomas. Up to 17% of IPs will recur after more than 5 years, including 6% after 10 years.2,3 Mirza et al.3 found that the mean time to develop a metachronous carcinoma was 52 months (range, 6–180 months), with an estimated frequency of 3.6%,3 supporting the need for long-term postoperative follow-up. McKay et al.5 found a higher rate of human papillomavirus (HPV) in dysplastic and malignant IPs, which suggests that patients with HPV-positive IPs might be candidates for more rigorous follow-up and surveillance because of the higher risk of malignant tumor transformation. Patients with persistent disease after surgery also have a higher risk of malignant transformation (11%) compared to those with complete resections.3 Therefore, patients with unresectable IP, or those not eligible for further surgery, should be regularly debulked or biopsied to monitor for malignant transformation.

Patients with higher-stage tumors also have an increased risk of recurrence. Two commonly referenced IP staging systems in use were published by Krouse6 in 2000 and Cannady7 in 2007 (see Supporting Information, Table 1, in the online version of this article). For both classifications, IPs involving the peripheral sinuses or those tumors with extension outside of the sinus cavities have increased rates of recurrence. Using both the Krouse and Cannady staging systems on over 445 patients with IPs, tumors in stage T4 (Krouse) or group C (Cannady) had recurrence rates of over 35%. Clearly, high-stage IPs (i.e., Krouse 3 or 4 or Cannady B or C) should be followed more closely postoperatively due to a higher incidence of tumor recurrence compared to low-stage tumors.

Based on the available literature, a suggested surveillance schedule for IPs is found in the Supporting Information, Figure 1, in the online version of this article. Tumors in the high-risk category (HPV+, high T stage, recurrent tumors) should be seen and evaluated more frequently than those tumors with no additional risk factors for malignant transformation. We advocate nasal endoscopy as the primary method of tumor surveillance postoperatively; however, if the original tumor site is not visible (such as in the lateral frontal sinus), then yearly or twice-yearly imaging studies might be required to evaluate for tumor, with MRI being the preferred modality. Lai et al.8 found that when comparing biopsy specimens to contrast-enhanced MRI for recurrent IPs, MRI exams yielded a sensitivity and specificity of up to 75% in the setting of granulation tissue and postoperative changes.

**BEST PRACTICE**

Regular surveillance for IP facilitates the early identification of small, asymptomatic recurrences and provides a tool for earlier management of these recurrences. Although the majority of IP cases will recur in the first year, more than 25% can recur many years after surgery, and thus long-term follow-up is indicated. We advocate regular follow-up endoscopic examinations, especially for tumors that are HPV positive, higher T stage, or for patients with unresectable or residual IP due a higher risk of recurrence and malignant transformation. Surveillance schedules can be based on those used for HNSCC. A majority of IPs will recur in the first 2 years, but late recurrences are not uncommon. Locations that are difficult to endoscopically visualize postoperatively (i.e., the lateral frontal sinus) may be followed with serial MRI exams.

**LEVEL OF EVIDENCE**

Recommendations for the frequency and benefit of surveillance after surgery for IP are based on published tumor recurrence rate data from systematic reviews (level III evidence) and case series (level IV evidence).

**BIBLIOGRAPHY**