What Is the Appropriate Timing for Endoscopic and Radiographic Surveillance Following Treatment for Sinonasal Malignancies?

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BACKGROUND

Sinosal malignancies are rare, representing only 3% of all head and neck neoplasms and approximately 1% of all malignancies. Given this low incidence and the diversity of pathologies, standardized protocols for post-treatment surveillance are lacking. Due to their advanced stage at presentation, sinonasal malignancies often have a poor prognosis, with recurrence rates ranging from 27% to 56%. Whereas the majority of recurrences occur within 2 to 3 years post-treatment, certain malignancies, such as adenoid cystic carcinoma, olfactory neuroblastoma, and melanoma, have a propensity to recur much later. The majority of recurrences occur locally and represent the leading cause of disease-specific mortality. Several factors, including complex anatomy, treatment-related changes, distortion due to resection and reconstruction, and sinonasal inflammation, complicate surveillance for recurrence. Due to these unique aspects, accepted surveillance guidelines for head and neck malignancies may not be directly applicable for sinonasal malignancies. Accordingly, distinct guidelines for post-treatment endoscopic and radiographic surveillance are needed.

LITERATURE REVIEW

The current available evidence is limited at best. Whereas surveillance protocols have been better defined in the management of head and neck squamous cell carcinoma, the limited incidence and varied pathologies in sinonasal carcinomas have hindered the development of standardized protocols for post-treatment surveillance. Despite differences in tumor biology, treatment modalities, and anatomical subsites, current clinical practice relies significantly on data published on general head and neck malignancies.

Khalili and colleagues retrospectively evaluated the efficacy of endoscopic and imaging surveillance in patients with sinonasal malignancies. In this study, endoscopic follow-up was completed every 1 to 3 months for the first 2 years, 3 to 6 months for the next 3 years, and annually beyond year 5, whereas imaging was obtained every 3 to 6 months for the first 2 years, and at 6 months to yearly intervals afterward. In their review of 100 patients, 30 patients recurred, with 22 patients (73%) recurring locally; regional and distant metastasis represented 17% and 10% of recurrences, respectively. The majority of patients (63%) recurred within 2 years. Seventy-seven percent of recurrences were diagnosed with imaging, whereas only 17% and 3% were identified via endoscopy or physical examination, respectively. Although the specificity of endoscopy and imaging was similar at 89% and 90%, respectively, imaging had a significantly higher sensitivity (75% vs. 25%), accuracy (86% vs. 73%), and negative predictive value (92% vs. 78%) with P values <.05. However, identification of recurrence by endoscopy was critical, as it resulted in better prognosis, likely due to the superficial nature of these recurrences, thus making them amenable to resection. The positive predictive value (PPV) was higher for imaging than nasal endoscopy, but the difference was not significant (72% vs. 43%, P = .07). Out of the imaging modalities, magnetic resonance imaging (MRI) had the highest PPV at 84%, significantly higher than computed tomography (CT) (44%) and positron emission tomography (PET)/CT (46%). However, PET/CT was critical in diagnosing distant recurrences in cases of mucosal melanoma. Furthermore, the presence of
suspicious symptoms significantly increased the PPV of endoscopy and imaging to 83% and 90%, respectively, compared to 13% and 55%, respectively, without suspicious symptoms.\(^1\)

In their retrospective series, Harvey et al. demonstrated that PET/CT can have excellent sensitivity and negative predict values (100%), but its functionality is hindered by poor specificity (40%) and PPV (53.8%) in the early postoperative period.\(^2\) This limitation exists due to the inability of PET/CT to distinguish between tumor recurrence and inflammatory change (i.e., from surgery and/or radiation therapy), reducing its utility in the early surveillance setting. Gil et al. also examined the role of PET/CT imaging for surveillance and reported specificity and PPV of 85% and 67%, respectively.\(^3\) For Harvey et al., PET/CT scans were obtained at a minimum of 3 months after treatment, but specific timelines were not provided. Gil et al. acquired the majority of their PET/CT scans (>80%) 6 months after treatment.\(^2,3\)

Unlike the previous studies, which evaluated the cross-sectional accuracy of PET/CT, Schwartz and colleagues performed a longitudinal analysis of PET/CT imaging in post-treatment surveillance.\(^4\) In this analysis, 76 patients were monitored with PET/CT imaging. The median time to recurrence was 20 months, with only four patients recurring before 5 months and 10 patients recurring by 24 months. Further subgroup analysis indicated that 17 of 18 local recurrences occurred in patients with advanced local disease or high-grade histopathology. In patients with no local recurrence of the sinonasal malignancies, standardized uptake value (SUV) data were subsequently grouped into various time points (2–4 months, 5–10 months, 5–12 months, 13–24 months), and compared using independent sample t tests. There was a statistically significant reduction in SUV between the 2- and 4-month and 5- and 12-month periods (\(P = .048\)) as well as between the 2- and 4-month and 5- and 24-month (\(P = .02\)) post-treatment period. The authors concluded that post-treatment inflammation in the sinonasal cavity exists beyond the 12-week period (commonly cited as the standard in the head and cancer literature), thereby increasing the number of false positives. They hypothesize that this inflammation persists due to communication of the nose and paranasal sinuses with the external environment, causing subsequent treatment-related disruption of mucociliary clearance.\(^4\)

The previously discussed studies highlight several key points. First, most recurrences occur locally within 24 months. Second, MRI has a superior PPV to PET/CT or CT. Finally, PET/CT imaging is vital in identifying distant metastasis, but can be limited due to post-treatment inflammation within the first 4 months following treatment.

**BEST PRACTICE**

Given the high recurrence rates in sinonasal malignancies, close, routine endoscopic and imaging surveillance is needed in the post-treatment setting. Endoscopy and imaging serve to complement each other.

Frequent endoscopic examinations can be completed at 1- to 3-month intervals, with MRI imaging at 3- to 6-month intervals for the first 24 months. Beyond this period, endoscopic examinations can be performed every 3 to 6 months until year 5 and then annually thereafter, whereas imaging can be performed every 6 months to yearly. PET/CT imaging can be deferred between 6 and 12 months post-treatment in most cases. However, PET/CT has a unique role in tumors such as melanoma, with propensity for distant metastasis or to better characterize equivocal findings on MRI beyond 4 months post-treatment. Ultimately, given the lack of level 1 evidence, endoscopic and imaging surveillance protocols should be left to clinical judgment given individual patient factors, tumor biology, and treatment modalities.

**LEVEL OF EVIDENCE**

At present, a limited number of studies evaluating the optimal post-treatment surveillance regimens for sinonasal malignancy exist. All of the present studies represent level 4 evidence. In the future, prospective, multi-institutional surveillance studies with long-term follow-up for individual tumor types are needed.

**BIBLIOGRAPHY**