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Evaluating the Potential Role of PET/CT in the Posttreatment Surveillance of Head and Neck Cancer

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The central rationale for active surveillance after curative treatment of head and neck squamous cell carcinoma (HNSCC) is the belief that earlier detection of recurrent or new primary cancers facilitates earlier initiation of therapy and can favorably impact clinical outcomes. The potential benefits of earlier detection have considerable appeal to many physicians and patients, outweighing the potential risks.

Active surveillance in some form is widely applied in oncology practice; however, a challenge facing the NCCN Head and Neck Cancers Panel is the relative lack of higher-quality evidence to inform specific surveillance recommendations. The panel currently recommends surveillance with (1) history and physical examinations, including mirror and fiberoptic examinations as clinically indicated; (2) posttreatment imaging of the primary site (and neck, if treated) within 6 months of treatment completion; (3) chest imaging as clinically indicated for patients with a smoking history, per the NCCN Clinical Practice Guidelines in Oncology for Lung Cancer Screening (to view the most current version of these guidelines, visit NCCN.org); and (4) a consideration of Epstein-Barr virus DNA testing in patients after treatment for nasopharynx cancer. PET/CT after treatment is only specifically mentioned in the context of a decision algorithm for assessing whether to perform a neck dissection or observe the neck after chemoradiation or radiation treatment.[1] Otherwise, the NCCN Guidelines for Head and Neck Cancers note no prescribed or routine role for surveillance imaging, including PET/CT, in the absence of suspicious signs or symptoms. At the 2014 guidelines panel meeting, available data were reviewed on the potential role of PET/CT in the posttreatment setting.

PET/CT scans are increasingly used for a variety of reasons in the diagnosis and management of advanced HNSCC. For example, in a review of 8 studies, experts were able to detect the unknown primary tumor using PET or PET/CT in 51 of 180 patients with an otherwise inconclusive workup.[2] Further, in patients receiving intensity-modulated radiation therapy, fused PET/CT images are used to refine gross target volumes and better tailor radiation treatment fields to reduce toxicity.[3] The potential utility of PET/CT in posttreatment management would seem a logical extension of its demonstrated value in these other settings.

As noted, the NCCN Guidelines for Head and Neck Cancers recommend considering a PET/CT scan during post-radiation or post-chemoradiation assessment as part of a risk-stratified approach to assess the need for elective neck dissection. In a meta-analysis of 51 studies involving 2335 patients, the weighted mean pooled sensitivity, specificity, positive predictive value, and negative predictive value (NPV) of PET/CT for the postradiation neck were 72.7% (95% CI, 66.6%–78.2%), 87.6% (95% CI, 85.7%–89.3%), 52.1% (95% CI, 46.6%–57.6%), and 94.5% (95% CI, 93.1%–95.7%), respectively.[4] Therefore, rather than all patients proceeding to adjuvant neck dissection, given the high NPV, observation can be considered for patients with non-FDG–avid neck lymph nodes measuring less than 1 cm. Sher et al[5] analyzed the value of incorporating PET/CT into this decision-making. The most cost-effective strategy for managing the post-chemoradiation neck is reserving neck dissection only for patients with residual disease on PET/CT.

The timing of posttreatment PET/CT imaging can impact its diagnostic accuracy. PET/CT scans are recommended no sooner than 12 weeks after treatment completion

to avoid high rates of equivocal and false-positive results.[6–8] The rate of equivocal studies declines with time since treatment.[9] In patients with initial posttreatment scans that are equivocal for residual disease, a repeat PET/CT scan may help identify patients who can safely undergo observation without neck dissection.[7]

Evidence supporting the utility of PET/CT in routine surveillance is less clear than to that available to inform its use in management. Although an initial posttreatment PET/CT serves to identify residual disease, studies have shown that a second PET/CT, usually after an interval greater than 6 months, could be useful in detecting late local recurrences.[10,11] For example, in a prospective study, Lowe et al[11] reported a 100% sensitivity of scheduled PET scans completed at 2 and 10 months after treatment in detecting all locoregional and metastatic disease. Ten of 16 recurrences were found on the first PET scan, and 90% of these were locoregional. Six of 16 recurrences were found on the second PET scan, and 50% were locoregional.[11] In a single-institution study using frequent routine PET/CT, Kostakoglu et al[12] reported earlier detection of recurrent disease by nearly 6 months compared with physical examination or high-resolution CT scans.

Ho et al[9] confirmed that surveillance with PET/CT (completed annually for 2 years in patients with a negative posttreatment scan at 3 months) leads to earlier detection of recurrent disease. However, this study reported no survival benefit at 3 years in an unselected cohort of patients with HNSCC diagnosed with PET/CT-detected versus clinically detected recurrent disease (including both local and distant failure).[9] Future studies are needed to better address whether additional PET/CT scans will lead to improved outcomes through the earlier detection of salvageable late local recurrences. In addition, further evidence is needed to better define how previous PET/CT results may predict the value of subsequent scans and to determine the optimal interval between assessments.

Debate is ongoing as to the role of routine PET/CT scans beyond the initial posttreatment assessment for the earlier detection of distant metastatic lesions. This debate is further intensified in the setting of human papillomavirus (HPV)–related oropharynx cancer, for which there are reports of atypical presentation of recurrent metastatic disease,[13,14] potentially longer survival after the development of recurrent disease,[15] and a possibly greater role for resection or local ablative therapy of distant disease. In a study of patients treated with chemoradiation for oropharynx cancer in prospective clinical trials, 86% of recurrences were detected within 3 years in patients with p16-positive tumors.[15] Whether additional imaging could facilitate earlier initiation of therapy and improve clinical outcomes in this cohort—with expected longer survival after recurrence—deserves further study. As experience and knowledge about the natural history of HPV-related oropharynx cancer expands, we will hopefully better understand which patients could benefit from early treatment of metastatic disease or whether additional imaging creates a leadtime bias associated with the detection of more indolent disease.

The diagnostic performance of PET/CT scans may provide valuable prognostic information and a means to possibly risk-stratify surveillance. Specifically, PET/CT has a very high NPV value in HNSCC for recurrent locoregional and metastatic disease. In a pooled analysis of more than 2300 patients, Gupta et al[4] reported a weighted mean NPV of a single posttreatment PET/CT scan for the primary site of 95.1% (95% CI, 93.5%–96.5%). Other studies have reported the NPV of a negative PET/CT scan closer to 100% when more than one scan is completed over time or completed later in follow-up.[10,12,16,17] Combining PET/CT results with clinical characteristics, such as HPV-status, may have a role in future guidelines to inform a more risk-stratified approach to posttreatment follow-up.

To date, once a patient is free of disease, no clear evidence is available to support

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routine use of PET/CT in the surveillance of asymptomatic survivors of HNSCC. The high sensitivity of PET/CT may lead to false-positive results that prompt and warrant subsequent follow-up, including biopsies, procedures, and imaging. Yet, when used at distinct decision points, PET/CT has proven effective at providing valuable diagnostic and prognostic information that affects management. In light of changing epidemiology, emerging therapeutic options, and incorporation of value considerations into clinical practice, a further look at the potential role of PET/CT as part of a strategy to better risk-stratify and individualize survivorship care will undoubtedly be part of future deliberations of the NCCN Head and Neck Cancers Panel.

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