Retrospective Review of Positron Emission Tomography With Contrast-Enhanced Computed Tomography in the Posttreatment Setting in Human Papillomavirus–Associated Oropharyngeal Carcinoma

Jason Y. K. Chan, MBBS; Giuseppe Sanguineti, MD; Jeremy D. Richmon, MD; Shanthi Marur, MD; Christine G. Gourin, MD, MPH; Wayne Koch, MD; Christine H. Chung, MD; Harry Quon, MD; Justin A. Bishop, MD; Nafi Aygun, MD; Nishant Agrawal, MD

Objective: To determine the value of positron emission tomography (PET) with contrast-enhanced computed tomography (CT) in assessing the need for neck dissection by retrospectively reviewing the pathology reports of patients with human papillomavirus (HPV)-associated oropharyngeal squamous cell carcinoma (SCC).

Design: Retrospective cohort study.

Setting: Tertiary medical center.

Patients: Seventy-seven patients with HPV-related SCC.

Main Outcome Measures: Seventy-seven consecutive patients with a diagnosis of HPV-related SCC who were treated with radiotherapy as the primary treatment between August 2007 and October 2010 were retrospectively evaluated for radiologic and pathologic rate of persistence of nodal metastasis after completion of definitive radiotherapy. Pretreatment and posttreatment imaging included contrast-enhanced CT and PET. Response to treatment was measured on CT, PET at standardized uptake value (SUV) thresholds of 2 and 2.5, and PET/CT by a neuroradiologist in a blinded fashion. Then, the pathology report of the patients who underwent neck dissections was reviewed for nodal status after resection and correlated with the imaging findings.

Results: Of the 77 patients, 67 met the study criteria, with an average follow-up PET/CT scan at 90.5 days after completion of radiotherapy. Ten patients did not undergo follow-up PET/CT imaging. Twenty patients underwent neck dissections after completion of radiation therapy. Of these 20 patients, 4 had persistent tumor and 16 did not have viable tumor. Using the final pathology report to correlate with imaging responses, CT had a negative predictive value (NPV) of 85.7% (95% CI, 48.7%-97.4%), PET with SUV thresholds of 2 had an NPV of 91.7% (95% CI, 64.6%-98.3%), PET with a cutoff SUV of 2.5 had an NPV of 85.7% (95% CI, 60.1%-96.0%), PET/CT with an SUV of 2 had an NPV of 100% (95% CI, 59.8%-100.0%), and PET/CT with an SUV of 2.5 had an NPV of 85.7% (95% CI, 48.7%-97.4%). The 47 patients who did not undergo neck dissection had a median follow-up of 26 months without an isolated neck failure. Analysis of all 67 patients in the cohort revealed the following values: CT had an NPV of 95.7% (95% CI, 85.8%-98.8%), PET with an SUV of 2 had an NPV of 98.2% (95% CI, 90.4%-99.7%), PET with an SUV of 2.5 had an NPV of 95.0% (95% CI, 86.3%-98.3%), PET/CT with an SUV of 2 had an NPV of 100.0% (95% CI, 92.0%-100.0%), and PET/CT with an SUV of 2.5 had an NPV of 95.7% (95% CI, 85.8%-98.8%).

Conclusions: Positron emission tomography combined with contrast-enhanced CT has a better NPV than either imaging modality alone in patients with HPV-associated oropharyngeal SCC. Furthermore, PET/CT with an SUV threshold of 2 used in patients with HPV-related SCC offers an imaging modality with a high NPV that may obviate the need for unnecessary neck dissections.

CME available online at www.jamaarchivescme.com and questions on page 999

A SUBSTANTIAL NUMBER OF patients with head and neck squamous cell carcinoma (SCC) present with metastatic regional disease. In fact, head and neck SCC arising from the oropharynx has clinically positive nodes in more than 50% of patients, and 30% to 40% of patients with clinically negative necks harbor occult disease in the neck.1 Human papillomavirus (HPV) has emerged as a risk factor for cancers of the oropharynx, with up to 50% of tonsil cancers testing positive for HPV.2-4

Patients with HPV-associated cancers have an improved overall and disease-specific survival.3 Treatment of oropharyngeal SCC...
(OPSCC) with curative intent includes either surgery with or without adjuvant (chemo)radiation therapy or radiation therapy with or without chemotherapy.\(^6,7\)

Management of the neck after radiation therapy with or without chemotherapy presents a treatment dilemma. In the past, a planned neck dissection was advocated for patients with N2 or greater disease.\(^8\) However, more recently, the indications for a salvage neck dissection have evolved, particularly for HPV-related disease. Currently, imaging with fludeoxyglucose F 18–positron emission tomography (FDG-PET) combined with computed tomography (CT) and physical examination is often used for initial staging and posttreatment monitoring for disease persistence or recurrence. If there are findings of persistent or recurrent disease on physical examination, anatomical imaging, and/or metabolic imaging 12 weeks after completion of radiation therapy, then a neck dissection is indicated. Given the published high negative predictive value (NPV) of PET/CT, negative findings of persistent or recurrent disease on physical examination, anatomical imaging, and/or metabolic imaging suggest deferment of a neck dissection.\(^9\) In other words, if there is complete radiologic and clinical response, neck dissection may be unnecessary in HPV-related disease given the favorable treatment responses of OPSCC associated with HPV. Herein, we report a retrospective review of the pathology reports of patients with OPSCC associated with HPV who underwent radiation therapy with pretreatment and posttreatment PET and contrast-enhanced CT to evaluate their function in response assessment and avoidance of neck dissections in this subgroup of patients.

**METHODS**

**PATIENT ELIGIBILITY**

Seventy-seven consecutive patients who received a diagnosis of HPV-related SCC of the oropharynx and received radiotherapy as the primary treatment between August 2007 and October 2010 were retrospectively evaluated for radiologic and pathologic persistence of nodal disease. The HPV status was determined by p16 immunohistochemical analysis (MTM Laboratories) and HPV DNA in situ hybridization (Ventana Inform HPV III Family 16 Probe [B] Kit; Ventana Medical Systems) that uses a probe set that captures HPV genotypes 16, 18, 33, 35, 45, 51, 52, 56, and 66. Cases that were immunoreactive with p16 (strong nuclear and cytoplasmic staining in at least 70% of the tumor) and showed dotlike HPV hybridization signals in tumor nuclei were regarded as HPV related. Seven cases with positive results on p16 immunohistochemical analysis but negative results on HPV DNA in situ hybridization were also considered HPV related.

**RADIOThERAPY AND SYSTEMIC TREATMENT**

Radiotherapy was either intensity-modulated radiation therapy or image-guided radiation therapy delivered to 70 Gy with once-daily fractionations of 2 Gy. Systemic therapy consisted of concurrent chemotherapy with cisplatin (50 patients), carboplatin (3 patients), or cetuximab (1 patient). Ten patients who were clinically determined to have high-risk disease received neoadjuvant chemotherapy consisting of fluorouracil, cisplatin or carboplatin, and docetaxel.

**ASSESSMENT OF RESPONSE**

Assessment of response was based on PET/CT imaging protocol by a blinded neuroradiologist, as discussed in the next section. No evidence of disease at least 6 months after the completion of PET/CT was considered confirmation of complete clinical response. Planned neck dissections (after complete response in the absence of clinical disease) were not performed.

**DIAGNOSTIC PET/CT IMAGING PROTOCOL**

Pretreatment and posttreatment imaging evaluation included PET/CT. Posttreatment PET/CT studies were performed with a commercially available PET/CT scanner (Discovery LS; GE Medical Systems) according to the following protocol. Patients fasted at least 4 hours before the PET acquisition and received an intravenous injection of FDG (8.14 MBq/kg [0.22 mCi/kg]). A tracer uptake phase of about 60 minutes was allowed, during which the patients sat in a quiet injection room without talking; 68Ge transmissions scans were used to generate a transmission map. The CT portion consisted of a multidetector helical CT scanner (LightSpeed Plus; GE Medical Systems). The parameters for CT acquisition were as follows: 140 kV, 80 mA, 0.8 seconds per CT rotation, and a pitch of 2. The CT images were reconstructed at 2.5-mm intervals. All CT examinations were performed after intravenous administration of iodinated contrast material unless it was contraindicated by prior allergic reaction or renal insufficiency. A board-certified neuroradiologist with expertise in head and neck imaging who was not aware of the clinical outcome identified target lesions on each side of the neck on pretreatment imaging and followed them up on posttreatment PET/CT scans. A target lesion was defined as a lymph node measuring 10 mm or larger in the short-axis diameter on transverse CT images with or without corresponding increased FDG uptake on the PET study. The maximum standardized uptake values (SUVs) normalized for lean body mass of all target lesions were recorded. When a lymph node smaller than 10 mm was suspected to be metastatic on pretreatment evaluation on the basis of CT attenuation, contrast enhancement, or FDG uptake characteristics, it was noted and followed up as a nontarget lesion. Response to treatment was defined as a target lesion measuring less than 7 mm or demonstrating more than a 70% decrease in short-axis diameter on posttreatment CT scans. We evaluated the response on PET scans at 2 different SUV (maximum [max]) thresholds: 2 and 2.5. Any SUV (max) measuring below these values was considered to represent a response regardless of the size of the node on CT scans. When a sizable lymph node metastasis on pretreatment CT scans demonstrated marked decrease in size on posttreatment CT scans with no measurable masslike lesion but persistent obscuration of fascial planes, it was considered a response as long as the SUV (max) was below the thresholds. All patients who developed new lesions and patients who had persistent nontarget lesions were considered to have no response.

**PATHOLOGIC RESPONSE ASSESSMENT**

The surgical records of all patients were also reviewed, and the patients who underwent a salvage neck dissection were identified. Without an international grading system for pathologic criteria in assessing the response of nodes after radiation therapy, pathology reports for these patients were reviewed and determined as node positive and node negative as reported by pathologists.
PET/CT scans and clinical examination. Complete response at the primary site on posttreatment imaging was 90.5 days (median, 88 days). All patients had the end of radiotherapy and follow-up PET/CT scanning was 38.5 days (median, 26 days). The average time between pretreatment imaging and the start of radiotherapy was 10.5 days. Of the 67 patients, 3 had distant metastases, 1 had a primary neck recurrence 19 months after treatment completion, and 1 had distant metastases with a neck recurrence (median, 15.6 months). A neck dissection was performed on 1 patient at 52.6 months because of a persistent necrotic node on PET/CT scans 6 and 9 months after chemoradiation therapy, and the pathology report was negative for residual disease. Of the 20 patients who underwent a neck dissection, 4 were positive for SCC and 16 were negative. Two of the patients with positive results were nonresponders based on all CT and PET cutoffs, with 1 patient a nonresponder on a PET SUV threshold of 2, and the other patient a nonresponder on CT and PET/CT cutoffs of SUV 2 and 2.5. Of the 16 patients with negative nodes, 6 had a response on all imaging categories, 4 had no response on all imaging categories, and 6 had no responses on CT but responses on PET SUV thresholds of 2 and 2.5. Of the 6 who had response on all imaging, 3 underwent neck dissections because of patient preference after discussion of planned neck dissections and because of persistent disease based on clinical examination and patient preference. Table 2 shows the sensitivity, specificity, PPV, and NPV in the group of patients who underwent neck dissections.

Forty-seven of 67 patients did not undergo neck dissections, with a mean and median follow up of 25.6 months and 26 months, respectively (range, 12-51 months). Of the 47 patients, 3 had distant metastases, 1 had a primary neck recurrence 19 months after treatment completion, and 1 had distant metastases with a neck recurrence (Table 3). No isolated neck failures were identified. Table 4 shows the sensitivity, specificity, PPV, and NPV of all imaging modalities for all 67 patients. Subgroup analysis of patients separated by N stage is shown in Table 5.

An interesting pattern emerged with respect to cystic nodal disease: 5 of the nonresponders based on CT findings had completely cystic masses remaining, with no solid enhancing component (Figure). Of note, all 5 had cystic nodal metastases before treatment. All 5 underwent neck dissection, with only 1 demonstrating scattered “viable tumor cells” on the background of necrotic tumor; this patient was a nonresponder. The remaining 4 patients with cystic residual masses had no viable tumor cells on histopathologic evaluation. Four of 5 patients with cystic masses—positive CT findings, including the 1 with positive tumor cells, had negative PET results on both SUV levels. One had false-positive PET results at SUV level 2 but negative results at SUV level 2.5.

In this retrospective cohort study, we evaluated CT, PET alone with SUV thresholds of 2 and 2.5, and PET/CT with the same SUV thresholds in the posttreatment management of neck disease in patients with HPV-related OPSCC. Our results suggest that there is a high NPV for PET/CT with an SUV cutoff of 2 and that PET/CT may be used to evaluate patients with HPV-related OPSCC after completion of therapy, consistent with other reports on the high NPV of PET/CT imaging. There are 4 pertinent issues related to diagnosis and management of the post-

#### ANALYSIS AND STATISTICAL METHODS

This was a retrospective cohort study with neck dissection considered as part of the treatment modality and not as failure. An isolated neck failure was defined as tumor recurrence in the neck with primary disease control. Data generated from the study were imported onto spreadsheets (Excel; Microsoft Corp). Sensitivity, specificity, NPVs, and positive predictive values (PPVs) were calculated using 2×2 tables for the entire cohort, with corresponding 93% confidence intervals using the Wilson score interval.

#### RESULTS

Sixty-seven of the 77 patients were included in the study, as 10 patients did not have posttreatment PET/CT scans available for evaluation. The demographics of the patients are shown in Table 1. The average time between pretreatment imaging and the start of radiotherapy was 38.5 days (median, 26 days). The average time between the end of radiotherapy and follow-up PET/CT scanning was 90.5 days (median, 88 days). All patients had complete response at the primary site on posttreatment PET/CT scans and clinical examination.

#### COMMENT

Twenty of the 67 patients underwent a neck dissection some time after completion of treatment (mean, 19.9 weeks; median, 15.6 weeks). A neck dissection was performed on 1 patient at 52.6 months because of a persistent necrotic node on PET/CT scans 6 and 9 months after chemoradiation therapy, and the pathology report was negative for residual disease. Of the 20 patients who underwent a neck dissection, 4 were positive for SCC and 16 were negative. Two of the patients with positive results were nonresponders based on all CT and PET cutoffs, with 1 patient a nonresponder on a PET SUV threshold of 2, and the other patient a nonresponder on CT and PET/CT cutoffs of SUV 2 and 2.5. Of the 16 patients with negative nodes, 6 had a response on all imaging categories, 4 had no response on all imaging categories, and 6 had no responses on CT but responses on PET SUV thresholds of 2 and 2.5. Of the 6 who had response on all imaging, 3 underwent neck dissections because of patient preference after discussion of planned neck dissections and because of persistent disease based on clinical examination and patient preference. Table 2 shows the sensitivity, specificity, PPV, and NPV in the group of patients who underwent neck dissections.

Forty-seven of 67 patients did not undergo neck dissections, with a mean and median follow up of 25.6 months and 26 months, respectively (range, 12-51 months). Of the 47 patients, 3 had distant metastases, 1 had a primary neck recurrence 19 months after treatment completion, and 1 had distant metastases with a neck recurrence (Table 3). No isolated neck failures were identified. Table 4 shows the sensitivity, specificity, PPV, and NPV of all imaging modalities for all 67 patients. Subgroup analysis of patients separated by N stage is shown in Table 5.

An interesting pattern emerged with respect to cystic nodal disease: 5 of the nonresponders based on CT findings had completely cystic masses remaining, with no solid enhancing component (Figure). Of note, all 5 had cystic nodal metastases before treatment. All 5 underwent neck dissection, with only 1 demonstrating scattered “viable tumor cells” on the background of necrotic tumor; this patient was a nonresponder. The remaining 4 patients with cystic residual masses had no viable tumor cells on histopathologic evaluation. Four of 5 patients with cystic masses—positive CT findings, including the 1 with positive tumor cells, had negative PET results on both SUV levels. One had false-positive PET results at SUV level 2 but negative results at SUV level 2.5.
treatment neck: (1) the role of planned neck dissection in head and neck surgery; (2) the role of planned neck dissection in HPV-associated OPSCC; (3) the role of PET/CT in determining the need for neck dissection; and (4) the criteria that are useful to determine the role of PET/CT in assessing the need for neck dissection.

**PLANNED NECK DISSECTIONS**

The main controversy of planned neck dissections revolves around patients with N2-N3 neck disease who have a complete response. Historically, advocates of planned neck dissections cite a low response to fractionated radiation therapy alone with histopathologic findings of occult residual disease. More recently, Brizel et al.13 showed an improved disease-free survival and overall survival rate at 4 years with planned neck dissection in patients with N2-N3 disease who achieved a complete response. However, studies increasingly show that there is little indication for planned neck dissections.14-16 Thariat et al.15 in a retrospective cohort review of 880 patients with SCC of the head and neck, showed a 92% 5-year regional control rate if there was a complete response on physical examination and contrast-enhanced CT 4 to 8 weeks after radiotherapy. Corry et al.16 showed that if a complete response (defined as complete response on clinical examination and contrast-enhanced CT) was achieved there were no isolated neck failures in 102 patients with N2-N3 disease with a median follow up of 4.3 years. Seventy-six percent of these patients had a primary tumor of the oropharynx, but HPV status was not evaluated.

Most of the studies cited herein predominantly involved N2 disease. The role of planned neck dissection in N3 disease is more ambiguous. Igidbashian et al.17 retrospectively evaluated 70 patients with N3 regional disease who had a clinical complete response based on CT and clinical examination findings and those with a partial clinical response who underwent neck dissections. The study reported that patients with a partial response in the neck and a complete response at the primary site who underwent neck dissections had a significantly improved disease-free survival but not a statistically significant difference in overall survival or regional relapse-free survival compared with patients who had complete responses at the primary and neck sites and who did not undergo a neck dissection. Also, Thariat et al.15 found that 5-year neck control and isolated neck control were lower in patients with oropharyngeal N3 neck disease than in patients with other N-stage disease. Despite the NPV of 100% with PET/CT and an SUV cutoff of 2 in our data for the N3 group, the sample size of our data for this population warrants further investigation.

**PLANNED NECK DISSECTION IN HPV-ASSOCIATED OPSCC**

Planned neck dissections in HPV-positive OPSCC remain controversial without a consensus. Currently, there is an epidemic of oropharyngeal cancer related to HPV, with the literature reporting that 50% or more OPSCC cases are HPV related.18-20 Both retrospective and prospective studies demonstrate an improved overall survival in HPV-related OPSCC vs non–HPV-related counterparts, an outcome that is believed to hold true for both surgical and nonsurgical treatment modalities.21,22 It would be useful to evaluate the need for planned neck dissections in this subgroup of patients. Shonka et al.23 in a retrospective review of 69 patients with OPSCC treated with radiotherapy with or without chemotherapy, reported that of the patients who underwent planned neck dissections, those with p16-positive disease were significantly less likely to have residual tumor in the neck than those with p16-negative disease. Furthermore, with no significant difference in clinical neck staging between p16-positive and p16-negative tumors, p16-positive tumors

---

**Table 2. Sensitivity, Specificity, Positive Predictive Value, and Negative Predictive Value for CT, PET, and PET/CT in Reviewing Responses to Therapy in 20 Patients Who Underwent Neck Dissection**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT70R</td>
<td>75.0 (30.1-95.4)</td>
<td>37.5 (18.5-61.4)</td>
<td>23.1 (8.2-50.3)</td>
<td>85.7 (48.7-97.4)</td>
</tr>
<tr>
<td>PET2</td>
<td>75.0 (30.1-95.4)</td>
<td>68.8 (44.4-85.8)</td>
<td>37.5 (13.7-69.4)</td>
<td>91.7 (64.6-98.5)</td>
</tr>
<tr>
<td>PET2.5</td>
<td>50.0 (15.0-85.0)</td>
<td>75.0 (50.5-89.8)</td>
<td>33.3 (9.7-70.0)</td>
<td>85.7 (60.1-96.0)</td>
</tr>
<tr>
<td>CT70PET2</td>
<td>100.0 (49.8-100.0)</td>
<td>37.5 (18.7-61.4)</td>
<td>28.6 (12.0-54.8)</td>
<td>100.0 (59.8-100.0)</td>
</tr>
<tr>
<td>CT70PET2.5</td>
<td>75.0 (30.1-95.4)</td>
<td>37.5 (18.5-61.4)</td>
<td>23.1 (8.2-50.3)</td>
<td>85.7 (48.7-97.4)</td>
</tr>
</tbody>
</table>

**Table 3. Representation of Failure Patterns in Patients Who Underwent Neck Dissection With Nodes Identified as Positive or Negative on the Pathology Report and Patients Who Had Negative PET/CT Imaging Results on Follow-up**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Node Positive (n = 4)</th>
<th>Node Negative (n = 16)</th>
<th>PET/CT Negative (n = 47)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isolated primary failure</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Isolated neck failure</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Isolated distant failure</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Primary and neck failure</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Distant and neck failure</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Death without preceding failure</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Abbreviations: CT70PET2, computed tomography (CT) with 70% reduction and positron emission tomography (PET) with a standardized uptake value (SUV) threshold of 2; CT70PET2.5, CT with 70% reduction and PET with an SUV threshold of 2.5; CT70R, CT alone with 70% reduction in short-axis diameter; PET2, PET with an SUV threshold of 2; PET2.5, PET with an SUV threshold of 2.5.
were more likely to have a complete cervical response, providing further evidence against planned neck dissections, particularly in this subgroup of patients.

**PET/CT IN NECK DISSECTION**

Monitoring of neck disease was historically based on clinical examination alone, which is a poor discriminator of response, giving a PPV and an NPV of around 40% and 75%, respectively. Additional imaging modalities, including ultrasonography, CT alone, PET alone, and PET/CT, have been used to monitor neck response after definitive therapy. There is a great deal of interest and excitement regarding the use of PET/CT as a modality for observing posttreatment response in the neck, and evidence suggests that PET/CT imaging has a greater than 94% NPV in nodal response. A retrospective review of 65 patients with head and neck SCC by Ong et al found PET/CT with an NPV of 97% in the neck. Chen et al prospectively evaluated a group of 30 patients and found that PET/CT was superior to contrast-enhanced CT alone, with greater accuracy and specificity in assessing regional disease. A prospective study by Porceddu et al involving 122 patients evaluated management of the neck based on PET alone for nodal response and had a low rate of neck dissection and no isolated neck failures in the PET-negative group. Within subgroup analysis, the p16-positive group had an NPV of 98.2% and 66.7%, respectively, for PET alone. The NPV is similar to our data, but the PPV was higher, possibly reflecting the use of different criteria for assessing positivity on PET. However, another prospective study by Moeller et al comparing PET/CT with CT alone in assessing radiation response in all patients with head and neck cancer found that PET/CT outperformed CT alone only in a subset of high-risk patients, eg, those with HPV-negative disease. This may be a function of an unselected study population as compared with the study by Porceddu and colleagues, in which they limited the analysis to those patients who achieved a complete response at the primary site.

**PET/CT CRITERIA IN NECK DISSECTION**

The utility of SUV thresholds in the posttreatment evaluation of treatment response has not been established. Recent studies using PET/CT in the evaluation of treatment response in the neck have not routinely used SUV thresholds for deciding clinical response; instead, response was based on other factors such as focal uptake.
as visually determined with respect to the background activity that corresponded to a structural abnormality. This is in contrast to the evaluation of PET imaging in the clinical staging of head and neck carcinomas, whereby SUV thresholds have been used to evaluate the likelihood of aggressive disease, response to therapy, and patient outcome. Herein, we reported using cutoffs of SUV 2 and 2.5 in PET/CT performed on average 90.5 days after completion of treatment to evaluate treatment response in the neck, with a better NPV obtained with a PET/CT SUV threshold of 2. The relatively low SUV levels were rationally selected before analysis in an attempt to achieve a high NPV, as the goal was to avoid missing residual neck disease that required a neck dissection. Likewise, the chosen CT criteria (lymph nodes <7 mm or >70% decrease in short-axis diameter) were more conservative than RECIST (Response Evaluation Criteria in Solid Tumors) 1.1 guidelines. Of note, there were no isolated neck failures in patients that were surveyed with PET/CT alone. One patient with initial N3 neck disease had disease progression that included distant metastases with neck lymphadenopathy, clinically and on imaging, likely representing aggressive disease, 7 months after completing chemoradiation therapy. A second patient had primary and regional failure 19 months after completion of treatment. In this patient, a surveillance PET/CT scan that was obtained 1 year after treatment demonstrated new metabolic activity in the right tongue base, and the patient subsequently developed new metabolic activity in the left side of the neck, which was detected 3 months later, representing a probable primary failure, with seeding in the neck, rather than a primary neck failure. However, given that this is a retrospective study, the use of PET SUV thresholds and CT response criteria should be evaluated prospectively to identify suitable levels for assessing treatment response to standardize observations of treatment response in the neck.

In 5 of our patients (7%), we found completely cystic but sizable residual masses on CT, with the results of PET being negative in all but 1 patient at SUV level 2. Only 1 of the 5 patients had a few scattered “viable tumor cells” on histopathologic examination. This scenario significantly contributed to the false-positive rates reported herein. No specific recommendation can be given for this subset on the basis of this study, but the likelihood of residual disease in cystic residual masses appears to be low.

In conclusion, given the reported favorable treatment responses in patients with HPV-associated OPSCC and the recent evidence against planned neck dissections, our study suggests that the use of PET/CT with an SUV cutoff of 2 as opposed to PET or CT alone provides an NPV that allows the continued observation of patients with a complete response based on PET/CT findings without the need for planned neck dissections.

Submitted for Publication: June 4, 2012; final revision received July 26, 2012; accepted August 28, 2012.

Author Affiliations: Departments of Otolaryngology–Head and Neck Surgery (Drs Chan, Richmon, Gourin, Koch, and Agrawal), Radiation Oncology and Molecular Radiation Sciences (Drs Sanguineti and Quon), Oncology (Drs Marur and Chung), and Pathology (Dr Bishop) and Division of Neuroradiology, The Russell H. Morgan Department of Radiology and Radiological Science (Dr Aygun), Johns Hopkins Medical Institutions, Baltimore, Maryland.

Correspondence: Nafi Aygun, MD, Division of Neuroradiology, Johns Hopkins University, 600 N Wolfe St, Phipps B112B, Baltimore, MD 21287 (naygun1@jhmi.edu); Nishant Agrawal, MD, Department of Otolaryngology–Head and Neck Surgery, Johns Hopkins Medical Institutions, 601 N Caroline St, Baltimore, MD 21287 (nagrawal@jhmi.edu).

Author Contributions: Drs Chan, Sanguineti, Aygun, and Agrawal had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Marur, Aygun, and Agrawal. Acquisition of data: Chan, Sanguineti, Aygun, and Agrawal. Analysis and interpretation of data: Chan, Sanguineti, Richmon, Gourin, Koch, Chung, Quon, Bishop, Aygun, and Agrawal. Drafting of the manuscript: Chan, Marur, Aygun, and Agrawal. Critical revision of the manuscript for important intellectual content: Chan, Sanguineti, Richmon, Gourin, Koch, Chung, Quon, Bishop, Aygun, and Agrawal. Statistical analysis: Chan, Sanguineti, and Agrawal. Administrative, technical and material support: Chan, Sanguineti, Marur, Quon, and Bishop. Study supervision: Richmon and Agrawal. Provided patients: Chung.

Image: Pretreatment positron emission tomography (PET) with contrast-enhanced computed tomography (CT). High uptake on PET in the upper left corner and a cystic neck mass with a solid component on CT without contrast in the lower left corner. After completion of chemoradiation therapy, CT with intravenous contrast reveals a persistent cystic mass in the neck in the lower right corner and a negative PET result in the upper right corner in a patient with no viable tumor on neck dissection performed after this imaging. A indicates anterior; P, posterior.
Conflict of Interest Disclosures: None reported.

Previous Presentation: This study was presented in part at the Eighth International Conference on Head and Neck Cancer, July 24, 2012; Toronto, Ontario, Canada.

REFERENCES