Positron emission tomography–CT prediction of occult nodal metastasis in recurrent laryngeal cancer

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ABSTRACT: *Background.* The purpose of this study was to evaluate the predictive value of positron emission tomography (PET)-CT in identifying occult nodal metastasis in clinically and radiographically N0 patients with recurrent laryngeal cancer undergoing salvage laryngectomy.

Methods. Retrospective review of 46 clinically and radiographically N0 patients with recurrent laryngeal cancer who underwent a PET-CT examination before salvage laryngectomy with neck dissection from January 1, 2002, to December 31, 2014, was performed.

Results. Two patients (16.7%) had true-positive PET-CT results, whereas 10 patients (83.3%) had false-negative scans, 1 patient (2.9%) had a false-positive result and 33 patients (97.1%) had a true-negative PET-CT. The sensitivity of PET-CT was 16.7% (95% confidence interval [CI], 3.5% to 46.0%) with a specificity of 97.1% (95% CI, 83.8% to 99.9%), positive predictive value (PPV) of 66.7% (95% CI, 20.2% to 94.4%), and negative predictive value (NPV) of 76.7% (95% CI, 62.1% to 87.0%).

Conclusion. PET-CT has poor sensitivity and NPV making PET-CT an imperfect predictor of nodal disease in recurrent laryngeal cancer. *Head Neck* **39:** 980–987, 2017

KEY WORDS: positron emission tomography (PET)-CT, salvage laryngectomy, laryngeal squamous cell carcinoma, occult nodal metastasis, recurrent laryngeal cancer

INTRODUCTION

Currently, laryngeal squamous cell carcinoma (SCC) is routinely treated with radiotherapy (RT) or concurrent chemoradiotherapy (CRT).[1–5] This approach has been adopted with the goal of maintaining speech and swallowing function while providing similar survival rates compared to primary surgery. Unfortunately, many of these patients develop recurrences and require salvage laryngectomy.[6–8]

The role of neck dissection during salvage laryngectomy is controversial. The management of patients with clinically apparent nodal disease is straightforward, however, there is no consensus regarding management of the clinically N0 neck. Additionally, neck dissection adds morbidity to total laryngectomy and is associated with a higher complication rate, including a higher rate of pharyngocutaneous fistula.[9]

The prevalence of occult nodal metastases in the N0 neck in recurrent laryngeal cancer has been reported to be from 4% to 20%.[9–13] Supraglottic tumors and advanced T classification tumors have been associated with an even higher occult nodal metastasis rate.[11–13] When taken together, patients with T4 supraglottic tumors have a 50% risk of occult nodal disease.[13] Efforts have been made to predict the likelihood of nodal metastases in these patients. The staging of the neck before initial therapy has been shown to correlate with the risk of occult nodal disease in neck dissection specimens.[11] Preoperative CT and MRI scans have been used to improve preoperative staging, however, these tests have poor sensitivity leading to an inadequate negative predictive value (NPV).[14–16]

The 2-[fluorine-18]fluoro-2-deoxy-d-glucose (FDG) positron emission tomography (PET), in combination with CT (PET-CT), is increasingly being used in the management of patients with head and neck cancer, including initial staging, assessing response to therapy, detecting recurrence, and identifying unknown primary tumors.[15,17–29] Additionally, PET-CT is increasingly used to improve the accuracy of staging in recurrent laryngeal cancer.[30] Although the ability of PET-CT to detect nodal metastasis in other tumors has been addressed, the predictive value of PET-CT in detecting nodal disease in patients with recurrent laryngeal cancer has not been well studied.[15,16,21,29–37] The purpose of this study was to evaluate the predictive value of PET-CT in identifying nodal metastasis in patients with recurrent laryngeal carcinoma with a clinically and radiographically

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N0 neck. The overall goal was to assess the ability of PET-CT to discriminate the need for elective neck dissection.

MATERIALS AND METHODS

A retrospective review was performed of a cohort of patients who underwent salvage laryngectomy with neck dissection without clinical or radiographic (CT or MRI) evidence of nodal disease at the University of Michigan from January 1, 2002, to December 31, 2014. All patients had a PET-CT before surgery. Salvage laryngectomy was defined as surgery for persistent or recurrent laryngeal SCC after initial RT or CRT. Patients were excluded if they had evidence of nodal disease on clinical examination or preoperative CT or MRI. Forty-six patients met inclusion criteria. Clinical and pathologic data were collected, including initial stage and treatment of the primary tumor as well as the staging of the recurrent or persistent tumor. Disease was staged based on the seventh edition of the American Joint Committee on Cancer staging system.

Patients who underwent a PET-CT at the University of Michigan (91.3%; 42 of 46 patients) and those who had a PET-CT at an outside institution (8.7%; 4 of 46 patients) were included in this study. The PET-CT was performed per institutional protocol. At the University of Michigan, patients were fasted for >4 to 6 hours and had glucose levels <250 mg/dL before imaging. Around 60 minutes after intravenous administration of 300 MBq (8 mCi) of FDG, sequential PET and CT imaging was performed on an integrated PET-CT scanner (Siemens Biograph T6; Siemens Medical Solutions, Hoffman Estates, IL). Helical CT from the skull vertex to the mid-thigh was performed with 5-mm collimation (low-dose CT parameters: 140 kV, 80 mA, tube rotation of 0.8 second per rotation, and pitch of 3:1), followed immediately by whole body PET at multiple overlapping bed positions (area covered: skull vertex to mid-thigh, step-and-shoot mode, 3 minutes per bed position). Then, a dedicated contrast-enhanced head and neck CT was performed with field of view 15 cm, commencing 40 seconds after intravenous injection of 100 ml volume of iopromide (Ultravist) at 1.5 ml/second, and coregistered to the whole body FDG PET dataset. Images were reviewed on a workstation (MedImage; MedView Pty, Canton, MI) by 2 readers (1 head and neck radiologist and 1 nuclear medicine physician) providing a single read per study.

Four of the PET-CT studies were performed at outside centers, with the imaging data transferred from compact disc to our local archive for review. This led to some heterogeneity in the imaging protocols used, as some outside centers performed dedicated head and neck PET-CT images acquired separately (in addition to the whole body PET-CT), whereas others performed only a whole body PET-CT (with a large field of view). Evidence of PET-CT positivity was determined by the official report of the reading radiologist at the time of the scan, on which patients' management was based. In addition, PET-CT images were reviewed by a single reader (author K.K.W., board certified in Nuclear Medicine) who was blinded to the results of the official report and final pathology, with interpretation compared with the initial clinical reads. There were no discrepancies between the official reports and the review by author K.K.W.

Cervical lymph nodes displaying FDG uptake above background were considered either suspicious or positive for regional nodal metastasis. PET-CT results were categorized as positive or negative. All nodes that were considered suspicious by the reading radiologist were categorized as positive. Final pathology results were collected and the nodal metastases were tabulated. For patients who underwent a unilateral neck dissection, only the dissected neck was included in the analysis.

Patient population

Forty-six patients, 84.8% (39/46) men and 15.2% (7/46) women with a mean age of 62.1 ± 9.7 years were included in our cohort. At the time of salvage surgery, 41.3% of patients (19/46) were current smokers and 58.7% (27/46) were former smokers. At the time of initial therapy, 47.8% of tumors (22/46) were located in the supraglottis, whereas 52.2% (24/46) were located in the glottis. The neck was initially staged as N0 in 71.1% of patients (32/45), N1 in 13.3% of patients (6/45), N2b in 6.7% of patients (3/45), and N2c in 8.9% of patients (4/45). The initial staging was missing in 1 patient who was previously treated at an outside institution. Of the patients, 41.3% (19/46) were initially treated with RT, 54.3% (25/46) were treated with CRT, and 4.3% (2/46) were treated with laser excision followed by adjuvant RT or CRT. The mean interval to recurrence was 20.4 months. Of the recurrent primary tumors, 52.2% (24/46) were located in the supraglottis, 45.6% (21/46) were in the glottis, and 2.2% (1/46) were centered in the subglottis. Recurrent tumors were staged as T1 in 4.3% of patients (2/46), T2 in 19.6% of patients (9/46), T3 in 32.6% of patients (15/46), and T4 in 43.5% of patients (20/46). Patient characteristics, staging, and treatment are shown in Table 1.

Statistical analysis

In our analysis, we initially compared PET-CT positivity to pathologic node status on a per patient basis. We subsequently evaluated each neck specimen separately with the left and right sides of the neck being analyzed individually. After analyzing the cohort as a whole, subgroup analysis was performed by tumor subsite, T classification, and those patients without nodal metastasis (N0) before initial treatment (RT or CRT). To calculate the sensitivity and specificity of PET-CT in predicting nodal metastasis, results of the PET-CT scans were compared to the final pathology (gold standard). Positive predictive values (PPV) and NPVs were calculated. Ninety-five percent confidence intervals (95% CI) were calculated using the method described by Agresti and Coull.[38] All statistical analysis was performed using IBM SPSS software version 20 (IBM, Armonk, NY) with consultation from the University of Michigan Center for Statistical Consultation and Research. This study was approved by the University of Michigan Internal Review Board (HUM00081554).

RESULTS

In our cohort of 46 patients, 3 patients (6.5%) had a positive PET-CT scan. Twelve patients (26.1%) were noted to have

TABLE 1. Baseline characteristics of the study cohort.

Characteristic	Value (n = 46)
Age at salvage surgery, y, mean (SD)	62.1 (9.7)
Sex	
Male	84.8% (39)
Female	15.2% (7)
Tobacco status at salvage	
Current	41.3% (19)
Former	58.7% (27)
Never	0% (0)
Alcohol status at salvage	
Current*	15.9% (7)
Former*	11.4% (5)
Never*	72.7% (32)
Missing data	3.8% (2)
Initial tumor subsite	
Supraglottic	47.8% (22)
Glottic	52.2% (24)
Subglottic	0% (0)
Initial stage	
I*	20.0% (9)
II*	26.7% (12)
III*	33.3% (15)
IV*	20.0% (9)
Missing data	2.2% (1)
Initial N classification	
N0	71.1% (32)
N1	13.3% (6)
N2a	6.7% (3)
N2b	8.9% (4)
N2c	2.2% (1)
Missing data	
Initial treatment	
RT	41.3% (19)
CRT	54.3% (25)
Laser excision with RT	2.2% (1)
Laser excision with CRT	2.2% (1)
Interval to recurrence, mo, mean (SD)	20.4% (20.0)
Recurrent/persistent tumor subsite	
Supraglottic	52.2% (24)
Glottic	45.6% (21)
Subglottic	2.2% (1)
Recurrence T classification	
T1	4.3% (2)
T2	19.6% (9)
T3	32.6% (15)
T4	43.5% (20)

Abbreviations: RT, radiotherapy; CRT, chemoradiotherapy.
Note: Initial tumor designates the tumor characteristics and treatment before the diagnosis of recurrence or persistence. Recurrent tumor designates that tumor treated by salvage laryngectomy with neck dissection.
* Data shown as a percentage of the known conditions of the variable excluding those patients with missing data.

nodal metastasis on final pathology, with 2 true-positive (16.6%) and 10 false-negative (83.3%) PET-CTs. Of the 34 patients without nodal metastasis on final pathology, there was 1 false-positive scan (2.9%) and 33 true-negative scans (97.1%; Table 2) The sensitivity of PET-CT when compared to the final pathology was 16.7% (95% CI, 3.5% to 46.0%) and the specificity was 97.1% (95% CI, 83.8% to 99.9%). In this cohort, the PPV was 66.7% (95% CI, 20.2% to 94.4%) and NPV was 76.7% (95% CI, 62.1% to 87.0%).

We then evaluated the cohort looking at each neck specimen separately. Eight patients either had a previous unilateral neck dissection as part of their initial therapy (n = 4) or only the ipsilateral neck was dissected (n = 4) at the time of salvage laryngectomy, and, thus, there were 84 neck specimens in our analysis. In total, 15 of the neck specimens (17.8%) contained nodal metastasis, 2 (13.3%) of which were detected by PET-CT. There were 69 neck specimens without nodal disease with only 2 (3.0%) having false-positive scans. The false-positive scans corresponded to 1 patient with a PET-CT suggestive of bilateral neck disease who had no pathologic lymph nodes on final pathology. The sensitivity of PET-CT when compared to the final pathology was 13.3% (95% CI, 24.8% to 39.1%) and the specificity was 97.1% (95% CI, 89.4% to 99.8%). In this analysis, the PPV was 50.0% (95% CI, 15.0% to 85.0%) and NPV was 83.8% (95% CI, 74.0% to 90.4%; Table 3).

In a subgroup analysis, we evaluated the 32 patients classified as N0 before their initial therapy. In this group, there were 10 patients (31.3%) with nodal metastasis on final pathology, 2 (20.0%) of which were identified on PET-CT with 8 false-negative scans. Of the 22 patients without regional metastasis, there was 1 false-positive (4.5%) and 21 true-negative (95.4%) PET-CT scans (Table 4). The sensitivity and specificity were 20.0% (95% CI, 4.6% to 52.1%) and 95.5% (95% CI, 76.5% to 99.9%), respectively. In this population, this corresponds to a PPV of 66.7% (95% CI, 20.2% to 94.3%) and NPV of 72.4% (95% CI, 54.1% to 85.5%).

We evaluated our cohort of patients who were classified as N0 before their initial therapy looking at each neck specimen separately. There were 58 neck specimens in our analysis. There were 13 neck specimens (22.4%) with pathologically confirmed nodal metastasis, 2 (15.4%) of which were identified

TABLE 2. Positron emission tomography-CT test results compared to final pathology (gold standard) in the entire cohort.

PET-CT evidence of nodal metastasis	Pathological nodal metastasis	
	Yes	No
Yes	2	1
No	10	33

Abbreviation: PET, positron emission tomography.
Sensitivity = 16.7% (95% confidence interval [CI], 3.5% to 46.0%).
Specificity = 97.1% (95% CI, 83.8% to 99.9%).
Positive predictive value = 66.7% (95% CI, 20.2% to 94.4%).
Negative predictive value = 76.7% (95% CI, 62.1% to 87.0%).

TABLE 3. Positron emission tomography-CT test results compared to final pathology (gold standard) in the entire cohort when evaluating the left and right sides of the neck separately.

PET-CT evidence of nodal metastasis	Pathological nodal metastasis	
	Yes	No
Yes	2	2
No	13	67

Abbreviation: PET, positron emission tomography.
Sensitivity = 13.3% (95% confidence interval [CI], 24.8% to 39.1%).
Specificity = 97.1% (95% CI, 89.4% to 99.8%).
Positive predictive value = 50.0% (95% CI, 15.0% to 85.0%).
Negative predictive value = 83.8% (95% CI, 74.0% to 90.4%).

TABLE 4. Positron emission tomography-CT test results compared to final pathology (gold standard) in patients who were previously N0 before initial therapy.

PET-CT evidence of nodal metastasis	Pathological nodal metastasis	
	Yes	No
Yes	2	1
No	8	21

Abbreviation: PET, positron emission tomography.
Sensitivity = 20.0% (95% confidence interval [CI], 4.6% to 52.1%).
Specificity = 95.5% (95% CI, 76.5% to 99.9%).
Positive predictive value = 66.7% (95% CI, 20.2% to 94.3%).
Negative predictive value = 72.4% (95% CI, 54.1% to 85.5%).

TABLE 5. Positron emission tomography-CT test results compared to final pathology (gold standard) in patients who were previously N0 before initial therapy when evaluating the left and right side of the neck separately.

PET-CT evidence of nodal metastasis	Pathological nodal metastasis	
	Yes	No
Yes	2	2
No	11	43

Abbreviation: PET, positron emission tomography.
Sensitivity = 15.4% (95% confidence interval [CI], 3.1% to 43.4%).
Specificity = 95.6% (95% CI, 84.4% to 99.6%).
Positive predictive value = 50.0% (95% CI, 15.0% to 85.0%).
Negative predictive value = 79.6% (95% CI, 66.9% to 88.4%).

on PET-CT with 11 false-negative scans. Of the 45 neck specimens without pathologically positive nodes, 43 (95.6%) had a negative PET-CT with 2 false-positive scans (Table 5). The sensitivity and specificity were 15.4% (95% CI, 3.1% to 43.4%) and 95.6% (95% CI, 84.4% to 99.6%), respectively. The PPV was 50.0% (95% CI, 15.0% to 85.0%) and the NPV was 79.6% (95% CI, 66.9% to 88.4%).

In order to better understand the performance of PET-CT, we analyzed our cohort based on the recurrent tumor subsite and recurrent tumor T classification (Table 6). The small size of each group limited the analysis. As expected, the NPV was highest in patients with low risk for nodal metastasis (T1 or T2 tumors and glottic primaries) and was lowest in patients who were at the highest risk for occult nodal disease (T3 and T4 tumors and supraglottic primaries). Although the sensitivity was slightly better in patients with T3 tumors compared with other T classifications, the differences were not statistically significant. This was due to the small number of true-positive scans in the cohort.

The patients who had false-negative PET-CT scans are of particular interest. Of the 10 patients in our overall cohort with false-negative PET-CT scans, 6 patients had 1 occult node, 1 patient had 2 occult nodes, 1 patient had 3 occult nodes, 1 patient had 7 occult nodes, and 1 patient had 29 occult nodes that were positive for metastatic SCC on final pathology (Table 7). Histopathologic lymph node tissue was available for review in 5 of the 10 patients. The average size of metastatic deposit in the lymph node was 3 mm (range, 1–7 mm). Representative images of the PET-CT from the patient with 29 occult nodes are shown in Figure 1 and representative images of an occult node from this patient are shown in Figure 2.

DISCUSSION

PET-CT has proven to be a valuable tool in caring for patients with head and neck cancer. First described by Warburg[39] in 1956, PET-CT capitalizes on the concept that malignant cells exhibit increased glucose utilization by upregulating glucose transporters. FDG, a radiopharmaceutical analog of glucose, is taken up by malignant cells and undergoes phosphorylation by hexokinase to FDG-6-phosphate; however, unlike glucose, FDG is trapped intracellularly as an index of the metabolic activity of tumor cells.[39] This technology has proven useful in initial staging, assessing treatment response, monitoring for recurrence, and identifying distant metastasis in patients with head and neck cancer.[18,19,26,34,40,41] Although PET-CT has been shown to have increased sensitivity when compared to CT or MRI, the role of PET-CT in guiding treatment of the neck, especially in the salvage setting, is evolving.[13–15]

TABLE 6. Positron emission tomography-CT performance based on recurrent tumor subsite and T classification.

Variables	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
T1/T2	NA*	100%	NA*	100%
(*n* = 11)		(71.2% to 100%)		(71.2% to 100%)
T3	33.3%	100%	100%	85.6%
(*n* = 15)	(56.3% to 79.8%)	(71.2% to 100%)	(16.8% to 100%)	(58.8% to 97.2%)
T4	11.1%	90.1%	50.0%	55.6%
(*n* = 20)	(0.0% to 45.7%)	(60.1% to 100%)	(9.5% to 90.6%)	(33.7% to 75.5%)
T3/T4	16.7%	95.7%	66.7%	68.8%
(*n* = 35)	(3.5% to 46.0%)	(77.3% to 100%)	(20.2% to 94.4%)	(51.3% to 82.2%)
Supraglottis	0%	100%	NA†	66.7%
(*n* = 24)	(0% to 37.2%)	(77.3% to 100%)		(46.6% to 82.2%)
Glottis	50.0%	94.4%	66.7%	89.5%
(*n* = 21)	(15.0% to 85.0%)	(72.4% to 100%)	(20.2% to 94.4%)	(67.4% to 98.3%)

Abbreviations: 95% CI, 95% confidence interval; PPV, positive predictive value; NPV, negative predictive value; NA, not applicable.
* No patients with T2 tumors had positive nodes on final pathology.
† There were no positive positron emission tomography-CT scans.

TABLE 7. Number of positive nodes on final pathology in patients with false-negative positron emission tomography-CT.

Patient number	Nodes positive in right side of neck	Nodes positive in left side of neck	Total positive nodes	Largest metastatic deposit, mm
1	1	0	1	MD
2	4	3	7	MD
3	20	9	29	7
4	1	1	2	1.5
5	0	1	1	MD
6	0	1	1	MD
7	NA*	1	1	1
8	1	NA*	1	1
9	NA*	3	3	MD
10	0	1	1	3

Abbreviations: MD, missing data; NA, not applicable.
* Unilateral neck dissection performed.

To the best of our knowledge, this is the largest study to evaluate the ability of PET-CT to detect nodal metastasis in patients with recurrent laryngeal carcinoma. In our study of clinically and radiographically (based on CT or MRI) N0 patients, the sensitivity of PET-CT was 16.7% with a specificity of 97.1%. In our population, this yielded an NPV of only 76.7%. When we compared our results to other reports in the literature, we noted a wide range of reported sensitivities and specificities. In these studies, the reported sensitivity ranges from 71% to 89% and specificity ranges from 82% to 100%.[21,32,36,40,41] In the largest meta-analysis of 1236 patients in 32 studies, PET-CT had pooled sensitivity of 79% (95% CI, 72% to 85%) in detecting cervical nodal metastases with a specificity of 86% (95% CI, 83% to 89%). Notably, PET-CT had an even lower sensitivity of 50% (95% CI, 37% to 63%) in detecting occult nodal metastasis in the clinically N0 patient, although it did have a reasonable specificity of 87% (76% to 93%).[42]

The current study reports a sensitivity that is substantially lower than previous reports. This is likely because of the differences in study design. The previous studies included patients with head and neck cancer from all subsites, with laryngeal primaries making up a small proportion of the population. Additionally, the previous studies included patients who were previously untreated, whereas our study only included patients who were previously treated with RT or CRT. This is important as chemotherapy and radiation alter the lymphatics with decreased vascularity of the residual nodes. Thus, many of the pathologically positive

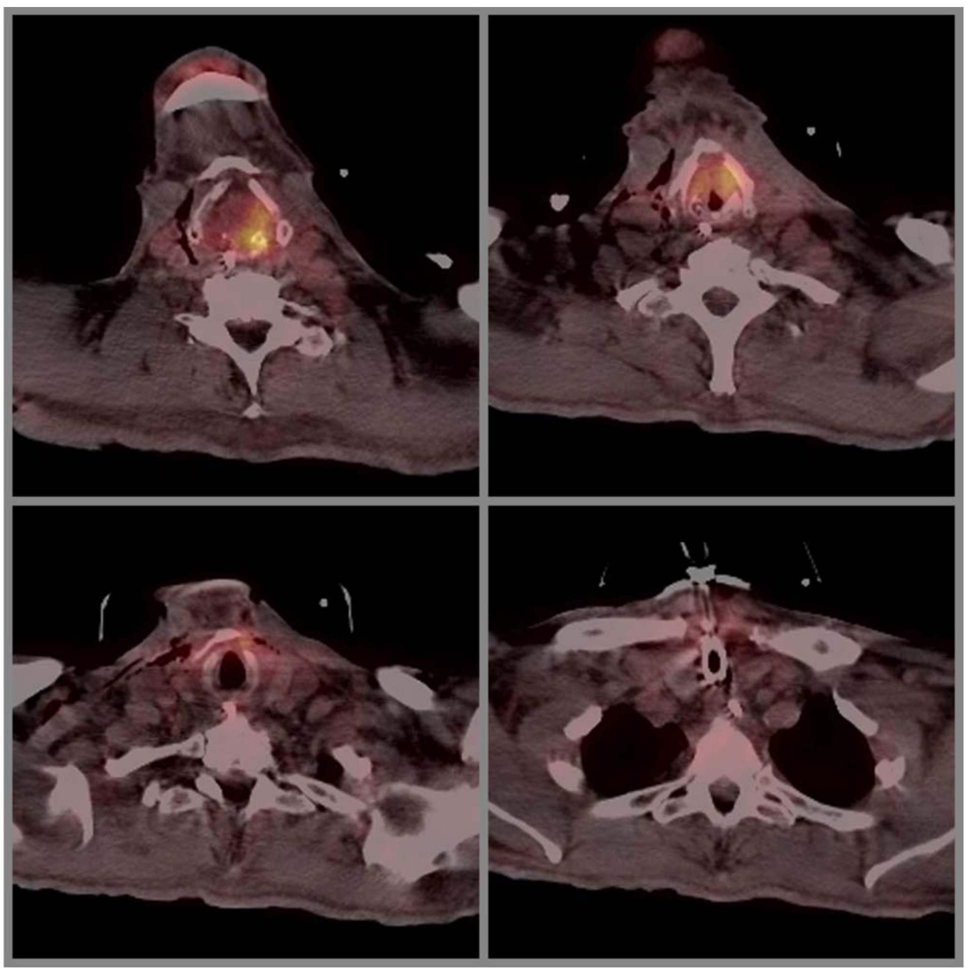

FIGURE 1. Representative images from a false-negative positron emission tomography-CT (patient number 3 in Table 6). Final pathology revealed 29 positive nodes. [Color figure can be viewed at wileyonlinelibrary.com]

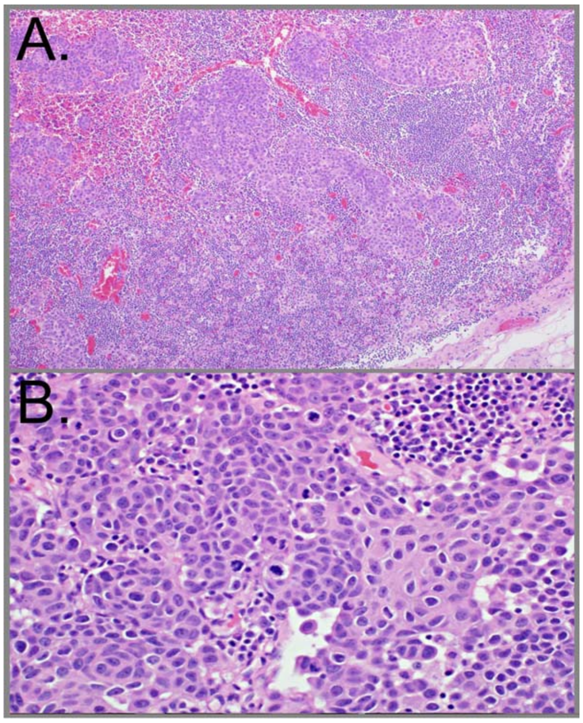

FIGURE 2. Representative images from the final pathology of an occult node from a patient with a false-negative positron emission tomography (PET)-CT (patient number 3 in Table 6, PET-CT shown in Figure 1). (A) Low powered view (original magnification ×10). (B) High power view (original magnification ×40). [Color figure can be viewed at wileyonlinelibrary.com]

nodes would be below the size detection limit of PET-CT (6–8 mm), which would, in turn, limit the sensitivity.[43] Perhaps most importantly, all other studies included patients with clinically or radiographically apparent nodes. Including patients with known nodal metastasis would increase the number of true-positive scans, which, in turn, would increase the calculated sensitivity. This study design fails to answer the question regarding the ability of PET-CT to detect occult nodal disease. This phenomenon is demonstrated in the meta-analysis by Kyzas et al[42] as the sensitivity drops from 79% to 50% when patients with clinically evident nodes are excluded. The current study is the only study evaluating the utility of PET-CT to evaluate the neck before salvage laryngectomy in a cohort of patients previously treated with CRT or RT with no clinical or radiographic nodal metastasis before PET-CT. This difference in clinical design almost certainly accounts for the difference in sensitivity seen in our study.

The closest report to the current study was published by Gilbert et al.[31] This study consisted of a review of 15 patients with SCC of the larynx who underwent elective neck dissection at the time of salvage laryngectomy. In their study, they reported a sensitivity of 70% (95% CI, 39% to 90%), specificity of 100% (95% CI, 51% to 100%), and NPV of 63% (95% CI, 30% to 87%). Once again, this study included patients with and without clinically apparent nodal disease, which led to a higher sensitivity than the current study, as described above. Based on these results, the authors concluded that the false-negative rate is too high to defer neck dissection based solely on PET-CT results, and this conclusion is supported in our study.[30]

By using the pre-test probability of occult nodal disease, the sensitivity and specificity of PET-CT from this study can be used to calculate the PPV and NPV of a particular patient population based on previously described methods.[44] This allows the clinician to determine the posttest probability of occult nodal disease, and it is the posttest probability of occult disease that should drive the decision regarding whether or not a neck dissection should be performed. In patients with clinically apparent nodal disease at the time of the laryngectomy, the decision to proceed with neck dissection is straightforward; however, the decision becomes more complicated in the previously treated neck with no evidence of disease. In the original article by Weiss et al[45] in 1994, decision analysis was used with the conclusion that the N0 neck should be treated if the risk of occult nodal metastasis is greater than 20%. Ferlito et al,[46] in their review of neck dissection in laryngeal cancer, suggested that the neck should be treated if the risk of metastasis is 15%.

Careful consideration of the risk of occult nodal disease is important in deciding to perform a neck dissection, as salvage laryngectomy is already associated with impaired wound healing and wound-related complications. Furthermore, neck dissection is associated with increased morbidity, including a higher fistula rate.[9,47–49] Unfortunately, there are few remaining treatment modalities available to the patient undergoing salvage laryngectomy, and neck dissection becomes more difficult once a laryngectomy has been performed, especially if free tissue is used to reconstruct the pharynx. Thus, identifying those patients at high risk of regional failure is important. In the present study, 26% of patients had occult cervical metastasis not detected on either clinical examination or CT. PET-CT failed to identify the majority of these patients, as 23% of patients with a negative PET-CT had occult nodal disease. Thus, based on the low sensitivity and low NPV, PET-CT alone is an inadequate test to withhold neck dissection.

When we considered why PET-CT had an unacceptably low sensitivity, there was no evidence that the high rate of false-negative scans was related to patient preparation factors, modality of treatment (RT vs CRT), or the timing of the PET-CT after treatment. It is believed that this was instead related to low volume disease in the previously treated neck with cancer deposits that were below the spatial resolution of PET-CT leading to partial volume effect and reduced sensitivity. On re-review of the histopathology in the patients who had false-negative PET-CT scans in our study, the average metastatic deposit was 3 mm, confirming the low volume of disease. Posttreatment lymph nodes with limited tumor burden fall below the detection limit of the PET-CT leading to false-negative scans.

There were limitations to our current study. Although this is the largest study evaluating the ability of PET-CT to detect nodal disease before salvage laryngectomy, the sample size was still relatively small. This retrospective study included PET-CT scans performed at our institution and also from outside centers leading to some heterogeneity in the imaging protocols used. Protocols performing dedicated head and neck PET-CT images acquired separately (in addition to the whole body PET-CT) could have improved conspicuity of small cervical nodes compared to protocols with whole body PET-CT acquired over a large field of view. However, excluding patients with outside imaging studies did not affect our sensitivity (18.2% vs 16.7%) and specificity (96.8% vs 97.1%) significantly. The retrospective nature of this study also limits the ability to draw conclusions from the dataset. Given these limitations, a prospective study of PET-CT in salvage laryngectomy is needed to fully address this question.

CONCLUSION

This study demonstrates that although PET-CT has a reasonable specificity and PPV, it has inadequate sensitivity and NPV. Based on these results, neck dissection should not be withheld solely on the basis of a negative PET-CT when performing salvage laryngectomy for recurrent laryngeal SCC.

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