WHAT DOES PET IMAGING ADD TO CONVENTIONAL STAGING OF HEAD AND NECK CANCER PATIENTS?

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Purpose: To determine the value of PET scans in the staging of patients with head and neck carcinoma.

Methods and Materials: The charts of 25 patients who underwent neck dissection, computed tomography (CT) scan, and F-18-fluorodeoxyglucose positron emission tomography (FDG-PET) imaging as part of their initial work-up for a head and neck squamous cell cancer between 2000–2003 were reviewed. All patients underwent clinical examination, triple endoscopy, and chest radiograph as part of their clinical staging, adhering to American Joint Commission for Cancer criteria. In addition to the clinical nodal (N) stage, PET findings were incorporated to determine a second type of N staging: clinical N + PET stage. The number of neck sides and nodal levels involved on CT or PET and on pathologic examination were recorded.

Results: The sensitivity and specificity for detection of nodal disease were similar for CT and FDG-PET. Positive and negative likelihood ratios were similar for both diagnostic tests. None of our 25 patients had unsuspected distant disease detected by PET.

Conclusion: The addition of PET imaging did not improve diagnostic accuracy in our patients compared with CT. PET scanning did not alter clinical management in any of the patients. © 2007 Elsevier Inc.

PET imaging, Head and neck carcinoma.

INTRODUCTION

F-18-fluorodeoxyglucose (F-18-FDG) positron emission tomography (PET) imaging is frequently used in patients with squamous cell carcinoma of the head and neck (SCCHN). Some studies have suggested that PET changes the extent of disease in 15%–20% of patients with head and neck cancer compared with computed tomography (CT) alone (1, 2). In 2001, Schecter et al. reviewed the literature and concluded that FDG-PET adds little to conventional imaging studies for the pretreatment detection of nodal metastases, detection of unknown primaries, or metastatic disease in the chest (3). Gregoire states that the staging of the head and neck nodes is a very good illustration of the uselessness of FDG-PET for target volume selection and delineation in the neck (4). Frank et al., however, suggest that the utilization of PET/CT is appropriate for head and neck cancer staging in the initial presentation (5). Thus, review articles discussing PET and CT/PET conclude that it is either a valuable modality in the initial evaluation of SCCHN or a useless modality (3–5). This study will attempt to define the incremental value of FDG-PET imaging for neck staging to conventional staging methods in surgically managed patients with SCCHN. The endpoints to be examined in this study include diagnostic sensitivity, specificity, and accuracy of CT vs. FDG-PET for neck nodal metastases. The imaging findings were compared with the gold standard: pathologic findings from neck dissection.

METHODS AND MATERIALS

Patients

The charts of 25 patients who had CT and PET for staging SCCHN followed by neck dissection from 2000–2003 were reviewed. A total of 38 neck sides were dissected in these 25 patients. Twenty-one patients had definitive surgery for their primary SCCHN. Neck dissections were divided into anatomic levels 1–5 using standard criteria by the operating surgeon. Clinical staging included history and physical examination, routine laboratory tests, and triple endoscopy in all patients. The study was approved by the Institutional Review Board of SUNY Upstate Medical University.

CT scans

The CT scans were contrast enhanced and done on several different scanners and interpreted by many radiologists without
any knowledge of the PET findings. From CT reports and scans, the first author determined the number of nodal levels and neck sides involved by disease. Similarly, the first author used operative reports and pathologic reports to determine the number of nodal levels dissected and the number of levels with metastatic involvement.

**PET scans**

The PET scans were done at 2 facilities and interpreted by several radiologists. Four of the 25 scans were CT/PET scans. The PET radiologist had access to the CT scans in about half of the cases. The first author used the nuclear medicine physician’s report of area(s) of increased uptake to determine the number of nodal levels and neck sides involved by malignant disease. There was no specific standard uptake value (SUV) used to identify malignant disease. PET scan was performed using the following method: Advance PET scanner or Discovery ST PET/CT system was used. Both systems were made by General Electric Medical Systems (Chalfont St. Giles, UK) and utilize bismuth germanium oxide detector technology. Patients were administered 10 mCi of F-18-FDG and PET imaging was performed in supine position in 2D mode. Transmission PET data were reconstructed using filtered back projection method, in 128 × 128 matrix, pixel size 4.25 mm, with Hanning filter, cutoff at 8.5 mm, real-time random subtraction, and geometric correction. Emission PET data were reconstructed using the OS-EM iterative method, in 128 × 128 matrix, pixel size correction was used, with Gaussian smoothing 8 mm, axial smoothing, and real-time random subtraction. Well counter used real-time random subtraction, geometric, decay, deadtime, and scatter correction.

**Staging**

Each patient was assigned a clinical nodal (N) stage by the first 2 authors according to the American Joint Commission on Cancer staging criteria, incorporating all clinical findings, as well as CT interpretation by the diagnostic radiologist. They also determined a clinical N + PET stage for each patient by incorporating the nuclear medicine physician’s findings. For example, if there was a 2-cm node on 1 neck side, the clinical N would be N1. If the PET was positive only at this site, clinical N + PET would be N1. Clinical N + PET would be N2 if another area was considered malignant in this neck; NO if the PET was read as normal for the neck.

**RESULTS**

Patient characteristics and treatment information are listed in Table 1. Most of the patients presented with locally advanced squamous cell carcinoma. Pathologic neck stage (pN) is compared with clinical N stage and clinical N + PET stage in Table 2. The ability of each modality to determine neck nodal level involvement in the 161 dissected nodal levels is listed in Tables 3 and 4. PET and CT both show significant and identical positive correlation with pathologic findings in Tables 3 and 4. However, although the overall discordance of CT and PET with pathologic findings is identical, the discordance is not in the

<table>
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<tr>
<th>Table 1. Patient characteristics</th>
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<td>Age (median, in y)</td>
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<td>No. of patients</td>
</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>Male</td>
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<tr>
<td>Female</td>
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<tr>
<td>Primary site</td>
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<td>Oropharynx</td>
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<td>Hypopharynx</td>
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<td>Pathologic AJCC stage</td>
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<td>III</td>
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<tr>
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<td>Radiation therapy</td>
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<td>Primary or adjuvant chemotherapy</td>
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<tr>
<th>Table 2. Comparison of clinical N stage and clinical N stage + PET in 25 patients</th>
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<td>Clinical N stage + PET</td>
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<td>Clinical N stage</td>
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<th>Table 3. Comparison of nodal involvement on CT with pathologic involvement in 161 nodal levels</th>
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<td>Pathologic involved nodal levels</td>
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<td>CT</td>
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<th>Table 4. Comparison of nodal involvement on PET with pathologic involvement in 161 nodal levels</th>
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<tr>
<td>Pathologic involved nodal levels</td>
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<td>PET</td>
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Chi-square tests for Tables 3 and 4 indicate a p < 0.001 with 1 degree of freedom.
identical patients or nodal levels. McNemar-matched proportional testing of CT vs. PET to predict pathologic nodal level involvement shows no difference; relative risk = 1.0. The median SUV of involved nodal levels is 5.8 with a range of 2–12.8. Three of 18 positive neck sides on PET are falsely positive (pathologically negative) with SUVs of 2, 2.7, and 8, respectively. Six patients are discordant between clinical N and clinical N + PET stage. The clinical N + PET was identical to pathologic N in 3 of these 6 patients; clinical N (including CT findings) was identical to pathologic N in the other 3 patients. Table 5 lists results of CT vs. PET in correctly identifying malignant disease in a neck side. Each neck dissection, whether partial or complete, is counted as a neck side dissection. Each of the two imaging modalities has an accuracy of 73%. Unsuspected distant malignant disease was not found by PET in any of the 25 patients reviewed.

**DISCUSSION**

Vermeersch et al. published the most extensive review in the literature of the role of PET imaging in the staging of SCCHN (6). Their article includes an evaluation of 17 articles comparing CT/MRI with FDG-PET for SCCHN. Several of the articles compare MRI or ultrasound with FDG-PET, and most do not correlate neck side or nodal extent of involvement with pathology. Vermeersch et al. conclude that there was a significantly higher sensitivity and specificity with PET than CT/MRI for detection of nodal metastases (6). However, they also explicitly state that “given the large variation in methods used by different authors to assess the presence or absence of disease, a straightforward meta-analysis of FDG-PET was not possible”.

For this study, the literature was reviewed for articles meeting the following criteria: (1) all patients had SCCHN and a CT and PET scan for staging, (2) all patients had neck surgery and pathologic nodal examination as the reference standard, and (3) CT and PET were compared with pathologic examination for neck side involvement and/or nodal extent of involvement. Three articles met our criteria (7–9). Two were included in the analysis by Vermeersch et al. (7, 9).

Jaeschke, Guyatt, and Sackett published criteria to guide readers to determine whether the findings in an article about a diagnostic test are valid (10). One of their criteria is that the diagnostic test (in this case CT or PET) should not influence the decision to perform the reference standard (neck dissection). Twenty-one patients in our study were treated with primary surgical intent for their primary disease, so the decision to do a neck dissection was driven by their primary disease, not the imaging findings. Four patients with unknown primary or SCCHN had neck dissection for clinically evident neck disease before radiation therapy. The neck imaging did not influence the decision to do a neck dissection. This series meets the criteria by Jaeschke et al. for valid data. The other three publications did not provide sufficient details to determine whether they meet these criteria. The four series differ in many respects. Two studies (7, 9) published by the same group of investigators were limited to squamous cell carcinomas of the oral cavity and palate. Schwartz et al. and this series included a variety of SCCHN, with a preponderance of locally advanced tumors (8). The series differed in patient numbers ranging from 20–106 patients. Also, two series compare individual pathologic nodal findings with imaging results (7, 9), whereas the others compare nodal level findings on pathologic examination with imaging results (8). Furthermore, Schwartz et al. compared CT/PET with CT, and the other series compared PET and CT. Radiologists do not have standardized criterion to identify malignant neck disease, particularly with PET.

The wide range of results is evident in Table 6; however, the average increase in accuracy by the addition of PET is about 5%. Among the series, Jaeschke et al. recommended using likelihood ratios to help determine whether the results of a diagnostic test will help in caring for patients (Table 7) (11). Positive likelihood ratios (LR+) are a ratio of posttest probability of disease vs. pretest probability of disease in a patient. The higher the ratio the better the test is at finding disease. Jaeschke et al. reported that positive likelihood ratios (LR+) >10 indicate the test often leads to conclusive changes in the probability of disease, whereas ratios 5 to 10 indicated moderate shifts in the probability of disease (11). Conversely, negative likelihood ratios (LR−) reflect the probability that disease is absent in a patient after the test compared with the probability before the test was done. The lower the ratio the more likely that the test is useful in detecting absence of disease. Jaeschke et al. reported that a LR− ≤0.10 indicated a frequent conclusive change by the test in probability that disease is absent, while a ratio between 0.1 and 0.2 generated moderate shifts in probability and ratios between 0.2 and 0.5 lead to small shifts in probability that disease is absent (13). The
The results of this analytic test on the four series are listed in Table 7. Adams et al. (7) was the only study where CT and PET were in different LR ranges using the criterion by Jaeschke’s et al. (8). Thus, three of the four series suggested similar efficacy of PET and CT in identifying neck disease by nodal level or lymph node group.

Adams et al. (7) found LR+ of CT showed it to result in small shift in probability that disease was absent (0.21), whereas PET led to a moderate shift that disease was absent (0.11). Schwartz et al. (6), however, reported that the LR+ of CT suggested a small shift in probability that disease was absent (0.22), and PET led to a frequent conclusive shift in probability of finding no disease in the neck (0.04). Stuckenson et al. (9) and our study show little difference in LR+ between CT and PET (Table 7). The trend observed in the analysis of these small series is that CT and PET are of similar efficacy in detecting the absence of neck disease.

This study confirms that the SUV is of limited value in evaluating malignant nodal disease in SCCHN because there is considerable overlap in the range of values seen in benign false-positive nodes and malignant nodes. This finding was previously reported by Adams et al. (7), who found a SUV range of 2–15.8 in benign inflammatory nodes and 2–11 in malignant nodes (8).

Both CT and PET identify malignant nodal disease with high accuracy in SCCHN with similar false-positive and -negative ratios. If every 1 of the 39,250 SCCHN patients diagnosed annually has PET imaging as part of the initial staging work-up, the cost in the USA alone would be about $100 million (12, 13). A very large prospective study would be required to prove that PET improves accuracy by the 5% estimated by the other series in Table 6. The high costs of performing such a study might not be justifiable for a diagnostic tool like PET, which rarely changes clinical management, or not at all as in this study. PET may have a more important role to play in early detection of persistent disease, which is being further investigated in RTOG protocol 0522 or in identifying recurrent disease (14). Currently, PET imaging remains investigational in the staging of SCCHN.

Table 7. Likelihood ratios of CT or PET in predicting the presence or absence of neck disease

<table>
<thead>
<tr>
<th>First author</th>
<th>LR(+)</th>
<th>LR(-)</th>
<th>LR(+)</th>
<th>LR(-)</th>
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<tbody>
<tr>
<td>Adams (7)</td>
<td>5.5</td>
<td>.21</td>
<td>15</td>
<td>.11</td>
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<tr>
<td>Schwartz (6)</td>
<td>52</td>
<td>.22</td>
<td>64</td>
<td>.04</td>
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<tr>
<td>Stuckenson (9)</td>
<td>2.5</td>
<td>.46</td>
<td>3.9</td>
<td>.37</td>
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<tr>
<td>Current series</td>
<td>9.9</td>
<td>.33</td>
<td>9.9</td>
<td>.33</td>
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Abbreviations: = LR(+), positive likelihood ratio; sens/(1-spec); LR(-), negative likelihood ratio; (1-sens)/spec.
REFERENCES


