Modern Staging and Utility of PET Imaging in Esophageal Cancer Management

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Key Words
Esophageal cancer, staging, FDG, PET, neoadjuvant therapy

Abstract
Esophageal cancer is the eighth most common cancer worldwide, and one of the most fatal diseases despite modern medical treatment. Because correct staging and surveillance of neoadjuvant therapy for esophageal cancer is mandatory for further treatment planning, choosing a modern imaging system is important. The development of $^{18}$F-fluorodeoxyglucose positron emission tomography ($^{18}$F-FDG-PET) has provided alternate means of tumor detection distinct from more conventional methods. This modality has extraordinary performance in detecting locoregional lymph node involvement and distant metastatic disease, and has been introduced as a powerful tool in many guidelines. However, some factors still lead to false-negative or -positive results, raising questions of its accuracy. This article discusses the clinical efficacy of PET in staging and surveillance of neoadjuvant therapy in esophageal cancer, comparing its accuracy with conventional imaging modalities. (JNCCN 2008;6:862–869)

Esophageal cancer is the eighth most common cancer in the world. The incidence rate differs according to geographic region, with 2- to 60-fold higher estimated incidence in endemic areas. In the United States, the incidence has been decreasing for many years. In developed countries, this may be from the declining incidence of squamous cell carcinoma of the esophagus, usually attributed to risk factors such as smoking and alcohol consumption, although esophageal adenocarcinoma has been increasing.

Currently, esophageal adenocarcinoma comprises 50% of all esophageal cancers in developed countries, with several increasing risk factors implicated, included obesity and gastroesophageal reflux disease. Although incidence has been changing, the prognosis remains disappointing, with 5-year survival rates of 34%, 17%, and 3% in localized stage, regional stage, and distant metastatic disease, respectively. Patients with early-stage disease are considered potentially curable with definitive surgery or multimodality therapy. In contrast, those with distant metastasis have the worst prognosis, and palliative treatment remains the first choice. As a result, establishing accurate staging before applying specific treatments is essential.

Conventional imaging is the mainstay in workup and surveillance of esophageal cancer. The introduction of endoscopic ultrasound (EUS) has an accuracy of 89% for T staging, and the highest accuracy (> 80%) compared with other methods for detecting metastatic disease in locoregional lymph nodes.

CT is another powerful tool that provides high accuracy in detecting liver or lung metastases and aortic involvement or tracheobronchial invasion. Both modalities rely on the structural detection of a tumor-involved area, leading to possible misdiagnosis if normal anatomy is not affected. In this respect, PET may be advantageous in its ability to detect biologic alteration of tumor-involved tissues.

In 2007, a multidisciplinary expert panel recommended PET be performed routinely for staging. In the NCCN Clinical Practice Guidelines in Oncology: Esophageal Cancer (in this issue; to view the most recent version of these guidelines, visit the NCCN Web site at www.nccn.org), it is currently a category 2B (non-uniform
response. Given the increasing popularity of this radiologic modality, this article reviews its application in detail.

**Mechanism of Fluorodeoxyglucose-PET**

Since its original inception for neuroanatomic research, PET scanning has been in development for several decades. The construction of a PET image begins with the infusion of radioisotope-labeled elements, such as $^{18}$O, $^{13}$C, $^{15}$N, and $^{18}$F, which become incorporated in tissues according to their normal biologic function. The natural decay of radioisotopes releases positron-emitting radioparticles that are detected with scanning machines to reveal the distribution and quantity of radioactivity.

Since the development of the widely used radioisotope 18F-fluorodeoxyglucose (18F-FDG), this glucose analog has successfully promoted the use of PET in the field of oncology. The advantage of 18F-FDG is its long half-life of 110 minutes. In contrast with other radioisotopes with half-lives of 20 and 2 minutes, such as $^{13}$C and $^{15}$O, respectively, the longer half life of 18F-FDG allows it to be manufactured commercially offsite. This decreases the cost of the imaging modality, making the price more reasonable for widespread public use.

In contrast to conventional imaging systems, FDG-PET is based on the alteration of metabolic activity in different tissues. As most malignant cells are inefficient in metabolizing glucose, it is not surprising that glycolysis is increased in tumor-involved areas. This phenomenon leads to increased uptake of glucose and FDG by transporter proteins. In contrast to its natural analog, intracellular FDG is rapidly converted into 18F-FDG-6-phosphate and becomes biochemically trapped in metabolizing tissues, commonly known as metabolic trapping. Accumulation of the radioisotope results in attenuated labeling by PET scanning, allowing an interpreting physician to judge the extent of tumor involvement.

Despite its widespread use in oncology, some limitations remain. Glucose consumption by granulocytes and mononuclear cells, which is noted in active infection, inflammatory disease, and radiated tissue, frequently results in false-positive detection. Another weakness is the limited spatial resolution in a reconstructed image, resulting in nondetection of tumors less than 1 cm in size. In addition, some troublesome factors, such as low-avidity tumors and uneven physical absorption of FDG in certain areas, often lead to misdiagnosis by the interpreting physician. Health care providers should always be aware of these circumstances in clinical practice.

**PET in the Staging of Esophageal Cancer**

Once esophageal cancer is diagnosed, mandatory tumor TNM staging based on the American Joint Committee on Cancer should be confirmed before specific treatment. Because prognosis and treatment are altered by the presence of adjacent lymph nodes or distant metastases, the choice of staging tools should be applied carefully. Popular modern imaging modalities include EUS accompanied by fine needle aspiration (FNA) biopsy, chest and abdomen CT scan, and PET.

Each method has its own advantages and disadvantages. EUS is the most powerful method to identify primary tumors and locoregional nodes, but the detection of disease is not reliable beyond 5 cm from the esophagus. CT is a popular, noninvasive tool for tumor staging, and is commonly applied to determine the presence of malignant lymph nodes and distant metastases. The accuracy may be impeded by normalized malignant lymph nodes or ones enlarged as a consequence of inflammation or other benign processes. Both conventional modalities are the current mainstay for staging per NCCN guidelines.

As PET becomes more popular, discussions of its efficacy in staging have been met with increasing enthusiasm. Because this modality detects metabolic alteration before structural change, most physicians expect it to be more accurate in imaging malignancies.

Several prospective studies have been published with variable results. For T staging, EUS is still believed to be superior to PET. A study by Lowe et al. recruited 75 patients to compare the differing modern imaging modalities. Both CT and PET had an accuracy of 42% in local tumor staging, which was inferior to EUS at 71%. Little et al. recently examined PET in superficial esophageal cancer and concluded that PET was not able to differentiate Tis from T1 by the degree of FDG uptake. In summary, PET is not the first choice in staging of primary tumor extent.

Unlike local staging of tumors, PET offers better detection of locoregional lymph node disease and distant metastases. PET is expected to provide more detailed information before an operation, which can
help avoid undertreating patients or performing unnecessary surgery. The real question is whether it provides better information than CT, which has been the first-line modality in staging for many years. In 1997, Block et al. reported that PET correctly identified 17 of 17 patients with metastatic disease, compared with 5 of 17 using CT, from a total of 58 patients with biopsy-proven esophageal cancer. Similarly, PET detected 11 of 21 patients with lymph node disease, compared with 6 of 21 using CT.

However, with the continued advancement of CT, PET may not offer such overwhelming advantages. More recent studies have shown that in detecting locoregional lymph node disease, PET offers sensitivity, specificity, and accuracy of 22% to 82%, 60% to 100%, and 48% to 83%, respectively (Table 1). The detection rate was not superior to CT but offered better specificity in most series. Sensitivity varied among studies, but this may be from differing gold standards for staging. Generally lower sensitivity for PET was reported in prospective studies in which patients were already preselected for surgery, and investigators relied on histopathologic examination of lymphadenectomy specimens for disease spread as the gold standard. The report by Lowe et al. reported a higher sensitivity for PET, but the gold standard for locoregional lymph node disease relied on FNA sampling using EUS and further sampling if suspicious lesions missed with EUS were seen by CT and PET. This may have biased the detection rate for PET and underestimated the true prevalence of locoregional disease. Similar findings were found in detection of distant metastases, with reported sensitivity, specificity, and accuracy of 22% to 82%, 89% to 93%, and 67% to 84%, respectively (Table 2). In a study by Lerut et al., PET correctly upstaged 5 patients (12%), preventing unnecessary resection of tumor. The reason for the superiority of PET may be its advantage in detecting disease outside the lung and liver. Moreover, novel integrated PET-CT provides 22% more information than PET alone through enabling additional structural analyses, resulting in a sensitivity of 96% and specificity of 59%, as seen in a prospective study in non–small cell lung cancer. Despite this advancement, mandatory histologic confirmation is still recommended to avoid a false-positive diagnosis.

Although PET is still far from thoroughly replacing conventional modalities in staging, it may play a complementary role. In fact, the combination of PET with conventional modalities is superior to any single imaging method, according to one prospective study. Nevertheless, in a study conducted by van Westreenen et al., the addition of PET failed to avoid unnecessary

<table>
<thead>
<tr>
<th>Author</th>
<th>Histology</th>
<th>Imaging Modality</th>
<th>No. Pts Enrolled</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
<th>P Value (Accuracy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yoon et al.</td>
<td>SCC</td>
<td>PET</td>
<td>81</td>
<td>30%</td>
<td>90%</td>
<td>82%</td>
<td>0.382</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CT</td>
<td></td>
<td>11%</td>
<td>95%</td>
<td>83%</td>
<td></td>
</tr>
<tr>
<td>Sihvo et al.</td>
<td>AC</td>
<td>PET</td>
<td>55</td>
<td>35%</td>
<td>100%</td>
<td>60%</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CT</td>
<td></td>
<td>42%</td>
<td>82%</td>
<td>58%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>EUS</td>
<td></td>
<td>85%</td>
<td>53%</td>
<td>72%</td>
<td></td>
</tr>
<tr>
<td>Sihvo et al.</td>
<td>AC</td>
<td>PET</td>
<td>55</td>
<td>35%</td>
<td>100%</td>
<td>60%</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CT</td>
<td></td>
<td>42%</td>
<td>82%</td>
<td>58%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>EUS</td>
<td></td>
<td>85%</td>
<td>53%</td>
<td>72%</td>
<td></td>
</tr>
<tr>
<td>Lerut et al.</td>
<td>SCC and AC</td>
<td>PET</td>
<td>42</td>
<td>22%</td>
<td>91%</td>
<td>48%</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EUS and CT</td>
<td></td>
<td>83%</td>
<td>45%</td>
<td>69%</td>
<td></td>
</tr>
<tr>
<td>Lowe et al.</td>
<td>SCC and AC</td>
<td>PET</td>
<td>75</td>
<td>82%</td>
<td>60%</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CT</td>
<td></td>
<td>84%</td>
<td>67%</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>EUS</td>
<td></td>
<td>86%</td>
<td>67%</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Flamen et al.</td>
<td>SCC and AC</td>
<td>PET</td>
<td>74</td>
<td>39%</td>
<td>97%</td>
<td>83%</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CT</td>
<td></td>
<td>63%</td>
<td>88%</td>
<td>85%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>EUS</td>
<td></td>
<td>22%</td>
<td>96%</td>
<td>78%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>EUS and CT</td>
<td></td>
<td>54%</td>
<td>90%</td>
<td>82%</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: AC, adenocarcinoma; EUS, endoscopic ultrasound; N/A, not applicable; NS, not significant; SCC, squamous cell carcinoma.
surgery, because exploratory surgeries were still needed for confirmation. In addition, 11% of patients had a false-positive diagnosis of distant disease because of a synchronous neoplasm or other cause, leading to unnecessary further investigation. Therefore, the advantage of adding PET in this situation is still questionable.

In conclusion, PET has an insensitive but specific detection rate for locoregional lymph node disease and a better detection rate for distant metastases. A meta-analysis of 12 studies confirmed this finding, showing a sensitivity rate of 0.51 (95% CI, 0.34–0.69) and 0.67 (95% CI, 0.58–0.76), and a specificity rate of 0.84 (95% CI, 0.76–0.91) and 0.97 (95% CI, 0.90–1.0) for detecting locoregional and distant metastases, respectively. The advantage is especially apparent in distant metastases, but with poorer performance in locoregional lymph node detection compared with EUS.

Use of PET in routine practice is still impeded by its high cost and inconclusive benefit against conventional methods. Because the spatial resolution of CT has increased with use of a multislice technique, PET is still far from completely replacing CT. Perhaps the value of applying PET in the staging of esophageal cancer is to provide an additional or alternative test to avoid unnecessary surgery when metastases outside of the lung and liver are suspected.

FDG-PET in the Assessment of Neoadjuvant Therapy

In advanced locoregional esophageal cancer, multimodality intervention has been the mainstay of treatment, starting with neoadjuvant chemotherapy with or without concomitant radiotherapy, followed by surgical resection. The most important factor for prognosis is achievement of a histologic complete response. Nevertheless, the histologic response is not commonly noted before an operation, and noninvasive methods have been studied as a surrogate for its evaluation.

Although EUS and CT cannot ascertain histologic response, PET is expected to offer some prediction of response even though absence of attenuation does not always equal complete histopathologic remission. A study by Swisher et al. compared the performance of PET, EUS, and CT before surgical intervention in 103 patients who completed preoperative chemoradiation. The study showed PET was more accurate in predicting pathologic nonresponse (76% vs. 68% and 62% in CT and EUS, respectively) using a standard uptake value (SUV) greater than 4 as a cutoff. Furthermore, an SUV less than 4 after chemoradiation significantly correlated with 18-month survival (77% vs. 34%; P = .01).

### Table 2  Prospective Studies of the Accuracy Between PET and Conventional Imaging Systems in Detecting Distant Metastases

<table>
<thead>
<tr>
<th>Author</th>
<th>Histology</th>
<th>Imaging Modality</th>
<th>No. Patients Enrolled</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
<th>P Value (Accuracy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luketich et al.</td>
<td>SCC and AC</td>
<td>PET</td>
<td>91</td>
<td>69.0%</td>
<td>93.4%</td>
<td>84.0%</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Sihvo et al.</td>
<td>AC</td>
<td>PET</td>
<td>55</td>
<td>53%</td>
<td>89%</td>
<td>76%</td>
<td>NS</td>
</tr>
<tr>
<td>Lerut et al.</td>
<td>SCC and AC</td>
<td>PET</td>
<td>42</td>
<td>77%</td>
<td>90%</td>
<td>86%</td>
<td>.094</td>
</tr>
<tr>
<td>Lowe et al.</td>
<td>SCC and AC</td>
<td>CT</td>
<td>75</td>
<td>81%</td>
<td>91%</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Flamen et al.</td>
<td>SCC and AC</td>
<td>EUS</td>
<td>74</td>
<td>74%</td>
<td>90%</td>
<td>82%</td>
<td>.004</td>
</tr>
</tbody>
</table>

Abbreviations: AC, adenocarcinoma; EUS, endoscopic ultrasound; N/A, not applicable; NS, not significant; SCC, squamous cell carcinoma.
Additional studies further validated the concept of PET predicting pathologic response, although various groups relied more on a percentage change in SUV than an absolute cutoff (Table 3). A systemic review by Westerterp et al. compared the accuracy of CT, EUS, and PET in assessing response to neoadjuvant therapy. In their analysis, CT was always feasible but had significantly lower accuracy than PET ($P < .006$) and EUS ($P < .003$). In contrast, EUS and PET had similar accuracy, but the former was not feasible in 6% of patients. In conclusion, the authors favored the clinical use of PET in assessing response because of its accuracy and feasibility.

Nevertheless, the concept was hampered because a study by Brink et al. failed to correlate percentage decrease of SUV with pathologic tumor regression grade in 20 consecutive patients, despite a significant decrease in SUV after radiochemotherapy. In addition, a retrospective study by Bruzzi et al. discovered that PET-CT had a low sensitivity, specificity, and accuracy of 57%, 46%, and 51.5%, respectively, for predicting pathologic response. One reason for this ambiguity is the high occurrence of therapy-induced esophagitis, in which active inflammation leads to the relative high FDG uptake in affected cells. However, the systematic review by Westerterp et al. showed the efficacy of PET in both chemotherapy and chemoradiotherapy trials, implying that the addition of radiation is not solely responsible for confounding the accuracy of PET in predicting histopathologic response.

PET can also be used to predict survival after induction therapy and before surgery. Many studies investigated this issue and reported that PET could differentiate patients with better or worse disease-free survival (DFS) and overall survival. This differentiation seems to be independent of whether patients undergo neoadjuvant chemotherapy alone or with concurrent radiotherapy (Table 4). One retrospective study showed that PET was equivalent to complete clinical response in predicting pathologic downstaging but superior in predicting DFS.

However, this interest in clinical practice is still impeded by several problems. First, the cutoff point of signal attenuation in studies remains diverse. A study by Mamede et al. recommended the absolute value of SUV for predicting DFS as opposed to its percentage change. Although the absolute value of SUV could be chosen as a cutoff point in predicting survival, other studies favored the percentage decrease of SUV or other methods (Table 4). This variation leads to obvious difficulties in integrating all data to apply a uniform standard for the use of PET. Another issue is the false-negative rate of detection of residual tumor, resulting in overestimation of treatment benefit.

These unsolved problems highlight the irreplaceable role of histologic response. Unless more advances in PET are made, it remains doubtful that it will be solely used to predict prognosis.

Perhaps the value of PET lies in early assessment of response to induction therapy. The major problem of preoperative therapy is the lack of early and reliable markers for predicting ultimate tumor response to avoid unnecessary treatment if the effect is limited. Because metabolism in tumor cells is altered earlier than size, many investigators believe PET may be able to overcome this dilemma.

In a prospective study, Weber et al. attempted to study the relation between early alteration of glucose metabolism and the ultimate response to chemotherapy. Using a cutoff value of a 35% reduction in initial FDG uptake, PET was able to predict clinical response with 93% sensitivity and 95% specificity 2 weeks after initiation of chemotherapy. This result was confirmed by a subsequent prospective study.

### Table 3 Reported Percentage Changes in Standard Uptake Value Pre- and Postchemoradiation Therapy Best Correlating With Prediction of Histologic Response

<table>
<thead>
<tr>
<th>Author</th>
<th>Study Design</th>
<th>No. of Patients</th>
<th>△SUV</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mamede et al.</td>
<td>Retrospective</td>
<td>25</td>
<td>32.3%</td>
<td>75%</td>
<td>62.5%</td>
<td>66.7%</td>
</tr>
<tr>
<td>Brücher et al.</td>
<td>Prospective</td>
<td>24</td>
<td>52%</td>
<td>100%</td>
<td>55%</td>
<td>N/A</td>
</tr>
<tr>
<td>Levine et al.</td>
<td>Prospective</td>
<td>64</td>
<td>10%</td>
<td>71.4%</td>
<td>66.7%</td>
<td>N/A</td>
</tr>
<tr>
<td>Port et al.</td>
<td>Retrospective</td>
<td>62</td>
<td>50%</td>
<td>77.8%</td>
<td>52.9%</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Abbreviations: △SUV, changes in standard uptake value; N/A, not applicable.

*Absolute decrease in SUV$_{\text{max1 hour}}$, which was calculated as the maximum value 1 hour post–radiopharmaceutical injection.
using the same 35% reduction in FDG uptake as a cut-off point, which also showed its prediction values in histopathologic response rate and survival times.39

These findings were applied in a clinical trial conducted by Lordick et al.,40 who integrated PET into the treatment algorithm for detecting early response to neoadjuvant chemotherapy. Using PET for reassessment 2 weeks after chemotherapy initiation, early metabolic response was determined as a decrement in the SUV of more than 35%. The results from this trial showed that prognosis differs between early metabolic responders and nonresponders, with a better survival outcome in the former (median overall survival not reached vs. 25.8 months; \( P = .015 \)). However, in the 50 metabolic responders, 21 patients still had confirmed histologic nonresponse, and their prognosis remained dismal despite being in this group, implying the robust role of histologic response.

Another question was raised regarding the management of metabolic nonresponders. The authors recommended future studies adding radiation or biologic response modifiers instead of proceeding to

Table 4 Cutoff Point for SUV, Decrease of SUV, and Other Methods for Predicting Histologic Response

<table>
<thead>
<tr>
<th>Author</th>
<th>Study Design</th>
<th>No. of Patients</th>
<th>Therapy</th>
<th>Cutoff Point</th>
<th>Survival (Better PET Responders* vs. Poorer Responders)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swisher et al.28</td>
<td>Retrospective</td>
<td>103</td>
<td>Chemoradiotherapy (CPT-11, taxane, 5-FU, and/or platinum-based)</td>
<td>SUV = 4</td>
<td>18-month survival: 77% vs. 34% (( P = 0.01 ))</td>
</tr>
<tr>
<td>Westerterp et al.37</td>
<td>Prospective</td>
<td>25†</td>
<td>Celecoxib (protocol therapy)</td>
<td>SUV_{BSAg} = 0.26</td>
<td>Significantly decreased recurrence-free period (( P_{\text{logrank}} = .001 ))</td>
</tr>
<tr>
<td>Downey et al.35</td>
<td>Prospective</td>
<td>17</td>
<td>Chemoradiotherapy (paclitaxel/cisplatin)</td>
<td>( \Delta \text{SUV} = 60% )</td>
<td>2-year DFS: 67% vs. 38% (( P = .055 )); 2-year overall survival: 89% vs. 63% (( P = .088 ))</td>
</tr>
<tr>
<td>Flamen et al.30</td>
<td>Prospective</td>
<td>30§</td>
<td>Chemoradiotherapy (cisplatin and 5-FU)</td>
<td>Major responders§</td>
<td>Median survival: 16.3 vs. 8.0 mo (( P = .01 ))</td>
</tr>
<tr>
<td>Brücher et al.29</td>
<td>Prospective</td>
<td>24§</td>
<td>Chemoradiotherapy (S-FU)</td>
<td>( \Delta \text{SUV} = 52% )</td>
<td>Median survival time: 22.5 vs. 6.7 mo (( P &lt; .0001 ))</td>
</tr>
<tr>
<td>Mamede et al.31</td>
<td>Retrospective</td>
<td>25</td>
<td>Chemoradiotherapy (CPT-11, taxane, 5-FU, platinum, and/or cetuximab-based)</td>
<td>SUV = 3.55**</td>
<td>Median survival: 19.4 vs. 9.5 mo (( P = .029 ))</td>
</tr>
<tr>
<td>Port et al.36</td>
<td>Retrospective</td>
<td>62</td>
<td>Chemotherapy (platinum-based)</td>
<td>( \Delta \text{SUV} = 50% )</td>
<td>Median DFS: 35.5 vs. 17.9 mo (( P_{\text{logrank}} = .03 )); 2-year DFS: 65.9% vs. 36.4%</td>
</tr>
</tbody>
</table>

Abbreviations: \( \Delta \text{SUV} \), changes in standard uptake value; 5-FU, 5-fluorouracil; CPT-11, irinotecan; DFS, disease-free survival; SUV, standard uptake value.

*Better PET responders are those with lower level of cutoff SUV, greater decrease than cutoff \( \Delta \text{SUV} \), or achieving major response. Poor PET responders are those not meeting the mentioned criteria.

†R0 resection.

‡SUV corrected for body surface area and plasma glucose concentration.

§Patients who received surgical resection.

¶Defined as post–chemoradiation therapy showing a complete remission or a quasi-complete response (almost complete disappearance of the primary tumor, a complete remission of all lymph node metastases observed on the pre–chemoradiation therapy PET, and the nonappearance of new lesions not seen on the pre–chemoradiation therapy PET).

**Averaged SUV of the entire tumor after therapy.
immediate operative resection to potentially improve survival outcomes.40

The use of PET in assessing response to neoadjuvant therapy was investigated by 2 other study groups, with differing conclusions.41,42 One notable difference between the studies was that Gillham et al.41 focused predominantly on adenocarcinoma histology, whereas Wieder et al.42 included only squamous cell carcinomas. The former found failure of PET to accurately predict histologic response, raising the issue of whether future studies with PET should distinguish between adenocarcinoma and squamous cell carcinoma histologies. Many articles cited herein did not distinguish between the 2 histologies, although most patients were of the adenocarcinoma subtype.

Song et al.43 also focused on patients with esophageal squamous cell carcinoma for using PET to assess histopathologic response after neoadjuvant radiotherapy. The authors noted that if analysis was limited to initially highly metabolically active primary tumors (SUV > 4), patients with complete pathologic response had a greater change in metabolic response (SUV) than pathologic nonresponders (87.9% vs. 68.4%; P = .006). However, this significant difference in change in SUV in the primary tumor did not translate for pathologic response or nonresponse in regional lymph nodes. More prospective trials are needed before expert panels can recommend the routine use of PET in early surveillance of neoadjuvant treatment.

Summary

Accumulating evidence has favored PET and PET-CT to be reliable modalities in staging and surveillance of postneoadjuvant response in esophageal cancer. This technology is not yet ready to replace conventional imaging methods, but may provide additional information in the detection of locoregional disease and distant metastases to avoid overtreatment. Nevertheless, further studies are needed to define the extent that routine use of PET and PET-CT improves overall outcomes for patients.

References

PET Imaging in Esophageal Cancer Management