Diagnostic Accuracy of Endoscopic Ultrasonography in Esophageal Cancer: A Single Center Experience

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Background/Aims: Determining the depth of tumor invasion and the presence of regional lymph node metastasis is important in deciding therapeutic strategies. We aimed to evaluate the diagnostic accuracy of EUS in detecting the depth of tumor invasion and regional lymph node metastasis.

Materials and Methods: A total of 141 consecutive patients underwent preoperative evaluation using EUS, CT, and PET CT from November 2005 to June 2009 in Pusan National University Hospital. We reviewed the patients’ medical records and compared EUS and pathologic findings.

Results: A total of 59 patients were included in the final analysis. The overall accuracy of EUS in predicting the correct T stage was 79.7% (95% CI, 66.8 – 88.6%). EUS accurately predicted T stage in 93.2% (95% CI, 82.7 – 97.8%) of T1 tumors, 79.7% (95% CI, 66.8 – 88.6%) of T2 tumors, and 86.4% (95% CI, 74.5 – 93.6%) of T3 tumors. Overall, EUS accurately predicted N stage in 83.1% of cases. EUS correctly predicted N stage in 91.4% of N0 tumors and 70.8% of N1 tumors.

Conclusions: Overall accuracy of EUS for the T and N staging of esophageal cancer was high. Thus, EUS is a useful diagnostic modality in determining the initial stage of esophageal cancer. (Korean J Helicobacter Up Gastrointest Res 2016;16:92-96)

Key Words: Esophageal neoplasm; Endosonography; Diagnosis

INTRODUCTION

The prognosis of esophageal carcinoma remains extremely poor despite advances in chemotherapeutic and surgical management. One reason for this is that the majority of patients have advanced disease at diagnosis. However, those with early-stage disease have significantly higher survival rates after surgical resection. Until now, surgery with or without neoadjuvant treatment has been considered the treatment of choice for advanced esophageal cancers. However, the 5-year survival rate in the resected group is still not higher than 30% to 35%.1,2

To optimize the selection of patients with esophageal cancer for curative or palliative treatment, it is important to determine the depth of infiltration of the tumor into the esophageal wall and the presence of malignant regional lymph nodes or distant metastasis. EUS has been shown to provide accurate assessment of the depth of tumor invasion and regional lymph nodes.3

The aim of this study was to evaluate the accuracy of EUS in detecting the depth of tumor invasion into the esophageal wall and regional lymph node metastasis.

MATERIALS AND METHODS

1. Patients

A total of 141 consecutive patients underwent preoperative evaluation using EUS, CT, and PET CT from November 2005 to June 2009 in Pusan National University Hospital (Busan, Korea). Of these, 59 patients (55 men and 4 women; mean age, 63.0±7.8 years) who underwent surgical resection were included in this study. The presence of esophageal carcinoma was confirmed by standard endoscopic biopsies performed in all patients before surgery. Patients in whom CT or PET CT showed evidence of distant metastasis were not considered candidates for surgery and were excluded from the study. Patients with high-grade malignant strictures that prevented the echoendoscope from being passed through the
length of the tumor were excluded. And patients who re-
ceived neoadjuvant treatment or other treatment were al-
so excluded from the study. All patients underwent
esophageal resection within 4 weeks of EUS.

This study was reviewed and approved by the
Institutional Review Board at Pusan National University
Hospital.

2. EUS

EUS was performed after an overnight fast with the
patient in left lateral position with the use of a mechan-
ical radial echoendoscope (GF-UM2000; Olympus Optical
Co., Tokyo, Japan) with variable frequencies of 5, 7.5, 12,
and 20 MHz by a single experienced endosonographer
(Kim GH) who had previously performed more than 1,000
examinations. Depth of tumor invasion (T stage) and
lymph node metastasis (N stage) were determined accord-
ing to the America Joint Commission on Cancer (AJCC)
TNM classification system:4 T1, invasion up to the third
wall layer (submucosa); T2, invasion into but not through
the fourth wall layer (muscularis propia); T3, invasion
beyond the fourth wall layer (adventitia); and T4, invasion
into the adjacent structures (i.e., aorta, pleura, lung, tra-
chea). Classification of regional lymph nodes used estab-
lished endosonographic criteria of echo texture, size,
shape, and border.5 Lymph nodes were considered to be
malignant if 3 or more of the following features were
present: a size greater than 5 mm, a sharp demarcation
of the borders, a round shape, and a central echo pattern,
which was homogeneous and echo poor.6-8 EUS classi-
fication of N stage was as follows according to the
sixth-edition AJCC TNM system: Nx, inability to assess re-
gional lymph nodes; N0, no regional lymph node meta-
stasy; and N1, regional lymph node metastasis.

3. Histopathology

Pathologic TNM classification was made on the esoph-
agectomy specimens. Esophagectomy by use of Ivor–Lewis
operation was performed in 51 patients (86.4%). Transhiatal
esophagectomy or minimally-invasive esophagectomy with
lymph node sampling was performed in 8 patients
(14.6%). Pathologic staging was assigned according to the
sixth-edition AJCC TNM system.

4. Statistical analysis

The sensitivity, specificity, positive and negative pre-
dictive values, and accuracy were calculated with 95% CIs
for each of the diagnostic measures for each individual T
and N stage, with pathologic stage as gold standard.
The statistical calculations were performed using the
SPSS version 12.0 for Windows software (SPSS Inc.,
Chicago, IL, USA).

RESULTS

A total of 59 patients (55 men and 4 women; age
range, 39∼84 years; mean age, 67 years) were included
in the study. The clinical, endoscopic, and pathologic tu-
mor characteristics are depicted in Table 1. Tumors were
located in the distal esophagus (n=21), mid-esophagus
(n=34) and proximal esophagus (n=4). All patients had
squamous cell carcinoma. Of them, 5 patients had histo-
logic subtype of basaloid carcinoma. Histopathologically,
most of tumors were well and moderately differentiated.

Table 2 shows the results of pathologic and EUS T
staging. The overall accuracy of EUS in predicting the
correct T stage was 79.7% (95% CI, 66.8∼88.6%). EUS
accurately predicted T stage in 93.2% (95% CI, 82.7∼
97.8%) of T1 tumors, 79.7% (95% CI, 66.8∼88.6%) of T2
tumors, and 86.4% (95% CI, 74.5∼93.6%) of T3 tumors.
Three patients with pT1 cancer were overstaged as having T2 lesions. Two patients with pT2 cancer were overstaged as having T3 lesions, and 1 patient with pT2 cancer was understaged as having T1 lesion. Six patients with pT3 cancer were understaged as having T2 lesions. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of EUS for individual T stages are shown in Table 3.

Pathologic and EUS N staging is depicted in Table 4. Overall, EUS accurately predicted N stage in 83.1% of cases. EUS correctly predicted N stage in 91.4% of N0 tumors and 70.8% of N1 tumors. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of EUS for individual N stages are shown in Table 5.

**DISCUSSION**

The majority of patients who are diagnosed with esophageal cancer have advanced diseases at presentation. At present, complete surgical removal of the tumor is the best treatment in these patients. Therefore, diagnostic process is focused on selecting patients who have no distant metastasis or local resectability. On the other hand, treatment for esophageal cancer has been changed in these days. Patients with superficial esophageal cancer confined to the mucosal layer can be cured with endo-

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**Table 2. Comparison of Pathologic and EUS T Stage in Esophageal Cancers (n=59)**

<table>
<thead>
<tr>
<th>Pathologic stage</th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>T4</th>
</tr>
</thead>
<tbody>
<tr>
<td>EUS stage</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>33</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>T2</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>T3</td>
<td>0</td>
<td>2</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>T4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Table 3. Diagnostic Accuracy of EUS by T Stage in Esophageal Cancers**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>91.6 (76.4~97.8)</td>
<td>95.7 (76.0~99.8)</td>
<td>97.1 (82.9~99.8)</td>
<td>88.0 (67.7~96.8)</td>
<td>93.2 (82.7~97.8)</td>
</tr>
<tr>
<td>T2</td>
<td>57.1 (20.2~88.2)</td>
<td>82.7 (69.2~91.3)</td>
<td>30.8 (10.4~61.1)</td>
<td>93.5 (81.1~98.3)</td>
<td>79.7 (66.8~88.6)</td>
</tr>
<tr>
<td>T3</td>
<td>62.5 (35.9~83.7)</td>
<td>95.3 (82.9~99.2)</td>
<td>83.3 (50.9~97.1)</td>
<td>87.2 (73.6~94.7)</td>
<td>86.4 (74.5~93.6)</td>
</tr>
</tbody>
</table>

Values are presented as percentage (95% CI).
Overall accuracy: 79.7%.

**Table 4. Comparison of Pathologic and EUS N Stage in Esophageal Cancers (n=59)**

<table>
<thead>
<tr>
<th>Pathologic stage</th>
<th>N0</th>
<th>N1</th>
</tr>
</thead>
<tbody>
<tr>
<td>EUS stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N0</td>
<td>32</td>
<td>7</td>
</tr>
<tr>
<td>N1</td>
<td>3</td>
<td>17</td>
</tr>
</tbody>
</table>

**Table 5. Diagnostic Accuracy of EUS by N Stage in Esophageal Cancers**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>91.4 (75.8~97.8)</td>
<td>70.8 (48.8~86.6)</td>
<td>82.1 (65.9~91.9)</td>
<td>85.0 (61.1~96.0)</td>
<td>83.1 (70.6~91.2)</td>
</tr>
<tr>
<td>N1</td>
<td>70.8 (48.8~86.6)</td>
<td>91.4 (75.8~97.8)</td>
<td>85.0 (61.1~96.0)</td>
<td>82.1 (65.9~91.9)</td>
<td>83.1 (70.6~91.2)</td>
</tr>
</tbody>
</table>

Values are presented as percentage (95% CI).
Overall accuracy: 83.1%. 
scopic resection. Patients with esophageal cancer beyond the muscle layer or regional lymph nodes seem to benefit from neoadjuvant chemotherapy before surgery.\(^{3,20}\) In this regard, accurate preoperative staging is important for determining optimal treatment option for esophageal cancer.

Over recent years, EUS has become a standard investigation in the T and N staging of esophageal cancer and is considered the locoregional staging modality of choice. EUS is considered to be the best modality for predicting the infiltration depth of esophageal cancer and the presence of malignant lymph nodes.\(^{11-13}\) In one study, EUS can accurately stratify patients into ‘early’ (T0-2 N0) or ‘advanced’ (T3-4 or N1) disease categories in 83% of patients, which is highly predictive of outcome and survival.\(^{12}\) In the present study, the T and N staging accuracy is comparable to that of past series evaluating EUS in esophageal cancer,\(^{11}\) as the overall accuracy of EUS for assessing the correct T and N stages was 79.7% and 83.1%, respectively.

EUS has some limitations, as this modality may involve understaging as well as overstaging. Overstaging of T2 tumor and understaging of T3 tumor appears to be a problem, because overstaging in T2 tumors may lead to an inappropriate administration of neoadjuvant treatment chemotherapy and understaging in T3 tumors may skip the chance of neoadjuvant treatment.

In our series, the relatively poor sensitivity of T2 tumors is not surprising; previous studies have shown that EUS evaluation of T2 tumors is generally less accurate than that for other degrees of infiltration.\(^{14,15}\) Tumor micro-invasion was found to be the most important cause of tumor understaging, whereas overstaging was mainly due to inflammatory changes surrounding the tumor and the tumor itself. In addition, the inability of EUS to clearly distinguish between the adventitial and the subadventitial layer is another source of error in the differentiation of T2 tumors that deeply infiltrate into the subadventitia and T3 carcinomas.\(^{16-18}\)

Our study has several limitations. Our data contains a narrow clinical spectrum of diseases, with patients who had T1 or T2 stage in 73%. In addition, all examinations were performed by a single endosonographer who was aware of clinical and endoscopic findings, so this might have influenced the interpretation of EUS.

In conclusion, the overall accuracy of EUS in the T and N staging of esophageal cancer was high. Thus, EUS is a useful diagnostic modality in determining the initial stage of esophageal cancer. However, it also has limitation in distinguishing T2 from T3 tumors.

REFERENCES