ROLE OF ENDOSCOPIC ULTRASOUND IN SUPERFICIAL ESOPHAGEAL CANCER

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SUMMARY. The recent increase in the incidence of superficial esophageal cancer and promising developments in potentially curative endoscopic therapies have placed endoscopic ultrasound in a central position with regard to decision making. This is a review of the literature to determine the role of endoscopic ultrasound and high frequency probe ultrasonography in the assessment of superficial esophageal carcinomas.

KEY WORDS: cancer, endosonography, esophagus.

INTRODUCTION

More than 90% of primary esophageal cancers are esophageal epithelial tumors (squamous cell carcinoma and adenocarcinoma). Marked epidemiologic changes have been observed over the last several decades. Until the 1970s, more than 90% of all esophageal cancers were squamous cell carcinoma. Over the last 40 years, esophageal adenocarcinoma has the fastest growing incidence rate of all cancers in the USA.1–4 This increase is most dramatic among white males. Currently, the majority of esophageal cancers in the western hemisphere are adenocarcinoma.2

Although esophageal cancer is an important cause of cancer mortality worldwide, it is relatively uncommon in North America. In the USA, estimated new cases and deaths due to esophageal cancer in 2007 are expected to be 15,560 and 13,940, respectively.5 The outcome depends on the depth of tumor invasion and presence of metastases. Given the extensive esophageal submucosal lymphatic network and absence of serosa,6 the risk of early nodal metastasis and local spread to surrounding tissues is common. Longitudinal, rather than segmental esophageal submucosal lymphatic drainage is probably the reason for skip metastasis in lymph nodes.7 A large portion of patients with esophageal cancer present with advanced stage, therefore, the prognosis is poor in the majority of cases.

STAGING OF ESOPHAGEAL CANCER

The outcome and treatment options of esophageal cancer depend on the stage of tumor. The degree of tumor invasion (T), the presence or absence of nodal metastasis (N), and distant metastasis (M) are used in the TNM classification for staging (Table 1).8 Accurate initial staging of esophageal cancer is critical, because initial triage of patients determines subsequent management. The initial evaluation of a patient diagnosed with esophageal cancer begins with the assessment of operative risk, investigation of the primary tumor region, and presence of metastatic disease. Computed tomography (CT) and/or positron emission tomography (PET) are used to evaluate for the presence of metastatic disease. Patients without evidence of distant metastasis should undergo locoregional staging. The precise differentiation of esophageal wall layers, direct imaging of the surrounding organs and tissues, and tissue sampling with fine needle aspiration (FNA) has allowed endoscopic ultrasound (EUS) to play a pivotal role in the staging of patients with esophageal cancer.

The transducer at the tip of an EUS scope emits ultrasound waves at several high frequencies. Higher frequency ultrasound improves resolution of the image but decreases the scanning depth. As in other locations within the gastrointestinal tract, the esophagus can be visualized as five layers with EUS scopes operating at frequencies from 5 MHz to 12 MHz.9 The layers are as follows: first hyperechoic layer, superficial mucosa; second hyperechoic layer, deep mucosa; third hyperechoic layer, submucosa; fourth hypoechoic layer, muscularis propria; and fifth hyperechoic layer, adventitia. The esophagus

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may be seen as nine layers with miniprobes operating at higher frequencies (20–30 MHz).

The detailed visualization of esophageal wall layers and surrounding tissues allows accurate tumor staging. Esophageal wall layers cannot be delineated with other imaging techniques such as CT and PET; therefore, the extent of tumor invasion cannot be determined as accurately as EUS with other imaging modalities. CT imaging relies only on the size and shape of a lymph node; however, EUS not only assesses the imaging characteristics such as size, shape, echotexture, and margins of a suspicious lymph node, but can also allow cytological evaluation of a suspicious lymph node by using FNA. With this method, a metastatic lymph node can be distinguished from reactive hyperplasia or inflammatory nodes. Celiac lymph nodes are the most important lymph node group to assess. In the setting of proximal and middle esophageal cancer, presence of celiac lymph node metastasis is a sign of distant metastasis and unresectability. These patients are staged as M1b. However, involvement of celiac lymph node with metastatic cells in distal esophageal or gastroesophageal tumors is considered as regional metastasis and staged as M1a. EUS accuracy in esophageal cancer staging has been evaluated in multiple studies; it was found to be the most accurate imaging modality in the assessment of tumor invasion and locoregional lymph node status.8–10

SUPERFICIAL ESOPHAGEAL CANCER

Superficial esophageal cancer is a terminology used for tumors confined to the mucosa or submucosa. Early esophageal cancer is a localized lesion with low risk of lymph node metastasis and a high potential for cure following complete resection. Recently, as a result of frequent use of endoscopic screening for upper gastrointestinal cancers and advances in endoscopic techniques to detect high-grade dysplasia and early esophageal carcinoma, the incidence of superficial esophageal cancer defined as Tis and T1 lesions have been increased in some Asian countries as well as the western world.20–22 Carcinoma in situ (Tis) is the earliest stage, in which malignant cells are confined within the epithelium and the lamina propria is intact.8 This is a histopathologic description and cannot be imaged endosonographically. When malignant cells invade the lamina propria, the tumor is then defined as a T1 lesion.8 T1 lesions can be subdivided into T1m (tumor invading lamina propria) and T1sm (tumor invading submucosa).23–30 The prognostic importance of the depth of tumor invasion required a more comprehensive subclassification of T1 lesions based on the depth of invasion. Mucosal lesions are subdivided into three groups: m1, carcinoma limited to the epithelium; m2, carcinoma with invasion into the lamina propria; and m3, carcinoma with invasion into but not through the muscularis mucosa. Submucosal lesions are also subdivided into three groups: sm1, lesions with invasion into the superficial one-third of submucosa (<200 μm); sm3, lesions with invasion into the deepest one-third of submucosa; and sm2, lesions with penetration into the intermediate one-third of submucosa (Fig. 1).

This subclassification is important for appropriate prognostication of superficial esophageal cancers as well as consideration of potentially curative endoscopic therapeutic options such as endoscopic mucosal resection (EMR),31–33 or endoscopic ablative therapies such as photodynamic therapy34–36 or argon plasma coagulation.37 The major advantage of EMR over endoscopic ablative therapies is the opportunity for histologic examination of the resected specimen. EMR can serve dual purposes – being both a staging tool and also having curative potential in early esophageal cancers. Recently published studies on both superficial esophageal adenocarcinomas and squamous cell carcinomas revealed virtually nonexistent lymph node metastasis with m1 and m2 lesions.38–43

Table 1  TNM classification system of esophageal cancer

<table>
<thead>
<tr>
<th>T-staging</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>Tx</td>
<td>Tumor not assessable</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>Tis</td>
<td>Tumor in situ</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor invading lamina propria (T1m) or submucosa (T1sm)</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor invading muscularis propria</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor invading through the muscle layer into the adventitia</td>
</tr>
<tr>
<td>T4</td>
<td>Tumor invading local structures</td>
</tr>
</tbody>
</table>

<table>
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<tr>
<th>N-staging</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>Nx</td>
<td>Nodal involvement not assessable</td>
</tr>
<tr>
<td>N0</td>
<td>No evidence of nodal involvement</td>
</tr>
<tr>
<td>N1</td>
<td>Evidence of nodal involvement</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>M-staging</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mx</td>
<td>Metastases not assessed</td>
</tr>
<tr>
<td>M0</td>
<td>No evidence of metastatic disease</td>
</tr>
<tr>
<td>M1a</td>
<td>Celiac nodes involved in lower esophageal cancer</td>
</tr>
<tr>
<td>M1b</td>
<td>Beyond locoregional node involvement i.e. cervical nodes in lower esophageal cancer and celiac nodes in upper esophageal cancer</td>
</tr>
</tbody>
</table>

Fig. 1  Subclassification of esophageal T1 tumors (m1: limited to the epithelial layer; m2: invades lamina propria; m3: invades into but not through muscularis mucosa; sm1–sm3: invades different thirds of the submucosa) (published with the permission of Springer). ep, epithelium; lpm, lamina propria mucosae; mm, muscularis mucosa; sm, submucosa; mp, muscularis propria.
Endoscopic therapies are performed for curative intent in m1 and m2 lesions. The risk of lymph node metastasis when there is invasion of the muscularis mucosa (m3) is approximately 7%, ranging between 4 and 12% of cases.\(^\text{38-43}\) When the tumor invades into the superficial submucosal layer, the average risk of lymph node metastasis is 15%, with a range of 0–32%.\(^\text{38-43}\) This increase in the prevalence of lymph node metastasis in patients with submucosal invasion is probably related to the rich submucosal lymphatic network. The presence or absence of lymph node metastasis has direct impact on the outcome of esophageal tumors. This is best demonstrated by the study of Westerterp \textit{et al.}, which showed a 5-year recurrence-free survival rate of 97% in patients with T1m1–3/sm1 lesions versus 57% in patients with T1sm2–3 lesions.\(^\text{41}\) Although the risk of lymph node metastasis is small with m3 and sm1 lesions, endoscopic therapies carry a potential risk for inadequate treatment. Therefore, the optimal treatment for these patients remains controversial and should be individualized. Surgical resection is considered as standard treatment for tumors with submucosal invasion. EUS with FNA may potentially play an important role in the risk stratification of early esophageal cancer by detecting malignant lymphadenopathy. Further studies are needed to accurately determine which patients with m3 and sm1 lesions would benefit from endoscopic therapies with potential curative intent. The indications and contraindications of endoscopic resection of superficial esophageal tumors are beyond the scope of this paper; Pech \textit{et al.} recently published a review on this topic.\(^\text{44}\)

**ROLE OF EUS IN SUPERFICIAL/EARLY ESOPHAGEAL CANCER**

Given the considerable morbidity and mortality of esophagectomy, accurate EUS staging of early esophageal cancer is crucial to choose among endoscopic, surgical, or palliative therapies. The ability to visualize different esophageal wall layers is the major advantage of EUS over other imaging modalities. EUS imaging with higher frequencies produces more detailed visualization of esophageal wall layers in trade off with depth of penetration. EUS is currently considered to be the most accurate noninvasive method to determine the depth of esophageal tumor invasion.

Until recently, most of the studies comparing EUS and CT focused on the staging of advanced esophageal malignancies. Increasing number of patients with early esophageal tumors and encouraging results from curative endoscopic therapies elicited the need for accurate staging of early esophageal cancers.

A study by Pech \textit{et al.} was the first prospective evaluation of the accuracy of EUS and CT on the TNM staging of early cancer in Barrett’s esophagus.\(^\text{45}\) T1 and >T1 could not be differentiated by CT. However, differentiation between T1 and >T1 using EUS was possible in all cases (with sensitivity, specificity, positive predictive value, and negative predictive value of 100%). On the other hand, even with the use of high-frequency probes, differentiation between T1m and T1sm was suboptimal; sensitivity of EUS for submucosal tumor invasion in the setting of Barrett’s esophagus was found to be only 27%. The overall accuracy of EUS for T-staging was 76%. EUS was also found to be superior to CT scan for N-staging. Sensitivity of EUS and CT was found to be 75 and 38%, respectively. Because the CT scan did not provide any information on TNM staging in patients with early cancer in Barrett’s esophagus beyond that of EUS, it was suggested to discontinue the use of CT in early cancer in Barrett’s esophagus.

EUS has been evaluated for use in patients with Barrett’s esophagus and high-grade dysplasia to detect occult malignancy. Falk \textit{et al.} evaluated the role of EUS (7.5 and 12 MHz) to detect endoscopically non-visualized tumors in nine patients with Barrett’s esophagus with high-grade dysplasia.\(^\text{46}\) One out of three patients with cancer was identified, but this lesion was overstaged. EUS incorrectly identified invasive carcinoma in two out of six patients with high-grade dysplasia, and correctly identified absence of carcinoma in four patients. Overstaging was attributed to esophageal wall inflammation, overlapping folds pulled up by the balloon, or tangential esophageal wall imaging. The authors concluded that conventional EUS could not reliably differentiate benign and malignant wall thickening in Barrett’s esophagus with high-grade dysplasia. However, in the study by Scotiniotis \textit{et al.} on the accuracy of EUS (7.5 and 12 MHz) in Barrett’s esophagus with high-grade dysplasia and intramucosal carcinoma, EUS detected all five cases of tumor with submucosal invasion based on disruption of the third sonographic wall layer and one case with lymph node involvement.\(^\text{47}\) EUS was false positive for submucosal involvement in one patient and for lymph node malignancy in four patients. The sensitivity, specificity, and negative predictive values of preoperative EUS for submucosal invasion were 100, 94 and 100%, respectively, while the values for lymph node involvement was 100, 81 and 100%, respectively. Presence of a nodule or stricture was found to be associated with increased likelihood of submucosal invasion.

There are several challenges in performing EUS on small early carcinomas. Localization of early esophageal tumors with the side-viewing EUS scopes can sometimes be difficult. Overdistention of the water-filled balloon surrounding the EUS transducer may compress the esophageal wall layers and compromise accurate tumor staging. As an alternative to the echoendoscope, small-caliber high-frequency EUS probes (15–30 MHz) can be introduced through the
working channel of standard endoscopes and placed over the lesion under direct visualization. Because the esophagus is filled with water, EUS probes do not need a balloon to obtain acoustic coupling. High-frequency probes produce nine esophageal layers. The mucosa consists of four layers; the first two (m1 and m2) represent the epithelium, the third layer (m3) is the lamina propria, and the fourth layer (m4) is the muscularis mucosa. The fifth layer is hypechoic and represents submucosa. The muscularis propria is composed of three layers; the sixth layer is the circular muscle, the seventh is an interface connective tissue, and the eighth layer is the longitudinal muscle. The ninth layer represents adventia. High-frequency ultrasound probes limit the penetration depth of the ultrasound beam; therefore, the visualization of mediastinal lymph nodes is suboptimal.

Larghi et al. initially staged 48 patients with Barrett’s esophagus with high-grade dysplasia and adenocarcinoma with EUS (5–20 MHz). Patients with disease confined to the mucosa underwent EMR. Patients with T1sm or deeper lesion or regional lymph node metastases were referred to surgery. The staging accuracy of EUS was found to be 85% (41 out of 48 patients). Surgical or EMR pathologic staging revealed that one patient was overstaged and six patients were understaged by EUS. Surgical pathology confirmed endosonographic submucosal invasion in seven out of eight patients. One patient with endosonographic T1m disease was overstaged. Submucosal invasion was identified on EMR specimens of 6 out of 15 (40%) patients with intramucosal adenocarcinoma staged by EUS. EMR following EUS provided valuable information to accurately stage patients with high-grade dysplasia and early cancer confined to the mucosa in the setting of Barrett’s esophagus.

Hasegawa et al. compared the accuracy of a high-frequency EUS probe (15 MHz) with a standard endoscopic (12 MHz) in preoperative staging of superficial esophageal carcinoma. The accuracy rates of the depth of invasion by the ultrasound probe were 86% (6 of 7 patients) for mucosal carcinoma and 94% (17 of 18 patients) for submucosal carcinoma, with an overall accuracy of 92% (23 of 25 patients); accuracy by EUS were 71% (5 of 7 patients) for mucosal carcinoma and 78% (14 of 18 patients) for submucosal carcinoma, with an overall accuracy of 76% (19 of 25 patients). The accuracy of lymph node metastasis was found to be 56% by ultrasound probes and 67% by EUS. The authors concluded that the ultrasound probe was more convenient to use and more accurate than EUS in the evaluation of the depth of invasion of superficial esophageal carcinoma. The study by Murata et al. accurately determined cancer limited to the lamina propria in 84% of cases with high-frequency ultrasound probes (15 and 20 MHz). Correct differentiation between mucosal and submucosal cancers was reported in 94% (46 of 49 patients). Overall accuracy of high-frequency ultrasound probes in 54 patients studied was 75%.

A prospective evaluation of high-frequency probe ultrasonography revealed limited accuracy for identifying invasive cancer in patients with high-grade dysplasia or intramucosal carcinoma in the setting of Barrett’s esophagus. High-frequency probe ultrasonography correctly diagnosed the presence or absence of tumor in six of nine patients (67%); three without cancer and three with a T1 lesion. Cancer staging was correct in only one out of three cases detected by high-frequency probe ultrasonography. The results of high-frequency probe ultrasonography were false negative in two esophageal cases, both of which had T1 lesion in the resected specimen. In only four out of nine patients, preoperative high-frequency probe ultrasonography findings were in complete correlation with postoperative pathologic findings.

The largest study prospectively evaluating staging in early esophageal cancer using high-frequency ultrasonic probes revealed an overall accuracy of 80%. However, the sensitivity for submucosal invasion fell to 48%. The location of tumor with submucosal invasion was found to play an important role in staging. Submucosal tumors located in the tubular esophagus (10 of 11 patients) were significantly better staged than submucosal tumors close to gastroesophageal junction (2 of 14 patients). Tumors with deeper submucosal invasion were also found to be better staged than those with superficial submucosal invasion. In addition, this study also showed that high-resolution endoscopy was as good as high-frequency ultrasound probe in the assessment of early esophageal tumor penetration. Although the endoscopic characteristics of esophageal lesions have been classified according to the Japanese system for early carcinomas, this system has been felt to be too complex and impractical for use in the west. The recent availability of high-resolution endoscopes – chroendoendoscopy as well as endoscopic therapeutic modalities – have increased interest in the endoscopic classification of these lesions. Further prospective studies on high-resolution endoscopy and macroscopic classification of superficial esophageal neoplasms in comparison with EUS are needed. High-resolution endoscopic classification of superficial esophageal neoplasms and EUS findings would potentially be complimentary to each other in therapeutic decision making.

A retrospective study evaluating 106 lesions (52 adenocarcinoma in Barrett’s mucosa and 54 squamous cell carcinoma) with high-frequency probe ultrasonography (20 or 30 MHz) had an accuracy, sensitivity and specificity to differentiate T1sm from T1m tumors of 73.5, 62 and 76.5%, respectively. No significant difference between the two frequencies was found. Among lesions with incorrect tumor invasion
assessed by high-frequency probe ultrasonography, 70% were erroneously overstaged as submucosal lesions, while histopathologic examination of these lesions (endoscopically or surgically resected specimens) revealed only mucosal cancer. Given the risk of overstaging, the authors suggested considering EMR for T1sm lesions in surgically high-risk patients. A risk factor for misinterpretation was the location of the tumor; almost 90% of tumors located in mid- to upper esophagus were correctly staged; however, less than half of the lesions in distal esophagus were correctly staged. The diagnostic accuracy that decreases progressively from the upper esophagus toward the gastroesophageal junction has also been described by others. This has been attributed to the difficulty in creating an acoustic interface by water filling at the gastroesophageal junction. Unfortunately, balloon-sheathed catheters did not overcome this problem. To the contrary, staging with water-filled lumen was found to be superior to the balloon-sheathed catheters, likely secondary to the pressure applied by the balloon to the mucosa. The histological type of esophageal cancer (adenocarcinoma and squamous cell carcinoma) did not significantly affect the accuracy of endosonographic staging of early esophageal cancers. Statistically nonsignificant greater accuracy for squamous cell carcinoma is likely due to the more proximal location of squamous cell carcinomas relative to adenocarcinomas within the esophagus, rather than histopathological architectural differences of these tumors. This assumption is supported by the study of Chemaly et al. which showed incorrect staging of all of the squamous cell carcinomas located in the distal esophagus. Only 19% of the squamous cell carcinomas were incorrectly staged in other locations of the esophagus. Presence of a nodule or protruding lesion is another factor that negatively affected the diagnostic accuracy of EUS. This is probably secondary to the changed pattern of the sonographic layer from inflammatory changes.

A recent evaluation of 55 patients with high-frequency probe ultrasonography (12 and 20 MHz) in superficial esophageal carcinomas (33 adenocarcinoma, 21 squamous cell carcinoma, 1 lymphoepithelial-like carcinoma) pathologically confirmed the absence of submucosal invasion in 86% of patients staged with T1m on EUS and confirmed the presence of submucosal invasion in 66% of patients staged with T1sm on EUS. The positive predictive value of EUS for submucosal invasion was 67%, negative predictive value was 86%, sensitivity and specificity were 88% and 62%, respectively, and diagnostic accuracy was 75%. The accuracy of EUS to determine lymph node metastases was 71%, with a negative predictive value of 84%. This imperfect nodal staging accuracy is likely due to the use of only endosonographic criteria, rather than EUS-FNA to identify malignant lymph nodes. Similar to other studies, the diagnostic accuracy of EUS was worse in the distal esophagus than in proximal to mid-esophagus. Presence of a nodule or protruding lesion is one of the factors that negatively affected the diagnostic accuracy of EUS. In the literature, the diagnostic accuracy of high-frequency probe ultrasonography for superficial esophageal cancer ranges between 65 and 93% (Table 2).

### Table 2: Accuracy of high frequency probe ultrasonography (HFPUS) in the assessment of the depth of invasion of superficial esophageal carcinoma

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of lesions</th>
<th>Frequency of HFPUS (MHz)</th>
<th>Histopathology</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Larghi</td>
<td>48</td>
<td>20</td>
<td>ACa</td>
<td>85</td>
</tr>
<tr>
<td>Hasegawa</td>
<td>25</td>
<td>15</td>
<td>SCC</td>
<td>92</td>
</tr>
<tr>
<td>Murata</td>
<td>54</td>
<td>15 and 20</td>
<td>SCC</td>
<td>75</td>
</tr>
<tr>
<td>May</td>
<td>100</td>
<td>20</td>
<td>81 ACa, 19 SCC</td>
<td>80</td>
</tr>
<tr>
<td>Chemaly</td>
<td>106</td>
<td>20 or 30</td>
<td>52 ACa, 54 SCC</td>
<td>74</td>
</tr>
<tr>
<td>Rampado</td>
<td>55</td>
<td>12 and 20</td>
<td>33 ACa, 21 SCC</td>
<td>75</td>
</tr>
<tr>
<td>Kawano</td>
<td>96</td>
<td>20</td>
<td>N/S</td>
<td>93</td>
</tr>
<tr>
<td>Yama(*)</td>
<td>17</td>
<td>20</td>
<td>SCC</td>
<td>67</td>
</tr>
</tbody>
</table>

ACa: Adenocarcinoma; N/S: not specified; SCC: squamous cell carcinoma.

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![Fig. 2 Algorithm for Suspected Early Esophageal Cancer. EUS is performed for T- and N-staging. Tumors that are T1N0 and less than or equal to 2 cm in size are amenable to endoscopic mucosal resection (EMR) with curative intent. If final pathology shows positive margins, submucosal infiltration or poorly differentiated histology, surgery should be performed. Otherwise, patients may be followed with endoscopic and endosonographic surveillance. Patients with nodes identified should undergo endoscopic ultrasound (EUS)–guided fine needle aspiration (FNA), if possible. FNA-negative patients may be candidates for EMR if the other criteria are fulfilled.](https://example.com)
The risk of missing a lymph node metastasis in a patient undergoing an EMR for an early esophageal malignancy has important implications. Originally, lymph node echo features such as size greater than 1 cm, echo-poor appearance, distinct margins and round shape were used to predict malignant involvement of a lymph node. The accuracy of predicting malignant involvement of a lymph node is 80% when all four endosonographic criteria are present in a lymph node; however, only 25% of malignant lymph nodes had all four criteria. Conventional EUS was found to be superior to high-frequency probe ultrasonography for N-staging in early esophageal cancers. Although there are a number of endosonographic criteria, EUS-FNA has been found to be superior to lymph node echo features alone. The important role of EUS in early esophageal cancer is not only limited to T-staging, but may also significantly change the management course in 20% of patients by detecting unsuspected malignant lymphadenopathy by EUS-guided FNA in patients with Barrett’s esophagus with high-grade dysplasia and intramucosal carcinoma. In this study, because of the presence of malignant lymphadenopathy, five out of 25 patients were excluded from EMR. To emphasize the importance of EUS-FNA over the use of only endosonographic criteria to exclude malignant lymph node involvement, two of the

Fig. 3  (A) Endoscopic picture showing esophageal nodule in the setting of Barrett’s esophagus. (B) Endoscopic ultrasound image showing a mucosal hypoechoic lesion consistent with superficial esophageal tumor without invasion of submucosal layer. (C) Endoscopic image showing esophagus following endoscopic mucosal resection.
positive lymph nodes were less than 10 mm in size in this study.

A recent study by Esaki et al. compared two different media for acoustic coupling. Overall accuracy of high-frequency EUS probes (20 MHz) for the diagnosis of invasion depth in superficial esophageal cancer was 78% by a jelly-filled method and 59% by a water-filled method.

Endosonographic evaluation of superficial esophageal tumors also has limitations. The accuracy of EUS is operator-dependent. Catalano et al. demonstrated that operator’s experience and machine-dependent factors play an important role in the accurate staging of esophageal carcinoma. Improvement in technology will probably decrease instrument-dependent factors causing artifacts. Fockens et al. showed a definite learning curve for endosonographic T-staging of esophageal tumors and concluded that 100 procedures are needed to achieve acceptable accuracy rates.

Taken together, these studies indicate that EUS is superior to CT for locoregional staging of esophageal cancer. In patients with macroscopically evident tumors, EUS has good accuracy to determine T-stage and for detecting and sampling nodal metastases. However, EUS – even with high-frequency probes – has limited accuracy in differentiating early tumors that are confined to the mucosa from those that invade the submucosa. In these cases, EMR is useful for staging and may be curative in superficial lesions.

CONCLUSION

The recent increase in the incidence of superficial esophageal cancer and promising developments in potentially curative endoscopic therapies have placed EUS to a central position in decision making (Figs 2, 3). EUS should be performed to identify potential candidates for EMR. These include patients with T1 disease confined to the mucosa, well-differentiated histopathology, with a tumor size less than 2 cm and no suspicious adenopathy. Suspicious nodes should be sampled via EUS-guided FNA, if possible. Patients who do not meet these criteria should be treated surgically or referred for neoadjuvant therapy protocols. EUS cannot reliably differentiate between T1m and T1sm disease, and may not supplant the importance of histopathology on the EMR specimen. Patients with T1sm lesion on histology should be offered surgery as this stage is associated with a higher risk of residual cancer and also of lymph node metastasis. Because of its inability to exclude T1sm, EUS may not be accurate enough to select cancer patients for ablative therapies such as photodynamic therapy and Argon plasma coagulation, if EMR is not also performed. In patients with Barrett’s esophagus with high-grade dysplasia, EUS is primarily useful for the evaluation of discrete lesions prior to EMR. The role of EUS in patients with flat dysplastic Barrett’s is controversial.

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