—Original Article—

The application of linear endoscopic ultrasound in the patients with esophageal anastomotic strictures

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ABSTRACT

Objectives: To evaluate the role of linear endoscopic ultrasound (EUS) in the diagnosis and treatment of the anastomotic stricture after esophagectomy for locally advanced esophageal cancer (EC). **Materials and Methods:** A retrospective analysis was performed in patients undergone EUS assessment and endoscopic treatment for anastomotic stricture after esophagectomy for locally advanced EC from January 2010 to December 2014 at Shengjing Hospital. The linear EUS was performed in all the patients to assess the thickness of the esophageal wall, the length and width of the lesion, and to evaluate the severity of anastomotic stricture. According to the EUS features of the lesion, different endoscopic therapy were performed. **Results:** There were 92 patients enrolled in this study. All the lesions of the patients were assessed by EUS. Eighty-six patients had cicatricial stricture of the esophagus confirmed by EUS, and were treated by endoscopic balloon dilation. Five patients were suspected to have tumor relapses, and the other one had lymphatic metastasis. All the six patients were undergone endoscopic metal stent implantation. The EUS diagnoses of all the patients were confirmed by pathological biopsy. **Conclusion:** Linear EUS is safe and effective for distinguishing the nature of the anastomotic stricture, and should be performed before endoscopic or surgical treatment.

Key words: Anastomotic stricture, endoscopic treatment, endoscopic ultrasound, esophagectomy

INTRODUCTION

Esophageal cancer (EC) is one of the most common malignant tumors, which takes 300,000 lives away every year.[1] Current comprehensive therapy with the dominant of surgeries is vastly used in the treatment of this disease. As one of the most common postoperative complications, anastomotic stricture always occurs after the surgery and brings the patients difficulty in swallowing and other psychological burden, which seriously compromising the life quality of the patients.

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Most of the anastomotic strictures after esophagectomy are cicatricial anastomotic strictures, and a small part is related to tumor recurrence.[2,3] The diameter of the anastomotic stricture which may induce the onset of symptoms is <10 mm in general condition. At present, the most widely used examination methods are gastroscopy, gastrointestinal (GI) contrast examination, computed tomographic (CT), and endoscopic ultrasound (EUS).[4] However, the use of linear EUS was rarely reported. In this study, we use linear EUS to examine the anastomotic stricture and to evaluate the nature of stricture.

MATERIALS AND METHODS

This was a retrospective study evaluating the role of EUS in the treatment of esophageal anastomotic strictures after the EC surgery. Written informed

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consent was obtained by all patients before the procedure. This study was approved by the Institutional Review Board of China Medical University in accordance with the Helsinki Declaration.

All the relevant medical records of patients with anastomotic stricture following esophagectomy or cardia carcinoma resection from January 2010 to December 2014 at Shengjing Hospital of China Medical University were collected.

The upper GI tract contrast studies, gastroscopy with biopsy, CT and EUS were performed in each patient. The upper GI contrast study was used to evaluate the length and severity of the stricture. The gastroscopy was used to identify the stricture location and length and to get the specimen for pathologic examination. CT scan of the chest and abdomen with intravenous contrast was performed to define the local extent, nodal involvement, and metastasis of EC. EUS was performed to show the length, width and severity of the stricture.

The EUS characters of anastomotic stricture pathogenesis, including scar stenosis and tumor recurrence, were recorded and compared.

Devices

All examinations were carried out by two experienced endosonographers with an EUS (Pentax EG3870 UTK with Hitachi EUB-6500).

Procedure

Place the linear ultrasonic probe to the anastomotic stricture of esophagus and rotate the probe for 360° for scanning. The distal walls of the GI tract could be observed when the probe travels through the stricture, meanwhile, check whether there were lymph nodes outside the esophageal wall. During the scanning of the anastomotic stoma, the thickness of the esophageal wall, the length of anastomotic stricture and the width of anastomotic stoma should be brought to the forefront. Elastography could be adopted for those suspected as any signs of recurrence or metastasis.

Statistical analysis

The data were analyzed using SPSS version 18 (SPSS Inc., Chicago, IL, USA). For analysis of the EUS characters difference of anastomotic stricture with different pathogenesis, including scar stenosis and tumor recurrence, three separate independent samples *t*-tests were used to compare the two groups on the thickness, length and width in EUS. $P = 0.05$ was considered significant for all statistical tests.

RESULTS

Patient characteristics as well as tumor histology and staging are presented in Table 1. There were 92 patients enrolled in this study, including 78 males and 14 females. The patients aged from 43 to 83 years, with a median age of 65 years. The predominant histology was adenocarcinoma ($n = 66$, 71.74%) while 28.26% were squamous cell carcinoma ($n = 26$). Prior to esophagectomy, nearly two-thirds of patients presented with stage III disease ($n = 58$, 63.04%), while one-third had stage II ($n = 34$, 36.96%). The onset time of difficulty in swallowing was 33 days to 15 months. All the patients were found with strictures under gastroscopy. The gastroscope cannot pass through strictures in 88 patients. The CT scan was given to all and found enlargement of lymph nodes in the mediastinum in one patient. The patients were subjected to EUS before the endoscopic therapy to evaluate the nature of the lymph node and of the anastomotic stricture.

Table 1. Patient characteristics, histology, and staging

Characteristic	*n* (%)
Total patients	92 (100.00)
Gender	
Male	78 (84.78)
Female	14 (15.22)
Age (years)	
Median age	65
Range	43-83
Tumor histology	
Adenocarcinoma	66 (71.74)
Squamous cell carcinoma	26 (28.26)
Preoperative stage	
II	34 (36.96)
III	58 (63.04)
Tumor recurrence	
Yes	5 (54.34)
No	87 (95.96)
Stage of disease after endoscopic treatment	
NED	87 (95.96)
II	3 (3.26)
III	1 (1.09)
IV	1 (1.09)
Endoscopic treatment	
Balloon dilatation	86
Metal stent implantation	6

NED: No evidence of disease

Scanning was given successfully to all of the 92 patients, 86 out of which were suspected to have cicatricial stricture of the esophagus in the EUS. The ultrasound endoscope found the esophageal wall has a 5-layer structure, while which was merged into a low-level echo in the anastomotic stoma. The thickness of anastomotic stoma wall was 2-4 mm, length was 6-8 mm and the width was 2-5 mm. There was no lymphatic metastasis outside the esophageal wall [Figure 1]. Balloon dilatation under endoscope was given for treatment, after which, gastroscope could travel through the anastomotic stoma for pathological examination of the digestive tract and visualize inflammation changes, no malignancy was found.

Tumor recurrence was suspected in EUS in five patients and visualized no 5-layer structure of the esophageal wall but a low-level echo with a thickness over 1 cm. The texture of the lesion was harder than the normal esophageal wall found by EUS elastography. The low-level echo was found with a length over 1cm in the both sides of the anastomotic stoma adjacent to esophagus and stomach, the width of the anastomotic stoma was 2-5 mm. There was no lymphatic metastasis outside the esophageal wall [Figure 2] in these five patients. Four of the five patients were found with tumor recurrence at the side adjacent to esophagus. A deep biopsy under EUS was performed in these four patients. One of the five patients had tumor recurrence at the side adjacent to the stomach, and the relevant specimen was obtained by gastroscopy in the stomach after small balloon dilation. The endoscopic metal stent implantation was performed in all of the five patients.

An enlarged lymph node pressing anastomotic stoma was found by EUS in one patient, and lymphatic

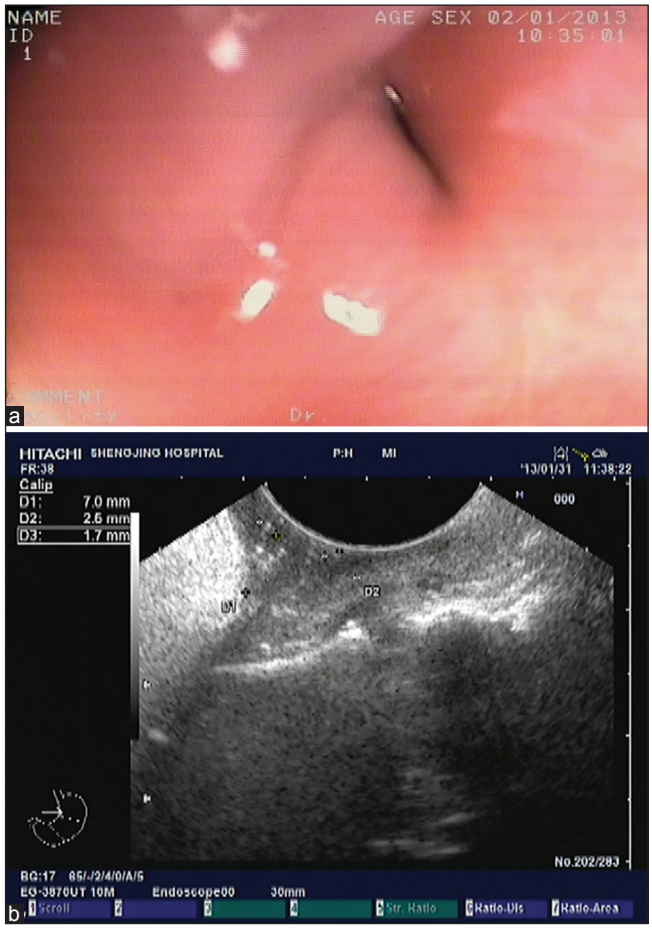

Figure 1. (a) The gastroscopy showed anastomotic stricture (b) The endoscopic ultrasound indicated the esophageal wall had 5-layer, however the location of anastomotic stoma was merged into a low level echo area. The length of anastomotic stoma wall was 7 mm (D1), the thickness was 2.5 mm (D2) and the width was 1.7 mm (D3). There was no lymphatic metastasis outside the esophageal wall

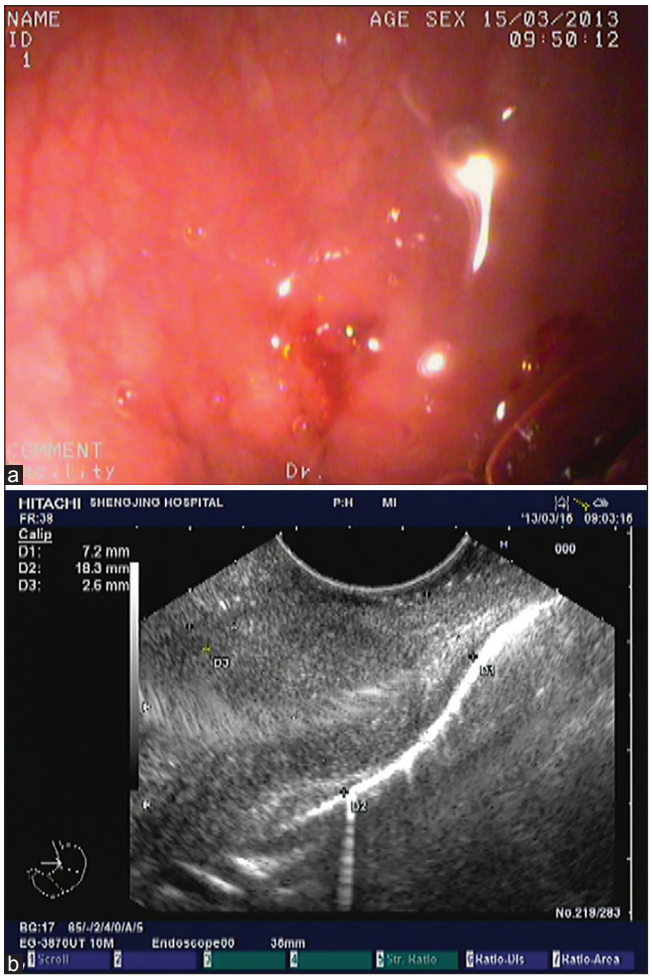

Figure 2. (a) Gastroscopy image obtained revealed anastomotic stoma occlusion (b) Endoscopic ultrasound visualized no 5-layer structure of the esophageal wall but a low level echo area, the thickness of which was 18.3 mm (D2). The normal 5-layer structure of the esophageal wall could be found with 7.2 mm (D1) in thickness, and 2.6 mm (D3) in width. There was no lymphatic metastasis outside the esophageal wall

metastasis was suspected. The EUS found the thickness of esophageal wall was 2-4 mm with a clear 5-layer structure. The length of anastomotic stoma was <1 cm. An oval heterogeneous hypoechoic structure with the size of 45 mm × 32 mm was found outside the esophageal wall. The texture of the hypoechoic structure was harder than the normal esophageal wall. In EUS, the structure was found to be pressing to the esophageal wall and the anastomotic stoma locally. The lymphatic metastasis was suspected and was confirmed by EUS guided fine needle aspiration and pathologic histology. The endoscopic metal stent implantation was performed in this patient [Figure 3].

The analysis of the EUS characters difference of anastomotic stricture with different pathogenesis, including scar stenosis and tumor recurrence was shown in Table 2. The thickness and length of the anastomotic stricture in EUS were significant larger in patients with tumor recurrence than scar stenosis, the *P* values were all smaller than 0.001 in the two comparisons. The width of the lesion were significant smaller in patients with tumor recurrence than scar stenosis ($P = 0.001$).

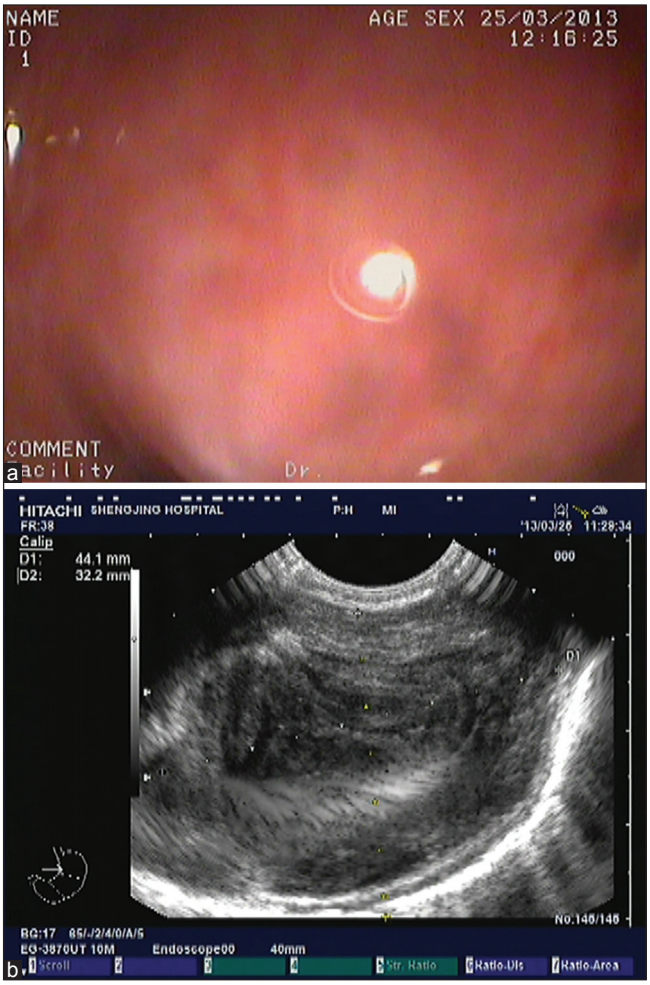

Figure 3. (a) Extrinsic prominence of esophageal wall above anastomotic stoma was seen in gastroscopy image (b) The thickness of esophageal wall was 2 mm in endoscopic ultrasound (EUS) and with clear 5-layer structure. An oval heterogeneous low level echo mass with an area of 45 mm × 32 mm was found outside the esophageal wall. Elastography found the texture was harder than esophageal wall. The mass oppressed the esophageal wall and the anastomotic stoma locally. EUS guided fine needle aspiration was applied to the lymph nodes and tumor metastasis is confirmed by pathologic histology

DISCUSSION

The treatment methods for anastomotic stricture after EC surgery currently available are including bougienage, laser, microwave ablation, balloon dilatation, permanent and temporary stent dilation.[5-8] The principle of treatment for cicatricial stricture is different from that of malignant stricture. Thus, the nature of stricture should be clarified before the treatment.

Gastroscopy is the most commonly used method in the examination after esophageal carcinoma resection. Due to its limitation, only the mucosa of the digestive tract could be observed under gastroscopy, leaving out other layers of the digestive tract and structures outside the digestive tract. The diagnoses yield of gastroscopy for cancer recurrence without involving the mucosa is limited, let alone to the recurrence in the stomach wall and enlargement of lymph nodes outside the wall.[9,10] As for the gastroscopy for anastomotic stricture, the pathological examination may only find cicatricial tissue and mucosa inflammation. The recurrence at the early stage might be misdiagnosed.

Computed tomographic scanning could be adopted for observing the thickness of digestive tract wall and assess whether there is enlargement of lymph nodes in the mediastinum, while it is difficult to distinguish the incrassation of anastomotic stoma induced by inflammatory reaction and recurrence, and hence the CT scanning is not accurate for diagnosing the recurrence at the early stage, but it could be used for observing the conditions of mediastinal lymph nodes.[11,12]

Table 2. Statistical analysis of anastomotic stoma stenosis with different pathogenesis

Features of the stenoses	Scar stenosis group	Tumor recurrence group	*t*	*P*
n	86	5		
Thickness (mm)	3.5±0.50	15.8±1.58	−17.363	<0.001
Length (mm)	6.9±0.64	17.2±1.99	−11.461	<0.001
Width (mm)	3.6±0.52	2.8±0.24	3.303	0.001

The difference between both groups was statistically significant

Endoscopic ultrasound could be used for visualizing the layer structure of digestive tract wall and the echoes, facilitating the finding of small pathological changes. It is mostly applied for diagnosing esophageal carcinoma and gastric cancer and provides a better tumor node metastasis staging for the guidance of subsequent treatment.[13,14] An important limitation of EUS is that a benign anastomotic stricture precluding passage of an endoscope after cervical esophagogastrostomy will develop in approximately 30% of patients[15] Flamen *et al*.[4] reported a case series, which indicated that in 84.6% (11/13) patients full passage of the echoendoscope was impossible, precluding accurate EUS diagnosis. However, in this study, the linear scanning EUS was adopted for scanning the anastomotic stoma. The ultrasound probe is installed at the head end of the endoscope, which makes a better contact with the scanning sites and good imaging effect. The scope can be placed to the anastomotic stoma, rather than passed the stoma. Radial EUS might fail because it is very difficult for the probe to pass through the anastomotic stoma. Although a microprobe may get through the partial anastomotic stoma, the imaging quality is inferior to that obtained by linear EUS.

Through the statistical analysis of the scar stenosis group and tumor recurrence group, we found the clear differences in thickness, length and width of anastomotic stricture between them. We can summarize the EUS imaging characteristics in order to judge the nature of anastomotic stricture. The benign strictures of the anastomotic stoma are mostly induced by suturing and inflammatory reactions[16] With EUS, a 5-layer structure of digestive tract wall could be visualized, and the accurate measurement of its thickness, the length and width of nastomotic stricture could also be obtained.[17,18] Cicatrical stricture shall be suspected if the EUS images of gastroesophageal anastomotic stoma meet the following criteria:

1. A clear 5-layer structure of anastomotic stoma is seen, and the wall thickness is <1 cm;
2. The anastomotic stricture is <1 cm; and
3. No lymphatic metastasis outside the esophageal wall is seen.

Strictures induced by tumor recurrence shall be suspected if the EUS images of gastroesophageal anastomotic stoma meet the following criteria:

1. The 5-layer structure of anastomotic stoma disappeared and merged into low-level echo, the wall thickness is larger than 1 cm, and elastography finds the texture was harder than the esophageal wall;
2. The low-level echo was found with a length over 1 cm in the both sides of the anastomotic stoma adjacent to esophagus and stomach;
3. Lymphatic metastasis outside the esophagus wall is seen and pressing the digestive tract wall.

For the recurrent stricture, the pathological diagnosis could be performed based on the clear layer structure of the digestive tract wall and features of the echo and combined with deep biopsy and fine needle puncture.[18] For the patients whose anastomotic stoma might be covered with cicatricial tissues, cicatricial inflammations are always obtained by gastroscopy if the tissues are not broken by the recurrent lesions, leading to delayed diagnosis. While during the scanning of linear EUS, the biopsy forceps are inserted into the lesion under the guidance of endoscope for deep biopsy, which could significantly improve the positive rate of the biopsy and avoid bleeding and perforation. For the enlarged lymph nodes are suspected as recurrence outside the esophageal wall, the cytologic examination and histological examination could be performed according to the samples collected by accurate fine needle puncture into the specific site of digestive tract and periphery areas under the guidance of the high resolution images of EUS. In addition, the three-dimensional reconstructing function, second harmonics imaging, and elastography also could help the physician with more information in the EUS examinations.[19-22]

Although the EUS obtains high-resolution images, locates and measures accurately, under which, deep biopsy in the digestive tract wall and fine needle puncture into the tissues outside the wall could be performed, the operation and the image interpretation are profoundly limited by the professional skills of the physician. Therefore, summarization of the features of the images and targeted scanning will greatly help the relevant physicians. As we all know, linear echoendoscope is oblique-view, so forward-viewing visualization is not optimal with it. It should be introduced into the gut lumen gently to avoid damage to the gut wall and perforation. Moreover, it cannot replace pathologic diagnosis since it is only a modality of radiology. So specimen should be obtained in the cases suspective of recurrent malignancies for biopsy.

CONCLUSION

Endoscopic ultrasound could distinguish the nature of the anastomotic stricture, and should be considered as an effective and safe examination method before endoscopic or surgical treatment.

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