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Fluoroscopic guidance biopsy for severe anastomotic stricture after esophagogastrostomy of esophageal carcinoma

A STROBE-compliant article

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Abstract

To determine the safety and effectiveness of fluoroscopic guidance biopsy in the diagnosis of serve anastomotic stricture after esophagogastrostomy for esophageal carcinoma.

A total of 55 patients with severe anastomotic stricture were enrolled for forceps biopsy between June 2013 and July 2017. Chest computed tomography (CT) and esophagogram were used to determine the location and extent of stricture. Specimens were collected from the site of stricture by using biopsy forceps under fluoroscopic guidance. Stooler's dysphagia score was compared before and after treatment.

The technical success rate of fluoroscopic guidance biopsy was 100%, with no serious complications occurred. A total of 38 patients were diagnosed as benign stricture, of which, 2 patients were further diagnosed as cancer by further biopsy, with a missed diagnosis rate of 5.3%, and 1 patient developed squamous cell carcinoma after 5 months. Thus 20 cases were diagnosed as cancer, 3 cases were adenocarcinoma and 17 cases were squamous cell carcinoma. Balloon dilation was performed for 20 patients (33 times) of benign stricture, and 9 patients (10 times) of malignant stricture. A total of 26 esophageal covered stents were implanted for benign restenosis after repeated balloon dilation. A total of 8 esophageal covered stents were implanted for malignant stricture. After esophagus stenting, dysphagia was immediately alleviated. The dysphagia score decreased from 3.4 ± 0.1 to 0.7 ± 0.1 ($P < .001$) after treatment.

Fluoroscopic guidance biopsy is a safe and effective procedure for directing appropriate treatment of anastomotic stricture after esophagogastrostomy, and it may be an alternative approach for patients who cannot tolerate fibergastroscopy.

Abbreviations: CI = confidence Interval, CT = computed tomography, SEM = standard error of mean.

Keywords: anastomotic stricture, biopsy, esophageal cancer, fluoroscopy, pathology

1. Introduction

Dysphagia due to anastomotic stricture is a common complication of esophagogastrostomy in patients of esophageal carcinoma,[1,2] which can lead to malnutrition and seriously impair the quality of life of patients. The objective of treatment is to relieve the dysphagia from esophageal obstruction.[3] Anastomotic stricture can be detected either by radiologic imaging or direct visualization. However, the radiologic or macroscopic examination sometimes is nonspecific, and pathologic finding often is required to establish a definitive diagnosis.[4,5] Endoscopic mucosal biopsy and brush cytology under direct visualization are the standard procedures.[4,6] Fibergastroscopy and biopsy are often used in patients with moderate anastomotic stricture; however, this examination is difficult in patients with severe anastomotic stricture. A severely stenosed esophagus may be too narrow to pass through a fibergastroscopy; moreover, there is a risk of hemorrhage during the fibergastroscopy and biopsy. Currently, the fluoroscopic guidance forceps biopsy was used to determine the pathological cause of anastomotic stenosis after cholangiojejunostomy [7] and severe airway stenosis [8] in our department. This retrospective analysis involved 55 patients with severe anastomotic stricture after esophagogastrostomy in patients of esophageal carcinoma. Our study is to determine the feasibility, safety, and effectiveness of fluoroscopic guidance biopsy in the diagnosis of serve anastomotic stricture, and its value for establishing appropriate treatment strategies.

2. Materials and methods

2.1. Patients

This retrospective study was approved by the ethics committee of Zhengzhou University. Informed consents were obtained from all patients in accordance with the guidelines and regulations for

Editor: Heye Zhang.

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This work was supported by the National Natural Science Foundation of China (Grant No. 81501569) and the National 863 Plan of China (Grant 2015AA020301).

The authors report no conflicts of interest.

The author(s) of this work have nothing to disclose.

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Medicine (2018) 97:37(e12316)

Received: 2 June 2018 / Accepted: 13 August 2018

http://dx.doi.org/10.1097/MD.0000000000012316

clinical study. Between April 2012 and June 2017, 55 patients (39 men and 16 women), with a mean age of 66.5 ± 1.4 years (95% CI, 63.6–69.4 years) were admitted to our department with severe dysphagia due to anastomotic stricture after esophagogastrostomy. All these patients were symptomatic and selected by record review. Chest computed tomography (CT) showed secondary signs of severe esophageal stricture, such as thickening of esophageal anastomotic stoma and proximal extension. Esophagogram via oral contrast and fibergastroscopy were administered to confirm stricture. Patients showed severe dysphagia due to anastomotic stricture after esophagogastrostomy but failed to routine fibergastroscopy owing to severe anastomotic stricture (<5 mm in diameter) were enrolled. This study excluded patients with esophago-tracheal fistula, esophageal mediastinal fistula, bleeding tendency, severe systemic failure, or a short survival (<3 months).

2.2. Fibergastroscopy

Routine fibergastroscopy was unsuccessful due to severe stricture in all patients prior to intervention, which showed that the stenosed segment too narrow to tolerate fibergastroscopy. Post-interventional fibergastroscopy was used to study the change of anastomotic stricture about 1, 4, and 24 weeks after balloon dilation or stenting (Fig. 1).

2.3. Fluoroscopic guidance biopsy and treatments

Fluoroscopic guidance biopsy and treatments were performed by 2 operators with more than 10 years experience. The pre-interventional workup consisted of routine blood examination, electrolyte assay, electrocardiogram, and chest CT to localize the lesion of esophagus. A total of 5 mL to 10 mL of ioversol was used for per oral esophagogram to determine the location, length, and severity of anastomotic stricture (Fig. 2A). A total of 5 mL of lidocaine was toke for local anesthesia of oral cavity, moderate sedation was provided for psychentonia patients. The patient's face shifted to the right and promptly aspirated the sputum to protect airway from aspiration. Over a hydrophilic guide wire, a 5-French multipurpose catheter (Terumo Holding, Beijing, China) was introduced through the mouth and throat, into the gastral cavity. Ioversol was injected through catheter to confirm that the catheter was located in the gastric cavity. A stiff guide wire was inserted through catheter into gastric cavity. The 9–12F long sheath was introduced over the stiff guide wire (0.035 in. × 260 cm) to the site of anastomotic stricture; a biopsy forceps was then introduced through the sheath. Under fluoroscopic guidance, 2 or 3 specimens of grain size were obtained from different parts of esophageal lesions for histopathological analysis (Fig. 2B). An intestinal feeding tube was implanted via nasal cavity for enteral nutrition before further interventional treatments. The esophageal covered stents (Nanjing micro-tech Medical Polytron Technologies Inc,

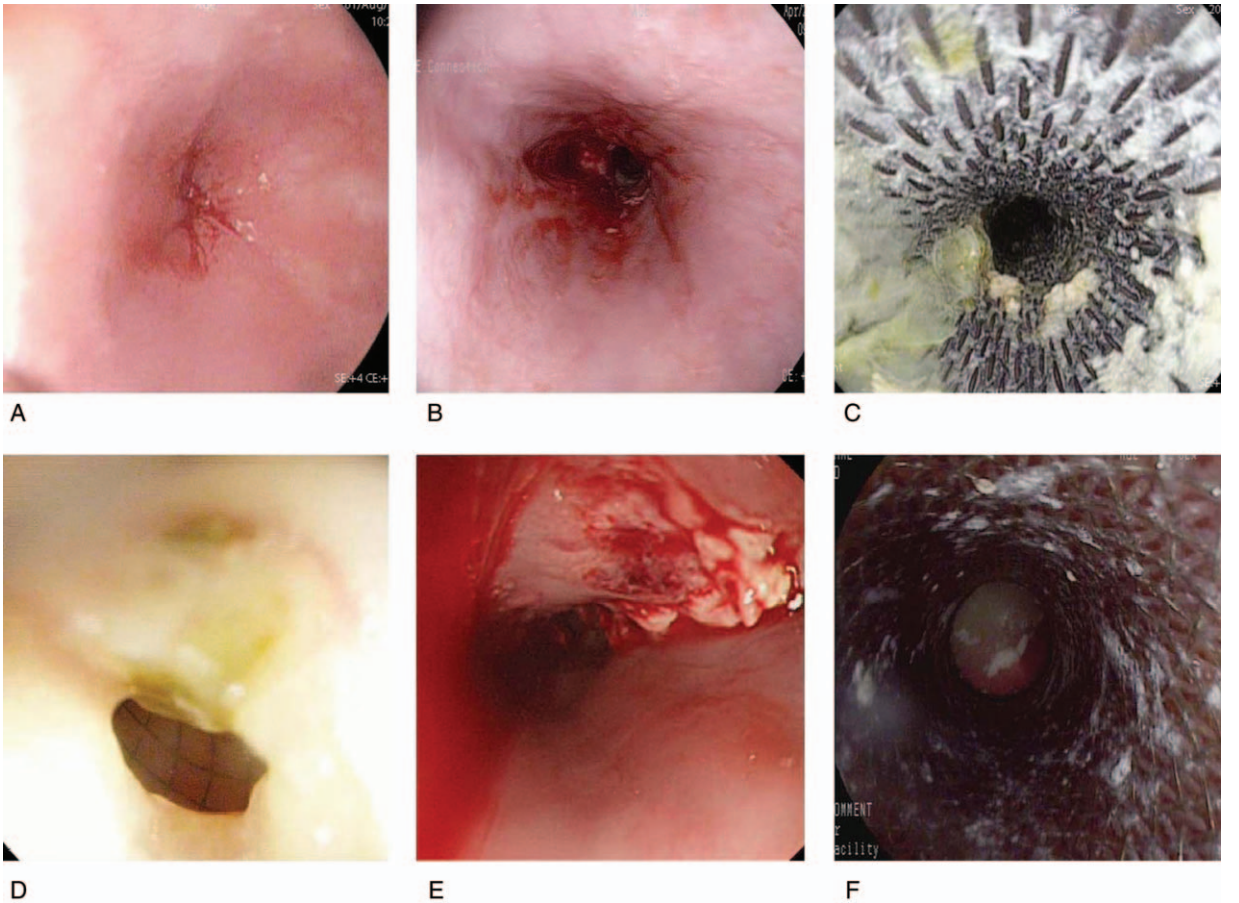

Figure 1. Fibergastroscopy examination for study the change of anastomotic stricture before and after balloon dilation or stenting. (A) A benign stricture was almost closed and the routine fibergastroscopy failed to examination after procedure, fibergastroscopy could pass through the lesion 1 week after balloon dilation (B). A covered stent was used for restenosed stricture after repeated dilation, which was patent after 5 weeks (C). Granulation tissue was shown above the covered stent after 8 weeks, which lead to restenosis of stent (D). For malignant stricture (E), stent seeded with iodine-125 was implanted, which showed patent after 10 weeks (F).

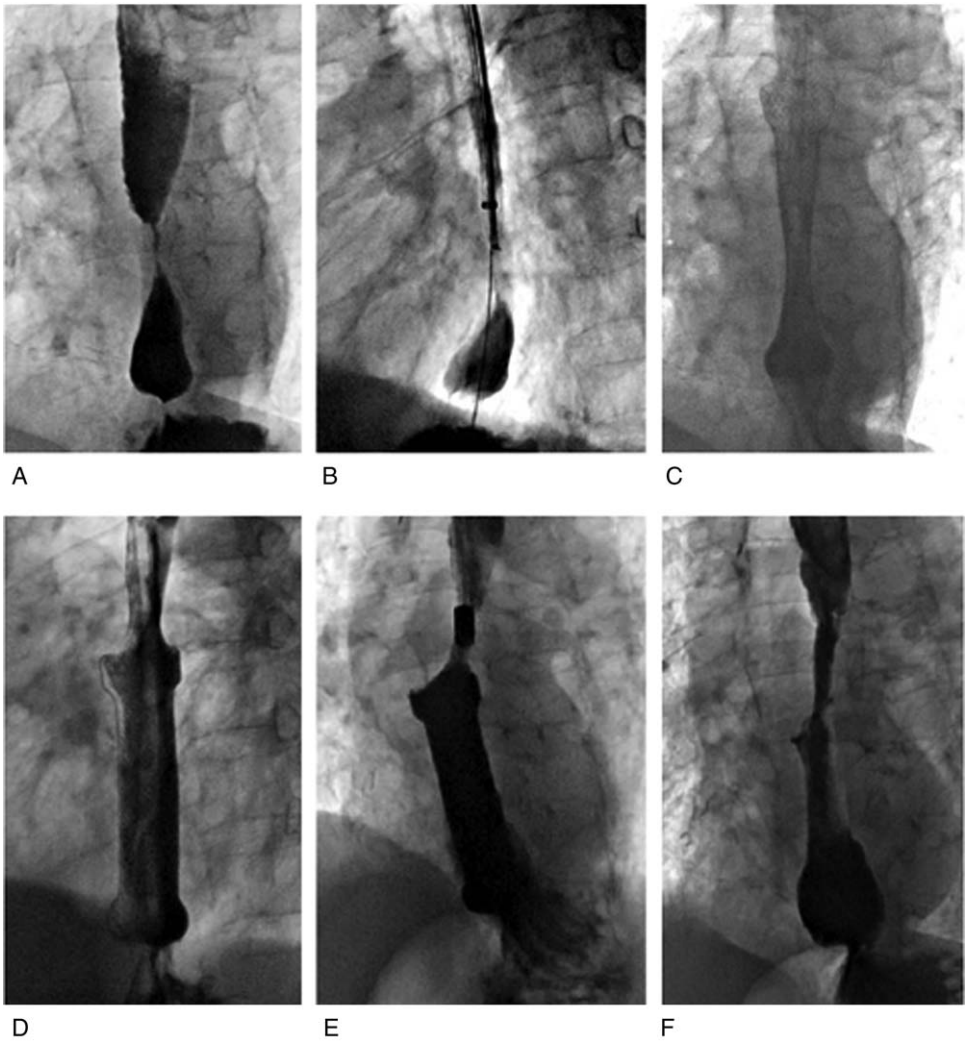

Figure 2. Fluoroscopic guidance biopsy and stenting. Per oral esophagogram showed a severe anastomotic stricture, which indicated the suspicious area (A). Biopsy forceps was introduced through the sheath and specimens were obtained under fluoroscopic guidance (B). The esophageal covered stents were implanted for benign restenosis after repeated balloon dilation (C), which was retrieved after about 3 month if dysphagia improved (D–F).

Nanjing, China) were implanted after repeated balloon dilation, which was retrieved after about 3 month if dysphagia improved (Fig. 2C–F). Besides, transcatheter arterial chemoembolization was performed for malignant stricture treatment.

2.4. Post-interventional treatment and follow-up

After the procedure, the patients' vital signs were monitored, and the presence or absence of bleeding and extent of relief from dysphagia were noted. Stooler's dysphagia score, ranging from 4 (aphagia) to 0 (no dysphagia), was used to assess the efficacy of treatment.[3] All patients were administered anti-inflammatory (cefoperazone sodium injections, 4.0 g/d). Further treatments, such as balloon dilation, stenting, or transcatheter arterial chemoembolization were administered according to the pathological results of biopsy. Chest CT was performed 1 week after procedure to observe the inflation of the stent.

2.5. Statistical analysis

All data were expressed as means ± Standard Error of Mean (SEM). Student t test was used for statistical analysis (Prism 5.0, GraphPad Software, Inc., SanDiego, CA). Differences were considered statistically significant at $P < .05$.

3. Results

Fluoroscopic guidance biopsy was performed successfully in all patients, with a mean biopsy time of 26.1 ± 1.7 minutes. Repeat biopsies were performed if pathology did not confirm pre-interventional examinations. There were no serious complications such as gastrointestinal perforation, esophageal fistula, and severe pain, except for minimal hemorrhage (less than 10 mL) in 11 patients. A total of 38 patients were diagnosed as chronic inflammation of mucous membrane or inflammatory granuloma, of which, 2 patients were further diagnosed as cancer by further biopsy, with a missed diagnosis rate of 5.3%, and 1 patient developed squamous cell carcinoma after 5 months. Among 20 cases of cancer, 3 cases were adenocarcinoma and 17 cases were squamous cell carcinoma, including one squamous cell carcinoma in situ (Fig. 3).

Balloon dilation was performed for 20 patients (33 times) of benign stricture, and 9 patients (10 times) of malignant stricture. The diameter of balloon was significantly smaller for malignant

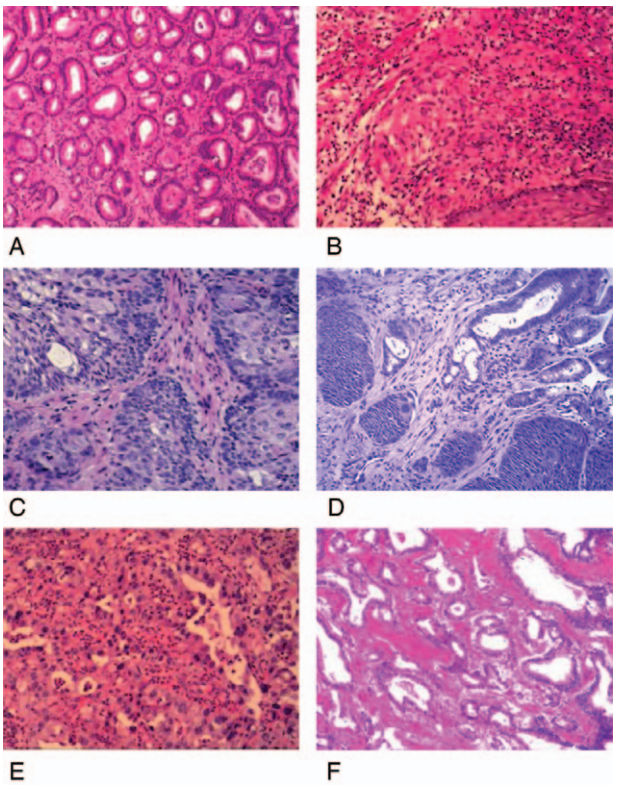

Figure 3. Pathologic diagnosis of serve anastomotic stricture after esophagogastrostomy. Pathologic examination showed chronic inflammation of mucous membrane (A) and inflammatory granuloma (B), squamous cell carcinoma (C–D), adenocarcinoma of mixture type (E) and intestinal type (F) according to Lauren classification.

stricture to avoid complications of rupture of esophagus and bleeding. A mean diameter of 14.1 ± 0.7 mm (Range: 10–16 mm) is effective and safe for dilation of malignant stricture to introduce esophageal stents or intestinal feeding tube (Fig. 4). For benign stricture, 26 esophageal covered stents were implanted for restenosis after repeated balloon dilation. A total of 10 stents were retrieved, with a mean indwelling time of 60.8 ± 14.8 days, including 4 migration, 3 restenosis, and 3 regular removals to protect complications. Besides, 3 patients underwent fundoplication and hiatal hernia repair. For malignant stricture, 8 esophageal covered stents were implanted, including 4 stents seeded with iodine-125, and 2 stents were withdrawn 34 days and 69 days after implantation due to restricture and migration of stents. Transcatheter arterial chemoembolization was performed in 8 patients,150 mg of oxaliplatin,1000 mg of fluorouracil, and 20 mg of pirarubicin were infused, and the feeding arteries of tumors were embolized with 350 to 560 um gelfoam particles (Fig. 5). A total of 5 of tracheal stents were implanted for patients of tracheostenosis caused by compress of esophageal tumors (Table 1).

All esophageal and tracheal stents were successfully placed at the first attempt. After esophagus stenting, dysphagia was immediately alleviated. The dysphagia score decreased from 3.4 ±0.1 to .7±.1 ($P<.001$) after stenting or repeated balloon dilation. Some discomfort, such as varying degrees of retrosternal chest pain, minimal hemorrhage, and foreign body sensation were observed in most patients at 1 week after procedure.

4. Discussion

Anastomotic stricture is the most common complication of esophagogastrostomy,[2] which is caused by many reasons, such as excessive scar caused by tissue repair response or reflux esophagitis. The treatments and prognosis of gastroesophageal anastomosis are quite different between benign and malignant stricture. Early diagnosis and treatment can improve the quality of life and prolong patient's life.[9] At present, the clinical diagnosis mainly depends on esophagogram, gastroscopy, and biopsy.[6] The esophageal biopsy under gastroscope can clearly show the location and shape of esophageal lesions, and take the biopsy tissue under direct vision. Gastroscopy biopsy is possible in patients of moderate anastomotic stricture, to visualize the entire lesion, determine the location and extent of the stricture, obtain biopsy specimens, and administer a number of effective treatments. However, this approach is not suitable for patients with severe anastomotic stricture, which may fail to pass through the lesion to observe the areas below the narrow wall, details of the stenosed segment cannot be ascertained, leading to a high risk of hemorrhage. The biopsy via gastroscope may fail, or merely

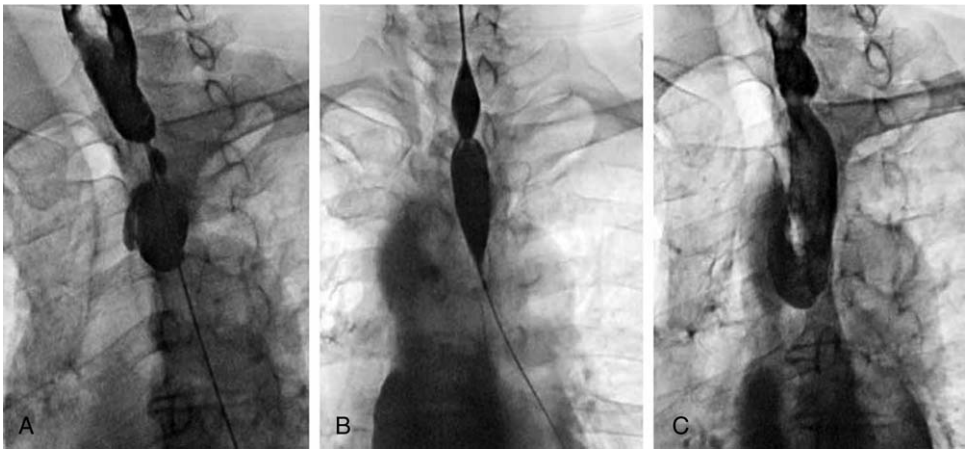

Figure 4. Balloon dilation for anastomotic stricture. A severe stricture was found in the level of articulationes sternoclavicularis (A), a balloon of 16 mm in diameter was used for repeated dilation (B). The diameter of stricture was increased immediately after dilation (C).

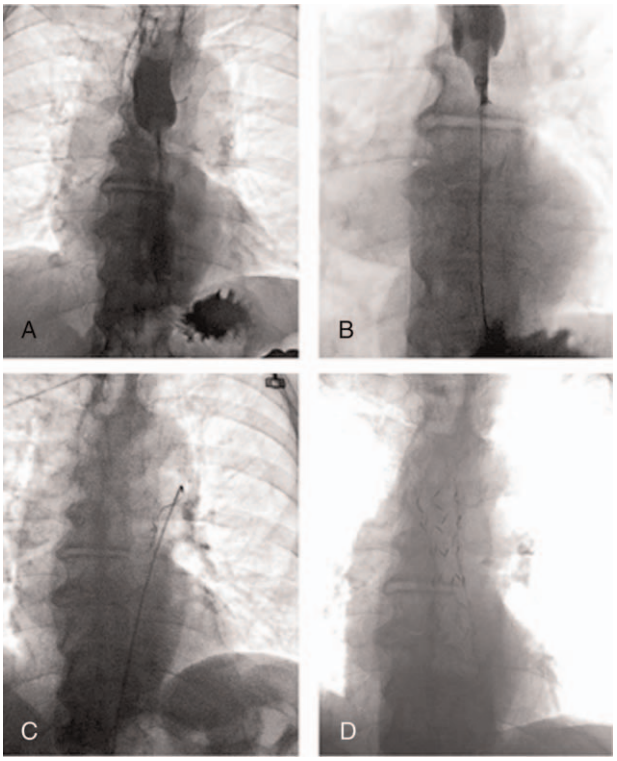

Figure 5. Fluoroscopic guidance biopsy and treatments for malignant stricture. Fluoroscopic guidance biopsy was performed under fluoroscopic guidance (A–B). Transcatheter arterial chemoembolization was performed with oxaliplatin, fluorouracil and pirarubicin, and the feeding arteries of tumors were embolized with 350–560 um gelfoam particles (C). A stent seeded with iodine-125 was then implanted (D).

obtain the above tissue or marginal tissue, but missed the real lesion, which may lead to misdiagnosis.

Fluoroscopic guidance biopsy specimens have been successfully obtained by inserting biopsy forceps through the vascular sheath in patients with biliary tract [10] and gastric lesions by endoscopy.[11] We performed fluoroscopy-guided biopsy through the vascular sheath in patients with severe anastomotic stricture, with accurate localization and high technical success, safety, and effectiveness to rapidly obtain samples for histopathological analysis. In our study, routine fibergastroscopy showed that the stenosed segment too narrow to tolerate fibergastroscopy. However, fluoroscopy-guided biopsy was performed successfully in all patients with no serious complications. Fluoroscopic guidance radiology biopsy revealed 20 cases of cancer, 35 cases of cicatricial stricture. Fluoroscopic guidance biopsy of gastroesophageal anastomotic stricture showed location and extension of lesion clearly, these strictures were identified as the suspicious regions, which can be easily achieved by adjusting the direction of the sheath. The location and depth can be well controlled during biopsy once the biopsy forceps tip location is revealed clearly, without causing perforation of esophagus, mediastinal abscess, bleeding, and other serious complications.[3] X-ray guided biopsy can achieve accurate sample, high detection rate and improved correct diagnosis rate. In addition, processing method for small tissue block and slicing method is also can affect the diagnostic accuracy.

Endoscopic biopsy and fluoroscopic guidance biopsy have advantages and disadvantages, for esophagogastric anastomotic stricture, the correct diagnosis rate of interventional biopsy will be higher than that of endoscopy. Fluoroscopic guidance biopsy is a viable alternative technology in diagnosis of severe anastomotic stricture after biopsy failure via gastroscopy. The author believes that the biopsy forceps can overcome the shortcomings of endoscopic biopsy if combined with X-ray guidance. The gastroscope can be inserted above the esophagogastric anastomotic stricture, biopsy forceps then was introduced under fluoroscopy for effective biopsy after position adjustment. The disadvantages of fluoroscopic guidance biopsy include the inability to repeat the biopsy after stent placement, if pathology is negative and its applicability to lesions within the esophagus lumen only.

The primary aim of treatment in such patients is to release the stricture in order to recover feeding function and improve nutritional status of the patient. Early implementation of radiotherapy or chemotherapy can greatly improve the survival rate and the prognosis for patients with cancer of esophagogastric anastomosis stricture. Esophagus stents bare or covered with a polyurethane or silicone coating, were placed after acquisition of the pathological material. Covered stents are effective and relatively safe for palliation of patients with complicated or recurrent esophagogastric cancer after partial or complete gastrectomy.[3,12] Temporary placement of a stent for a benign stenosis of the duodenum,[13] as well as malignant strictures.[14] The drawback of bare stents is obstruction caused by tumor ingrowths, and the main drawbacks of covered stents are the risk of migration.[3] The complication rate is higher in patients who have previously received chemoradiotherapy.[3] In this study, 2 stents were withdrawn 34 days and 69 days after implantation due to restricture and migration of stents. Besides, balloon dilation is effective and safe for patients with benign anastomotic stricture.[15] In this study, balloon dilation was performed for 20 patients (33 times) of benign stricture, and 9 patients (10 times) of malignant stricture.

There were limitations of this study. This was a retrospective study of small population without comparison and advantage of fluoroscopic biopsy over the standard endoscopic diagnosis had not been compared. Besides, some more theoretical analysis of the results is wanted in the further study. In summary, interventional forceps biopsy is a safe and effective procedure for directing appropriate treatment of anastomotic stricture after esophagogastrostomy, and it may be an

Table 1

Patient demographic data and treatment strategies.

	Benign stenosis	Malignant stenosis	*P*
n	35	20	
Gender, male (percentage)	25 (71.4%)	14 (70.0%)	1.00
Age, mean ± standard error, y	64.7 ± 2.0	69.7 ± 1.9	.10
Balloon dilation (frequency/patient)	33/20	10/9	
Mean diameter of balloon, mm	17.7 ± 0.3	14.1 ± 0.7	<.001
Mean length of balloon, mm	47.5 ± 3.1	42.2 ± 2.2	.25
Esophageal covered stent	26	8	
Mean diameter of stent, mm	18.7 ± 0.3	18.8 ± 0.5	.92
Mean length of stent, mm	98.9 ± 4.1	112.5 ± 5.3	.10
Retrieval of esophageal covered stent	10	2	
Mean indwelling days of esophageal stent	60.8 ± 14.8	51.5 ± 17.5	.80
Tracheal stent	2	3	
Transcatheter arterial chemoembolization	0	8	
Fundoplication and hiatal hernia repair	3	0	

alternative approach for patients who cannot tolerate fiber-gastroscopy.

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Visualization: Gang Wu.
Writing – original draft: Yonghua Bi.
Writing – review & editing: Yonghua Bi, Hongmei Chen, Xinwei Han, Jianzhuang Ren.

References

[1] Kesler KA, Ramchandani NK, Jalal SI, et al. Outcomes of a novel intrathoracic esophagogastric anastomotic technique. J Thorac Cardiovasc Surg 2018.
[2] Tambucci R, Angelino G, De Angelis P, et al. Anastomotic strictures after esophageal atresia repair: incidence, investigations, and management, including treatment of refractory and recurrent strictures. Front Pediatr 2017;5:120.
[3] Lambert R. Treatment of esophagogastric tumors. Endoscopy 2003;35:118–26.
[4] Vander Noot MR3rd, Eloubeidi MA, Chen VK, et al. Diagnosis of gastrointestinal tract lesions by endoscopic ultrasound-guided fine-needle aspiration biopsy. Cancer 2004;102:157–63.
[5] Emura F, Saito Y, Ikematsu H. Narrow-band imaging optical chromocolonoscopy: advantages and limitations. World J Gastroenterol 2008;14:4867–72.
[6] Terada T. A clinicopathologic study of esophageal 860 benign and malignant lesions in 910 cases of consecutive esophageal biopsies. Int J Clin Exp Pathol 2013;6:191–8.
[7] Li TF, Ren KW, Han XW, et al. Percutaneous transhepatic cholangiobiopsy to determine the pathological cause of anastomotic stenosis after cholangiojejunostomy for malignant obstructive jaundice. Clin Radiol 2014;69:13–7.
[8] Li ZM, Wu G, Han XW, et al. Radiology-guided forceps biopsy and airway stenting in severe airway stenosis. Diagn Interv Radiol 2014;20:349–52.
[9] Shin JH, Song HY, Ko GY, et al. Esophagorespiratory fistula: long-term results of palliative treatment with covered expandable metallic stents in 61 patients. Radiology 232D 2004:252–9.
[10] Kawashima H, Itoh A, Ohno E, et al. Transpapillary biliary forceps biopsy to distinguish benign biliary stricture from malignancy: how many tissue samples should be obtained? Dig Endosc 2012;24(Suppl 1):22–7.
[11] Kasuga A, Yamamoto Y, Fujisaki J, et al. Clinical characterization of gastric lesions initially diagnosed as low-grade adenomas on forceps biopsy. Dig Endosc 2012;24:331–8.
[12] Siersema PD, Schrauwen SL, van Blankenstein M, et al. Self-expanding metal stents for complicated and recurrent esophagogastric cancer. Gastrointest Endosc 54D 2001:579–86.
[13] Dormann AJ, Deppe H, Wigginghaus B. Self-expanding metallic stents for continuous dilatation of benign stenoses in gastrointestinal tract - first results of long-term follow-up in interim stent application in pyloric and colonic obstructions. Z Gastroenterol 39D 2001: 957–60.
[14] Lee JM, Han YM, Kim CS, et al. Fluoroscopic-guided covered metallic stent placement for gastric outlet obstruction and post-operative gastroenterostomy anastomotic stricture. Clin Radiol 56D 2001: 560–7.
[15] Kim JH, Shin JH, Bae JI, et al. Gastric outlet obstruction caused by benign anastomotic stricture: treatment by fluoroscopically guided balloon dilation. J Vasc Interv Radiol 2005;16:699–704.