

Original Article

Application of endoscopic OTSC in the treatment of intrathoracic esophageal anastomotic fistula post esophageal carcinoma resection

Yuanshan Yao, Yinjie Zhou, Zhenhua Yang, Hongbo Huang, Haibo Shen

Department of Thoracic Surgery, Ningbo No.2 Hospital, Ningbo City, Zhejiang Province, China

Received October 31, 2017; Accepted December 4, 2017; Epub January 15, 2018; Published January 30, 2018

Abstract: Objective: To evaluate the efficacy of rake-shaped endoscopic closure with over-the scope-clip system (OTSC) in treatment of 5 patients with intrathoracic esophageal anastomotic fistula after esophageal carcinoma resection performed in our hospital, as well as to conclude clinical experience. Methods: Clinical data of 5 patients with intrathoracic esophageal anastomotic fistula after esophageal carcinoma resection, who underwent the implantation treatment of OTSC in the Department of Thoracic Surgery of Ningbo No.2 Hospital between January, 2014 and December, 2016, were retrospectively analyzed. Supportive treatment was given to all patients for at least 7 d after diagnosis, and then endoscopic OTSC was implanted when their conditions became stable. After the endoscopic OTSC closure, efficacy and complications, etc. were assessed. Oral feeding time, length of stay and hospital charges were recorded. Besides, all patients were followed up for 6-24 months, and the time when OTSC fell off automatically and was excreted to the outside of the body, occurrence of other complications and recurrence of tumor were recorded. Results: All of the 5 patients received the endoscopic closure with OTSC successfully to treat anastomotic fistula, with an average operation time of 50.4 ± 1.72 min. Chest pain and foreign body sensation occurred in 4 cases after closure, all of whom got better or cured after corresponding therapies. No severe complications like massive hemorrhage occurred during or after the surgery. All the patients started taking food through mouth at 7-14 days, with an average length of stay of 20.20 ± 1.72 days and hospital charges of RMB 25.4 ± 2.3 thousand. The OTSC in all patients fell off automatically and were excreted to the outside of the body after the anastomotic fistula closed (within 1-2 months). Only one patient presented anastomotic stricture, but got improved after underwent endoscopic dilation. During the follow-up, no recurrence of tumor has ever happened. Conclusion: Endoscopic closure with OTSC is successful, effective and convenient to treat intrathoracic esophageal anastomotic fistula after esophageal carcinoma resection.

Keywords: Esophageal carcinoma, anastomotic fistula, OTSC

Introduction

Intrathoracic esophageal anastomotic fistula is a common complication and major cause of death after esophageal carcinoma resection. It was reported that its incidence was 4-17% and the mortality was 30% [1, 2]. The incidence of anastomotic fistula through right chest was higher than that of left chest [3]. Traditionally, esophageal anastomotic fistula was mainly treated depending on total thoracic drainage and sufficient nutrition support, characterized by obviously prolonged length of stay, high cost and high ratio of continued anastomotic fistula [4]. Clinically, many doctors treated anastomotic fistula with endoscopic covered stents and

normal titanium clips to shorten the length of stay [5]. However, covered stent may shift easily due to lack of sufficient tissue support [6]. As for common titanium clip, although it is cheap and easy to operate, its failure rate of closure increases because of its poor grasping force and it can merely close submucosa defect [7]. In 2010, application of the second-generation over-the-scope-clip system (OTSC) was approved by FDA. But in China, OTSC remains a newly arisen therapy; few patients accepted such therapy and less articles about its clinical efficacy were published [8]. Therefore, 5 patients with intrathoracic esophageal anastomotic fistula after esophageal carcinoma resections who underwent OTSC implantation in

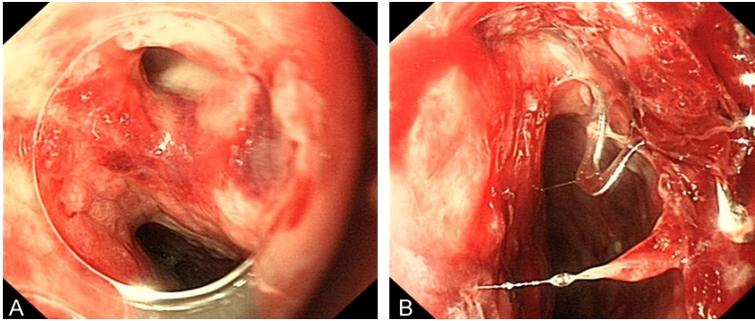


Figure 1. Treatment method of placing OTSC into the patients with intrathoracic esophageal anastomotic fistula after esophageal carcinoma resection. A. Visible esophagogastric anastomotic fistula under a gastroscopic; B. Esophagogastric anastomotic fistula was closed by OTSC, with no visible fistula under a gastroscopic and no visible side leakage all around.

our hospital between January, 2014 and December, 2016 were observed in this study. The results showed that the efficacy was better, so the clinical experience was concluded as follows.

Clinical data and methods

This study had been approved by the Ethics Committee of the hospital. As a retrospective study, it did not need the informed consent of patients.

General information

Clinical data of 5 patients with intrathoracic esophageal anastomotic fistula after esophageal carcinoma resection who received rake-shaped OTSC implantation in the Department of Thoracic Surgery of Ningbo No.2 Hospital between January, 2014 and December, 2016 were retrospectively analyzed. Among them, there were 3 males and 2 females, with an average age of 55 (45-72) years old; three patients were complicated with hypertension, two patients were complicated with diabetes and three patients were complicated with chronic obstructive pulmonary disease. Surgical methods: two cases underwent the anastomosis under the aortic arch from left chest; one case underwent the anastomosis above the aortic arch from left chest and two cases underwent the thoracic top anastomosis from right chest. Esophagogastric anastomotic fistula occurred at day 7-14 after esophageal carcinoma resection, characterized by sudden shiver and hyperpyrexia, irritable cough, accelerated heart rate, shortness of breath,

increased chest drainage and turbidity of drainage clinically; these patients demonstrated different levels of leukocyte elevation accompanied by a left shift. Hydropneumothorax under chest CT in accompanying shift to left; hydro-pneumothorax was observed during chest CT. Patients were diagnosed with a single fistula of intrathoracic esophageal anastomosis through orally giving meglumine diatrizoate for angiography. All patients were confirmed as a single fistula by gastroscopy, with a

diameter of about 0.86 ± 0.24 cm. See **Figure 1A**.

Methods

Once diagnosed as intrathoracic esophageal anastomotic fistula, the patients received supportive treatment for at least 7 days. After the patients were in stable condition, OTSC (German Ovesco) were implanted. See **Figure 1B**. Firstly, gastroscopes were implanted into 3 cases under general anesthesia and 2 cases under local anesthesia. Put OTSC into the releasing sleeve in the front of endoscope in advance and pulled the tissues at both sides of wound surface into hyaline cap with grasping forceps respectively; sucked more tissues into hyaline cap under negative pressure; pulled and released OTSC through connection by the supporting rotary trigger system or grabbed the tissue at one side of wound surface with foreign body forceps, sucked the tissue at the other side into hyaline cap under negative pressure and then released OTSC [9]. Postoperative chest drainage volume was less than 50 ml/d, body temperature returned to normal, CT showed abscess in the chest disappeared and small amount of liquid food were taken in through mouth for 3 days, patients can transit to take in semi-liquid food. Chest drainage tube could be removed with no discomforts two days after eating semi-liquid food.

Efficacy evaluation

Comprehensive assessment was conducted on the clinical efficacy, complications and so on. It could be observed whether the perforation or

Experience of endoscopic OTSC for intrathoracic esophageal anastomotic fistula

Table 1. Efficacy of OTSC

Outcomes	Value
Fistulas block success rate (n, %)	5 (100%)
Time of endoscopic closure (min)	50.4±1.72
OTSC fell off (n)	1
Complication	
Anastomotic stenosis (n, %)	1 (20%)
Death (n, %)	0 (0)
Chest pain (n, %)	4 (80%)
Postoperatively feeding (days)	7-14
Length of stay (days)	20.20±1.72
Hospital charge (RMB, thousand)	25.4±2.3
Tumor recurrence (n)	0

fistula was clipped and there was visible side leakage all around after the titanium clip was released. For patients whose titanium clips fell off, new titanium clips were implanted again in time. According to thoracic fluid drainage volume after surgery, second esophageal angiography was performed about 1-2 weeks later. The location of titanium clips and their blocking effect were specified and shift of titanium clips was observed.

Other outcome measures

Oral feeding time, length of stay and hospital charges were recorded. All patients were followed up until June, 2017 (6-24-month follow-up), and the time when OTSC fell off automatically and was excreted to the outside of the body, other complications and recurrence of tumor were recorded.

Results

Efficacy evaluation

Fistulas in all patients were successfully blocked under endoscope, and the average time of endoscopic closure was 50.4±1.72 min. There was no death postoperatively. Chest pain occurred in 4 cases, all of whom were successfully treated by drug analgesia. OTSC fell off in 1 case on day 7 after operation and then placed again under endoscope and the clip fell off automatically 5 weeks after placed and the fistula healed indicated by an endoscope (**Figure 1B**). All patients took a small amount of methylene blue orally on day 2 after esophageal stents were implanted, with no methylene blue flowing out of the thoracic duct.

All patients took food through mouth at 7-14 days after operation. Their average length of stay was 20.20±1.72 days and average hospital charge was RMB 25.4±2.3 thousand. OTSC in all patients fell off automatically and were excreted to the outside of the body after anastomotic fistula closure (within 1-2 months). One patient presented anastomotic stenosis and got improved after treated by endoscopic dilation. No one had tumor recurrence. See **Table 1**.

Discussion

For both trans left chest and trans right chest, gastroesophageal anastomotic fistula is always a severe complication after esophageal carcinoma resection, with an incidence of 4%-17% and mortality of 30% [1, 2]. Therefore, it is of great significance to treat gastroesophageal anastomotic fistula after esophageal carcinoma resection properly for the decrease of postoperative complications and mortality. Gastroesophageal anastomotic fistula is mainly treated through surgery and medical conservative treatment. Most domestic physicians believed that early secondary surgery for fistula closure should be done, once the fistula is surely diagnosed. Unsatisfied operative outcome results from delayed diagnose and severe chest, mediastinum infection and obvious edema and infection around fistulas make closure unsuccessful. Medical conservative treatment depends on thorough thoracic drainage and sufficient nutrition support, characterized by obviously prolonged length of stay, high cost and high ratio of continued anastomotic fistula [10].

Endoscopic therapy provides a new method for dealing with gastroesophageal anastomotic fistulas, mainly including metal covered stents and titanium clips. Metal covered stents have been widely used, but there are certain contraindications. For example, the anastomotic fistula above the aortic arch, as well as the intrathoracic anastomotic fistula located to the left of atrial impression, is among the contraindications of esophageal stent implantation because it may lead to serious artery rupture hemorrhage as a result of aorta and heartbeat friction, [11]. In addition, postoperative pain, foreign body sensation, upper gastrointestinal bleeding, stent displacement and persistent microfistula are common complications after

esophageal stent implantation. These limit the further application of metal stents [12]. Since only the defect of mucosal layer can be closed, peripheral edema of acute anastomotic fistula and proliferation of fibrous tissues around the chronic anastomotic fistula will reduce the performance of common titanium clips. Therefore, we decided to treat anastomotic fistula with OTSC. OTSC was approved by FDA in 2010 and it is made of the Nitinol with elastic memory. OTSC is installed on the head of endoscope, intended to capture and close the tissue more extensively and more efficiently without causing tissue ischemia and cutting. It is a special metal clip to achieve large area of mechanical compression for the gastrointestinal tract [7]. It is mainly used in endoscopic treatment of gastrointestinal bleeding, esophageal tracheal fistula and anastomotic fistula after esophageal carcinoma resection, etc. OTSC provides a new method for clinical treatment of anastomotic fistula after esophageal carcinoma resection. Theoretically, OTSC applies to anastomotic fistula in all sites.

Clinically, there is a certain controversy when endoscopic treatment should be performed for patients with gastroesophageal anastomotic fistula. Nishiyama et al. believed that endoscopic treatment should be taken immediately to block anastomotic fistula once confirmed, so as to prevent further infection [13]. However, Martinek et al. believed that fistula could be further ripped, expanded or even ruptured by endoscopic inflation once stent therapy was conducted immediately [14]. Therefore, conservative treatment could be taken at first, and stent therapy would be considered ten days after operation. But some suggested that fistula could be closed while conducting conservative treatment at early stage as long as there was a reliable thoracic drainage tube [15]. Based on our experience, immediate systemic supportive treatment should be carried out immediately once the gastroesophageal anastomotic fistula was diagnosed, and then esophageal stent can be implanted after general improvement of the body, which is generally performed about one week after anastomotic fistula is confirmed.

Four cases out of five patients in our group presented different levels of chest pain, which may be related to the characteristics of OTSC. If

OTSC could grab and close the fistula in large areas, patients would feel chest pain. Generally, chest pain would be relieved after symptomatic treatment. For another patient, OTSC fell off on day 7 after operation and presented anastomotic fistula again, with a diameter of 1.5 cm. Generally speaking, OTSC could effectively clamp the fistula with a diameter of within 3 cm and wouldn't cause strangulated necrosis of tissues because of OTSC's unique characteristic of closure. Therefore, it was speculated that this was related to the operation experience of the endoscopic surgeon. OTSC closure was performed again under general anesthesia. Re-examination with gastroscopy after OTSC fell off showed the fistula healed. For five cases in our group, their OTSCs fell off automatically after fistula healed. There was no need to pick clips out by gastroscopy, which is one of the advantages of OTSC, while the stent needs to be removed under gastroscopy after the end of stent therapy. The fistula wouldn't heal completely if too early, otherwise it is hard to pick out when the stent adhered tightly with mucous membrane if too late. All these made it difficult to determine the best time to remove stents [16]. The outcome in our group suggested that the success rate of OTSC was 100% with regard to short-term postoperative acute gastroesophageal anastomotic fistula. In our opinion, OTSC could be applied immediately when the lesions of acute anastomotic fistula were fresh and didn't transform into obvious fibrosis, the thoracic drainage tube was unobstructed and there were no apparent abscesses around anastomotic fistula. However, for patients with chronic anastomotic fistula, treatment efficacy was poor because of extensive fibrosis around the fistula.

Most clinical studies worldwide have reached positive conclusions on the application of OSTC in treatment of intrathoracic gastroesophageal anastomotic fistula, but there still exist some individuals who died from lung infection [17-20], which may be caused by the non-standard surgery procedure. In China, Dong et al. for the first time reported a case, of esophageal fistula closure using OTSC in 2016. The chest CT showed that the metal stent remained in position at one week after the surgery, and the adequate closure of the fistula was confirmed by gastroscopy at two weeks after the surgery. The patient returned to a full liquid diet 20 days

after the operation and showed no obvious discomfort after food intake [21]. In 2017, Yang et al. reported three cases who received endoscopic OTSC to treat esophageal fistula. The results suggested that fistulas of the three cases got closed successfully without severe complications, and the efficacy was better. The quality of patient's life was improved significantly than before [22]. These results were consistent with the conclusions reached in our paper, all of which indicated that OSTC had a good efficacy in treatment of intrathoracic gastroesophageal anastomotic fistula and was worthy of application and popularization. However, there are still few reports on the application of OTSC in treatment of digestive tract fistula currently in China. The application value of OTSC needs to be further studied.

Disclosure of conflict of interest

None.

Address correspondence to: Haiibo Shen, Department of Thoracic Surgery, Ningbo No.2 Hospital, No.41 Northwest Street, Ningbo City 315010, Zhejiang Province, China. Tel: +86-0574-83871083; E-mail: shenhaibo1026@163.com

References

- [1] Lambertz R, Holscher AH, Bludau M, Leers JM, Gutschow C and Schroder W. Management of tracheo- or bronchoesophageal fistula after Ivor-lewis esophagectomy. *World J Surg* 2016; 40: 1680-1687.
- [2] Seely AJ, Ivanovic J, Threader J, Al-Hussaini A, Al-Shehab D, Ramsay T, Gilbert S, Maziak DE, Shamji FM and Sundaresan RS. Systematic classification of morbidity and mortality after thoracic surgery. *Ann Thorac Surg* 2010; 90: 936-942; discussion 942.
- [3] Licht E, Markowitz AJ, Bains MS, Gerdes H, Ludwig E, Mendelsohn RB, Rizk NP, Shah P, Strong VE and Schattner MA. Endoscopic management of esophageal anastomotic leaks after surgery for malignant disease. *Ann Thorac Surg* 2016; 101: 301-304.
- [4] Luketich JD, Pennathur A, Awais O, Levy RM, Keeley S, Shende M, Christie NA, Weksler B, Landreneau RJ, Abbas G, Schuchert MJ and Nason KS. Outcomes after minimally invasive esophagectomy: review of over 1000 patients. *Ann Surg* 2012; 256: 95-103.
- [5] Sharaiha RZ, Kumta NA, DeFilippis EM, Dimairo CJ, Gonzalez S, Gonda T, Rogart J, Siddiqui A, Berg PS, Samuels P, Miller L, Khashab MA, Saxena P, Gaidhane MR, Tyberg A, Teixeira J, Widmer J, Kedia P, Loren D, Kahaleh M and Sethi A. A large multicenter experience with endoscopic suturing for management of gastrointestinal defects and stent anchorage in 122 patients: a retrospective review. *J Clin Gastroenterol* 2016; 50: 388-392.
- [6] Chen LL, Ma HS and Rao LQ. Clinical analysis of 26 cases of esophageal fistula treated with covered stent. *China Journal of Endoscopy* 2009; 15: 185-187.
- [7] Messenger M, Warlaumont M, Renaud F, Marin H, Branche J, Piessen G and Mariette C. Recent improvements in the management of esophageal anastomotic leak after surgery for cancer. *Eur J Surg Oncol* 2017; 43: 258-269.
- [8] Carrott PW Jr and Low DE. Advances in the management of esophageal perforation. *Thorac Surg Clin* 2011; 21: 541-555.
- [9] Markar SR, Koehler R, Low DE and Ross A. Novel multimodality endoscopic closure of postoperative esophageal fistula. *Int J Surg Case Rep* 2012; 3: 577-579.
- [10] Willingham FF and Buscaglia JM. Endoscopic management of gastrointestinal leaks and fistulae. *Clin Gastroenterol Hepatol* 2015; 13: 1714-1721.
- [11] Su GL. Clinical application of covered esophageal stent in the treatment of anastomotic leakage after resection of esophageal carcinoma. *Medical Information* 2015; 258.
- [12] Du ZH, Wang WQ, Li SQ, Chen L, Luo J and Zhou XQ. The postoperative anastomotic fistula treatment of esophagus cancer. *Journal of Frontiers of Medicine* 2016; 3: 95-96.
- [13] Nishiyama N, Mori H, Kobara H, Rafiq K, Fujihara S, Kobayashi M, Oryu M and Masaki T. Efficacy and safety of over-the-scope clip: including complications after endoscopic submucosal dissection. *World J Gastroenterol* 2013; 19: 2752-2760.
- [14] Martinek J, Ryska O, Tuckova I, Filipkova T, Dolezel R, Juhas S, Motlik J, Zavoral M and Ryska M. Comparing over-the-scope clip versus endoloop and clips (KING closure) for access site closure: a randomized experimental study. *Surg Endosc* 2013; 27: 1203-1210.
- [15] Yun CH, Zhao XG, Han YT, Wu ML and Peng CL. Application of the diagnosis and treatment of anastomosis fistula with drainage in thoracic cavity. *Shandong Medical Journal* 2015; 50: 51.
- [16] Aiolfi A, Bona D, Ceriani C, Porro M and Bonavina L. Stent-in-stent, a safe and effective technique to remove fully embedded esophageal metal stents: case series and literature review. *Endosc Int Open* 2015; 3: E296-299.
- [17] Armellini E, Crino SF, Orsello M, Ballare M, Saettone S, Tari R and Occhipinti P. New endo-

Experience of endoscopic OTSC for intrathoracic esophageal anastomotic fistula

- scopic over-the-scope clip system for treatment of a chronic post-surgical tracheoesophageal fistula. *Endoscopy* 2015; 47 Suppl 1 UCTN: E437-438.
- [18] Dogan UB, Akin MS and Yalaki S. Endoscopic closure of tracheoesophageal fistulas with the over-the-scope clip system. *J Coll Physicians Surg Pak* 2014; 24 Suppl 3: S193-195.
- [19] Baron TH, Song LM, Ross A, Tokar JL, Irani S and Kozarek RA. Use of an over-the-scope clipping device: multicenter retrospective results of the first U.S. experience (with videos). *Gastrointest Endosc* 2012; 76: 202-208.
- [20] Disibeyaz S, Koksas AS, Parlak E, Torun S and Sasmaz N. Endoscopic closure of gastrointestinal defects with an over-the-scope clip device. A case series and review of the literature. *Clin Res Hepatol Gastroenterol* 2012; 36: 614-621.
- [21] Dong LL, Zhang N, Zhu LR, Wang WL, Huang P, Shi Q and Yao LQ. A case of anastomotic fistula after resection of esophageal carcinoma by endoscopic OTSC clip system. *Chinese Journal of Gastrointestinal Surgery* 2016; 19: 468.
- [22] Yang WF, Rao GH, Ban JH, Pang MZ, Long WY and Zou YB. Report of 3 cases with esophageal fistula treated by OTSC system in the endoscopic closure. *Journal of Minimally Invasive Medicine* 2017; 12: 272-273.