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Personalized Management of Anastomotic Leak after Surgery for Esophageal Carcinoma

Hong-yu Ye, Wei-zhao Huang*, Yin-meng Wu, Yi Liang,
Jun-meng Zheng, and Hai-ming Jiang

Department of Cardio-thoracic Surgery, Zhongshan Hospital of Sun Yat-sen
University (Zhongshan People's Hospital), Zhongshan 528403, China

Key words: esophageal surgery; anastomotic leak; resurgery; stent

Objective To summarize the management of anastomotic leak following surgery for esophageal carcinoma.

Methods The medical records of the patients developing digestive tract leak after surgery for esophageal carcinoma in our hospital from January 2003 to March 2011 were retrospectively analyzed.

Results A total of 36 patients were included, in whom 13 developed cervical anastomotic leak, 18 had intra-thoracic anastomotic leak, and 5 had intra-thoracic gastric necrosis. Of these patients, 7 were treated with resurgery, 6 with esophageal stent implantation, and 23 with conservative treatment. Treatment lasted for 5 to 181 days, averagely 47.0 ± 31.9 days. After management, 9 patients died (25.0%). Among seven patients with resurgery, four had deceased, two were cured, and one developed leak again and was switched to conservative treatment until discharged. All the 6 patients treated with stent implantation were cured. Of the 24 patients receiving conservative treatment (including one switched from resurgery), 18 (75.0%) were cured and 1 was not cured but survived.

Conclusions Anastomotic leak following surgery for esophageal carcinoma should be treated individually based on the onset time, location, size, and extent of the leakage. Conservative treatment is still a safe and effective method. The efficacy of stent implantation needs further investigation to confirm.

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ANASTOMOTIC leak following surgery for esophageal carcinoma is a severe and refractory complication. With improvement in anastomotic techniques, its incidence has been significantly reduced; however, due to a good number of reasons in-

cluding physiology and anatomy of esophagus, the possibility of developing leak cannot be totally eliminated.¹ Therefore the appropriate management of this condition is crucial for surgical patients. In the present study, we performed a retrospective analysis to summarize the experience in treating anastomotic leak after surgery for esophageal carcinoma.

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*Corresponding author, Tel: 86-760-89880323, Fax: 86-760-88841707,

E-mail: garming97@hotmail.com

PATIENTS AND METHODS

Patients

From January 2003 to March 2011, 554 patients with esophageal carcinoma were treated with surgery in the Department of Cardio-thoracic Surgery in our hospital, among which a total of 36 developed anastomotic leak, with an incidence of 6.5%. General items in medical records of those patients were reviewed, including demographic characteristics, tumor features, concomitant conditions, pathological staging (based on Union Internationale Contre le Cancer 2007 staging system), and surgical approaches. None of them underwent neoadjuvant therapy.

Management of anastomotic leak

Systemic treatment: Once anastomotic leak was confirmed, fasting was started. Gastric tube was placed and continued gastrointestinal decompression introduced. Nutrition support treatment was instituted. Sensitive antibiotics were given to control the infection based on the results of bacterial culture.

Local management: Three types of local management were adopted, namely surgical treatment (resurgery), stent implantation, and conservative treatment. In surgical treatment, operative re-exploration was performed. Necrotic gastric tissue was resected and leak closed by stapler. Pleural cavity was lavaged repeatedly and drainage tube inserted. In stent implantation, self-expanding metallic coated esophageal stent was inserted *via* endoscopy to seal the leak. The conservative treatment consisted mainly of drainage.

Statistical analysis

SPSS 13.0 software was used for statistical analysis. Continuous data are presented as means $\pm$ SD. Categorical data were compared using chi-squared test or Fisher's exact test. $P < 0.05$ was considered statistically significant.

RESULTS

General information of the patients

All the 36 patients were male, with a mean age of 64.1 ± 11.8 years (range, 44-77 years). All these 36 patients had pathologically confirmed esophageal squamous cell carcinoma, of which 11 had tumors located in upper thoracic segment, 19 in middle thoracic segment, and 6 in lower thoracic segment. Before surgery, concomitant hepatic cirrhosis was seen in 1 patient, primary hypertension in 6, and obsolete pulmonary tuberculosis in 5. Twenty-one

patients were long-term smokers. With pathological staging after surgery, the disease was rated as stage IIa in 9 patients, stage IIb in 13, and stage III in 14.

Surgical approaches

In 13 patients, the surgery started with the right thoracotomy. Affected esophagus was resected and left-cervical circular gastro-esophageal anastomosis performed (McKeown modification). Four of them were anastomosed by staplers and 9 by manual suture. Drainage tube was placed *via* cervical incision. During surgery, gastric tube was inserted nasally and jejunostomy performed. The other 23 patients received left transthoracic approach, and intra-thoracic circular gastro-esophageal anastomosis was performed by staplers. During surgery, gastric tube and jejunal feeding tube were inserted nasally. In one of these patients, wedge resection of left lung was performed concomitantly. Following surgery, 8 patients were given parenteral nutrition, 18 were given enteral nutrition, and the other 10 both parenteral and enteral nutrition.

Postoperative leakage

Patients with fever, chest pain, dyspnea, or increased white blood cell count took oral methylene blue, and those without any of these symptoms were given follow-up contrast esophagogram on day 7 following surgery. All the patients were thereby confirmed with digestive tract leak. Among these 36 patients, 13 had cervical anastomotic leak, 18 had intra-thoracic anastomotic leak, and 5 had intra-thoracic gastric necrosis. The leak developed within 1-3 days after esophageal carcinoma resection in 6 patients, within 4-7 days in 11 patients, and within 8-14 days in 19 patients.

Treatment and outcome

Treatment lasted for 47.0 ± 31.9 days (range, 5-181 days). Complications mainly included pulmonary infection (50%), respiratory failure (19.4%), sepsis (11.1%), multiple organ failure (2.8%), and hepatic failure (2.8%). Nine patients deceased (mortality, 25.0%). The cure rate of conservative treatment was significantly higher than that of resurgery [75.0% (18/24) vs. 28.6% (2/7), $P = 0.037$], but not higher than that of stent implantation [75.0% (18/24) vs. 100% (6/6), $P = 0.302$, Table 1].

Three patients with early onset anastomotic leak (within 3 days after surgery) and 4 patients with confirmed intra-thoracic gastric necrosis were given operative re-exploration. The patient with early onset cervical anastomotic leak died of multiple organ failure on day 5 after surgery despite surgical repair. In the 2 patient with intra-

Table 1. Treatment profile in 36 patients with anastomotic leak following surgery for esophageal carcinoma

Treatment	Leak type			Cure rate	Mortality
	Cervical leak	Intra-thoracic gastric necrosis	Intra-thoracic anastomotic leak		
Resurgery	1	4	2	2/7 (28.6%)	4/7 (57.1%)
Stent implantation	0	0	6	6/6 (100%)	0
Conservative treatment	12	1	10	18/24*(75.0%)	5/24 (20.8%)
Total	13	5	18	26/36 (72.2%)	9/36 (25%)

* $P=0.037$ compared with resurgery.

One patient in conservative treatment was switched from resurgery treatment, who was discharged with drainage tube attached, not completely cured, thus counted as neither cured nor dead case.

thoracic anastomotic leak receiving resurgery, 1 was cured. In the 4 patients with intra-thoracic gastric necrosis, necrosis of the gastric stump was found ruptured. Necrotic tissue was resected and sutured by stapler. Only one of the 4 was cured; while in the other 3 patients, leak developed again after surgical repair, causing 2 deaths because of severe infection and respiratory failure on day 21 and day 25, respectively. The remaining patient was switched to conservative treatment, receiving placement of pleural cavity drainage tube and repeated lavage. On day 90 after surgery, follow-up contrast swallow still revealed leak of contrast agent, which, however, was limited within thoracic apex, indicating small leak (Fig. 1A, B). The patient was told to keep to semi-fluid diet and was free from significant fever and chest pain. On day 120, follow-up esophagogram suggested that the leak was healed, and residual abscess cavity in thoracic apex markedly reduced (Fig. 1C).

In 6 patients who underwent stent implantation, drainage from thoracic cavity was significantly reduced 3-5 days after surgery, and fever and symptoms of pulmonary infection remarkably relieved. One week after surgery, they started oral intake. But one patient's stent migrated on day 8 after implantation and was replaced by a longer stent. The stent was removed under endoscopy in the 7th week, and the procedure was successful (Fig. 2).

Of 12 patients with cervical anastomotic leak, 7 with smaller leak were managed by local drainage and daily dressings. For the other 5 with larger cervical leak whose divergence of anastomosis was up to 50%, drainage tube was placed in *via* the fistula; then fresh dressing was maintained for the wound within 5-7 days. When granulation was formed locally, latex drainage tube was placed into the leak *via* the fistula and cervical incision, which was then sutured. The drainage tube was then connected to a negative pressure bottle for continued drainage. In 10 patients with intra-thoracic anastomotic leak, 1 asymptomatic patient had localized leak as indicated by radiology, and was only given gastric tube and drainage, rather than

thoracic cavity drainage. The other 9 patients were treated with traditional "three-tube" therapy, that is, gastric tube, feeding tube, and thoracic drainage tube, together with thoracic cavity lavage therapy. In the patients receiving conservative treatment, 1 with cervical leak, 1 with intra-thoracic gastric necrosis and 3 with thoracic leak de-

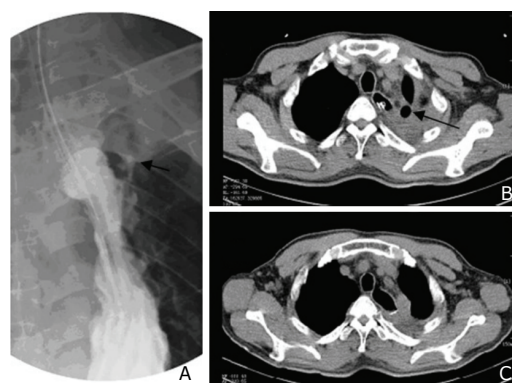


Figure 1. A follow-up contrast X-ray on day 90 after surgery (A) demonstrates an intra-thoracic anastomotic leak limited within thoracic apex (arrow). Computed tomography (CT) scan at the same time (B) shows the abscess cavity (arrow). The abscess cavity disappeared after 30 days in CT scan on day 120 (C).

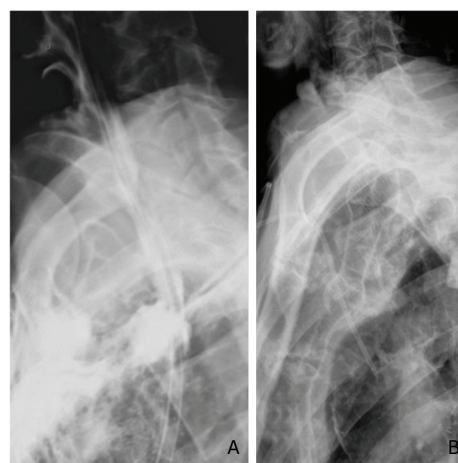


Figure 2. Intra-thoracic anastomotic leak (A) and implanted esophageal stent (B).

ceased in day 6-71 due to severe infection. After being treated for 181 days, a patient with intra-thoracic leak was not completely cured, but abscess cavity was limited, so the patient was discharged with abscess cavity drainage tube and jejunal feeding tube. The remaining patients were cured and discharged after being treated for 46.3 ± 14.9 days (range, 20-73 days). Among them, one patient with intra-thoracic leak had limited outflow and was thus only treated with placement of gastric tube and drainage; follow-up esophagogram after fasting for 2 weeks showed minimal outflow (Fig. 3), the patient started on semi-fluid diet and experienced no discomfort. In 5 patients managed with placement of drainage tube *via* fistula and cervical incision, the drainage tubes were removed on day 14 after placement. On day 21, the leak was cured and the patients started eating.

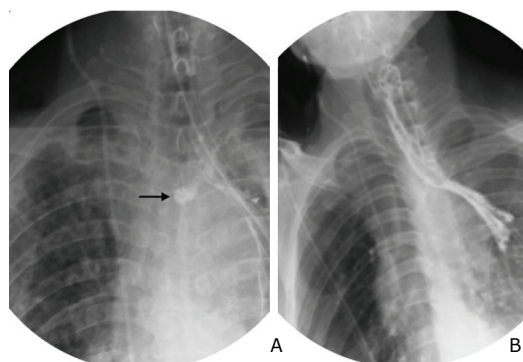


Figure 3. X-ray (A) shows a relatively small area of contrast extravasation contained by mediastinal structures (arrow). Esophagogram after fasting for 2 weeks (B) displays markedly reduced outflow.

DISCUSSION

Anastomotic leak is a serious complication of thoracic surgery, associated with high mortality and tends to necessitate long-term hospitalization.^{2, 3} In addition to systemic treatments including basic nutrition support and the use of broad-spectrum antibiotics, the most critical treatment is local management of the leak. Currently there is not standardized treatment. Turkyilmaz et al⁴ suggested detailed treatment processes, which was of certain reference significance.

Drainage is a basic surgical method in local management for anastomotic leak. Keeping an effective drainage is key to conservative treatment and can cure most anastomotic leak. Based on that principle, new methods of drainage have been introduced and achieved good results.^{5, 6} We presume that the closure of anasto-

motric leak is often the results of tissue adhesion around the leak, enclosure of the leak by granulation tissue, and finally coverage by digestive tract mucosa, rather than the healing of both ends of the leak. Effective drainage *via* gastric tube and thoracic cavity tube can ensure adequate drainage of digestive fluid from both inside and outside of gastric cavity, so as to allow tissue adhesion and healing around the leak. In 5 patients with cervical leak in this study, drainage tube was inserted *via* cervical fistula and connected to negative pressure device to collect outflowing digestive fluid. Thereby, tissue around the incision was free from contamination, so that granulation tissue could form around the drainage tube; the tube could be removed once the sinus tract was established. The rationale is similar to that behind the "T-tube" drainage for biliary duct. It is easy to take care of, takes shorter time compared with routine dressing changing and drainage, and is particularly applicable to larger cervical anastomotic leak. This method can also be used for refractory intra-thoracic anastomotic leak. Wang et al⁷ reported the resurgery in 9 patients and the placement of T-tube into the leak, of whom 8 were cured.

Resurgery for leak repair is a dilemma. Previous experience suggests that resurgery is associated with frequent complications and high mortality, but low rate of successful repair.⁸ Current literature presents controversial findings about the efficacy of resurgery. Zhang et al⁹ reported a cohort with intra-thoracic anastomotic leak; among 5 patients who underwent resurgery and repair or resection of anastomosis and re-anastomosis, outflow of digestive fluid was still seen after surgery at various degree. Crestanello et al¹⁰ reported a group of 20 patients receiving resurgery, in which 3 died after surgery, but no further leak was seen among these patients. We suggest that rigorous compliance to the indications of resurgery should be practiced, which include: early onset anastomotic leak; thoracic gastric necrosis; encapsulated empyema, with poor drainage by routine methods and significant concomitant toxic symptoms. Resurgery for these scenarios can produce better efficacy than conservative treatment. The objective of resurgery is to: transform an intra-thoracic anastomosis into a cervical anastomosis, so as to facilitate management; repair the leak as much as possible, which can be achieved by using omentum and muscle flap; clear digestive fluid and purulent secretion in thoracic cavity, so as to ensure good drainage, reduce absorption of toxic substances, and relieve toxic symptoms. In the present study, resurgery resulted in poor efficacy. The high mortality associated with resurgery in this study might be partly due to the conservative surgical procedure. The

choice of specific surgical procedures has yet to be further investigated.

Esophageal stent implantation *via* endoscopy has been gradually accepted and widely adopted as a treatment for anastomotic leak associated with cancers.¹¹⁻¹³ The application of stent is somehow limited, for instance, expansion of coated stent may cause avulsion of the tissue around anastomosis, stents can not seal a leak caused by gastric perforation, the anatomic angle of aorta does not allow for linear journey of the stent, the stent may injure vessel wall, and the stent may be displaced. However, the mortality of stent therapy for anastomotic leak was lower than that of traditional surgical treatment.¹⁴⁻¹⁷ For the present, it might be an optimal treatment strategy for intra-thoracic anastomotic leak. When the leak is sealed by the stent, thoracic exudation will be reduced. As solid adhesion forms along the pleura and the leak can be sealed from the outside, the stent can be removed. According to the method proposed by Leers et al,¹² the stent was removed in 6th to 8th week to avoid difficulty in removing resulting from adhesion of granulation tissue following prolonged placement of the stent.

In cases of localized intra-thoracic anastomotic leak, tube placement or resurgery is necessary to achieve adequate drainage for those with significant concomitant symptoms of infection, such as fever and chest pain. For asymptomatic localized anastomotic leak, capsulated residual cavity may exist for a long time, whereas complete healing of abscess or leak is not necessarily a prerequisite for restoration of normal diet. In management of localized anastomotic leak, patients should fast under observation for 1-2 weeks; if residual cavity is not expanding and infection not spreading, the patients can try to start semi-fluid diet. In a patient with intra-thoracic gastric necrosis who underwent resurgery in this study, localized leak still existed after the surgery, but the patient had no significant symptoms of infection, and follow-up esophagogram showed no increase in residual cavity, so the patient was allowed to start semi-fluid diet. In the follow-up visit one month later, residual cavity had already disappeared.

In conclusion, anastomotic leak after surgery for esophageal carcinoma can vary in location, onset time, size, and extent. For local management, personalized treatment should be decided based on patient's particular situations. Conservative treatment is still a safe and effective method and resurgery should be considered carefully. Stent implantation might be a prospective therapeutic option but needs further verification.

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