



Effectiveness and safety of bovine pericardium patch repair for cervical anastomotic leakage after oesophagectomy for cancer

Xionghuai Hua¹, Rulin Qian¹, Kefeng Shi¹, Xiufeng Wei², Heng Zhang¹, Ge Qu¹, Maolin Chen¹, Binbin Zhang¹

¹Department of Thoracic Surgery, Henan Chest Hospital, Zhengzhou 450000, China; ²Department of Thoracic Surgery, the First Affiliated Hospital of Xinxiang Medical University, Weihui 453100, China

Contributions: (I) Conception and design: X Hua; (II) Administrative support: R Qian, K Shi; (III) Provision of study materials or patients: H Zhang, M Chen, X Wei, G Qu, B Zhang; (IV) Collection and assembly of data: X Hua, X Wei; (V) Data analysis and interpretation: X Hua, X Wei; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Rulin Qian. Department of Thoracic Surgery, Henan Chest Hospital, Zhengzhou 450000, China. Email: xwnj2012@163.com.

Background: The objective of this study is to evaluate the effectiveness and safety of bovine pericardium patch (BPP) repair for cervical anastomotic leakage after esophageal squamous cancer.

Methods: Intractable cervical anastomotic leakage developed in 7 patients of esophageal squamous cell carcinoma undergoing cervical anastomosis. These patients received the BPP repair. The necrotic tissue around the cervical anastomosis was removed during the operation, and the defect was repaired with BPP according to the size of the leakage.

Results: The operative duration was 60–90 min (median, 75 min). There were no signs of recurrent anastomotic leakage in each patient undergoing BPP repair. Oral intake was initiated 5–8 days (median, 6 days) after the BPP repair operation without any discomfort.

Conclusions: The BPP repair is a safe and effective processing scheme for patients with cervical anastomotic fistula after resection of esophageal squamous cell carcinoma. This method may be recommended for appropriate patients with intractable cervical anastomotic fistula.

Keywords: Esophageal squamous cancer; esophageal reconstruction; cervical anastomotic leakage; bovine pericardium patch (BPP)

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Introduction

Resection of esophageal carcinoma is one of the surgical operations with the complex operation and high incidence of complications. In clinic, the conventional surgical methods of resection and digestive tract reconstruction of esophageal carcinoma are as follows: Ivor-Lewis esophagectomy, the McKeown approach, and the transhiatal technique. Especially, minimally invasive resection of the esophagus is becoming increasingly popular in recent years (1). In China, thoracic-laparoscopic esophagectomy is the current mainstream. Regardless of the technique, the residual stomach is the most commonly used replacement

organ after esophageal reconstruction (2). Cervical esophagogastric anastomotic fistula is one of the most common complications after esophageal squamous cancer. It may prolong the hospital stay, and cause severe mediastinal infections, even death in a short time (3).

Adequate drainage and active anti-infection treatment in the early stage are the key measures to control the further deterioration of cervical anastomotic leakage (4). Besides, it is necessary to correct the malnourishment. After a period of conservative treatment, if the fistula does not improve, further surgical or interventional intervention should be considered (5,6). In this study, we tried to use bovine pericardium patch (BPP) to repair cervical anastomotic

leakage after esophagectomy for cancer in order to evaluate its safety and effectiveness.

Methods

One hundred sixty-two patients with esophageal squamous cell carcinoma underwent radical resection at the Department of Thoracic Surgery, Henan Chest Hospital from June 2017 to June 2019. Among them, 142 patients underwent tubular gastric reconstruction with cervical esophagogastric anastomosis. The thoracoscopy combined laparoscopy and mediastinoscopy combined with laparoscopy surgical treatment were performed in 112 and 30 patients, respectively.

The end-to-side esophagogastric cervical anastomosis was performed in all patients by mechanical anastomosis by a 25-mm-diameter circular stapler. After the gastric stump was cut into a tubular gastric outside the abdominal cavity, it was pulled up to the neck along the posterior mediastinal esophageal bed. The distal end of the tubular gastric was cut, the circular stapler was inserted, and the gastric wall was penetrated. Then the center rod of the circular stapler was matched with the anvil which has been placed into the stump of the cervical esophagus. The gastric stump incision was closed with the linear cutting-closure device. Finally, the cervical anastomosis was intermittent and strengthened with 4-0 silk thread.

Anastomotic leakage was diagnosed in this study by salivary discharge, esophagography, or endoscopy. Cervical anastomotic leakage developed in 18 patients (12.7%) with esophageal squamous cell carcinoma undergoing esophagogastric cervical anastomosis. In these patients, 11 patients cured within 6 weeks by conservative treatment, including anti-infective therapy and adequate drainage. Finally, 7 patients developed into persistent and intractable anastomotic leakage. All of these patients with intractable anastomotic leakage were confirmed by routine endoscopic examination or angiography.

All patients were needed to sign an informed consent form before the operation. Moreover, all the BPP repair operation was performed under general anesthesia. The repair process of BPP mainly included two aspects. That was debridement of the leakage and repair of defect with BPP. The necrotic tissue around the leakage was removed, and the region of esophagogastric anastomosis leakage was exposed. Then according to the size of fistula, the appropriate BPP was made. Repair of the esophagogastric anastomosis defect was performed with continuous sutures

using 3-0 slide suture (Prolene W8558; Ethicon Inc.). Finally, a closed drain was inserted near the BPP (*Figure 1*).

Results

The clinical features of these 7 patients who underwent BPP repair were summarized (*Table 1*). Five of them were male (71.4%). The average age was 66.9 years (range, 55–78 years). Based on the stage of esophageal squamous cell carcinoma (TNM classification, 8th edition, UICC), patient classification was as follows: stage IB, 2 patients; stage IIA, 2 patients; stage IIIA, 2 patients; and stage IIIB, 1 patient. Gastric conduit reconstruction was performed in all patients. 3 patients underwent two cycles of neoadjuvant chemotherapy with Docetaxel combined with platinum. Thoracoscopy combined with laparoscopic resection was performed in 4 patients and mediastinoscopy combined with laparoscopic surgery in 3 patients. The posterior mediastinal esophageal bed pathway was used in all the patients. Moreover, all the patients undergoing surgery are squamous cell carcinoma.

The BPP repair was performed 35–60 days (median, 45 days) after radical operation of esophageal squamous cancer. The operative duration was 60–90 min (median, 75 min). Oral intake was initiated 5–8 days (median, 6 days) after BPP repair process. No patients had dysphagia. No patients developed surgical site infection. No sign of recurrence anastomotic leakage was found after BPP repair in each patient.

Discussion

Cervical anastomotic leakage is one of the most common complications after esophageal cancer surgery. The incidence of anastomotic leakage after the esophagus reconstruction was as high as 20–25% (7). Tubular gastric is the common alternative organ after resection of esophageal squamous cell carcinoma. Either it is manual or mechanical anastomosis depends on surgeons' preferences and technology to some extent. Related studies showed that there was no significant difference in the incidence of an anastomotic fistula between mechanical and handsewn anastomotic techniques (8). Compared with cervical esophagogastric anastomosis, intrathoracic anastomosis is associated with higher complications and mortality. The incidence of cervical anastomotic leakage is higher than that of intrathoracic anastomotic leakage (9). The main reason for this difference is the longer distance that the blood

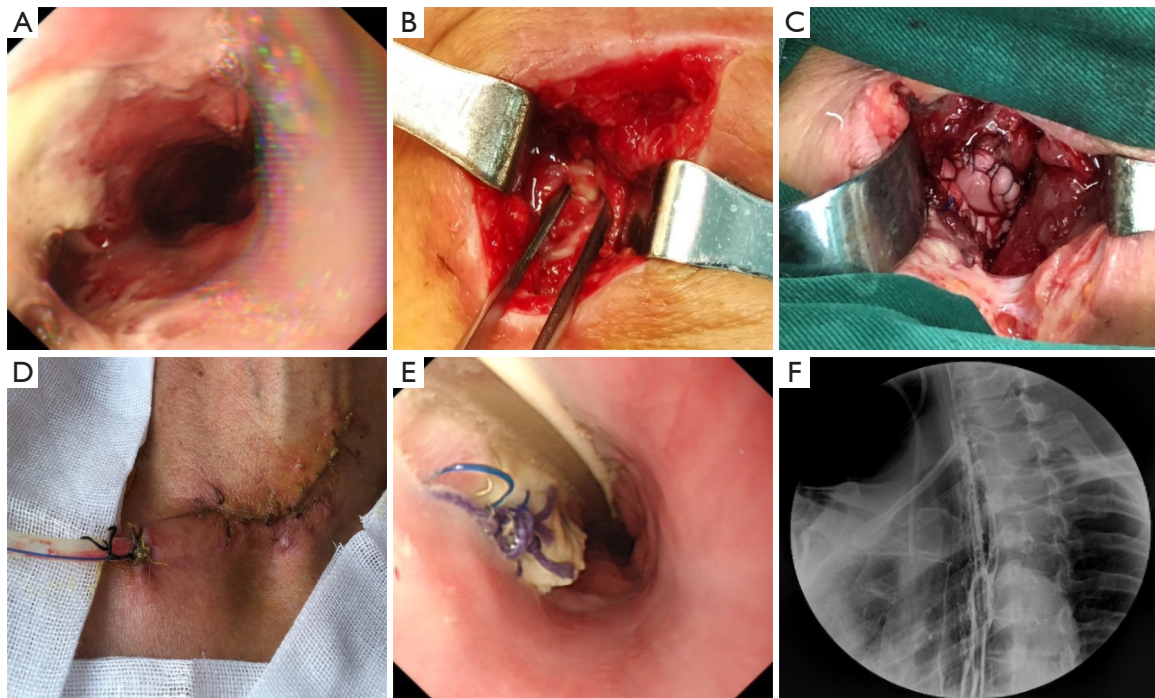


Figure 1 BPP repair and follow-up of cervical anastomotic leakage. (A) Postoperative endoscopy confirmed the neck anastomotic leak; (B) intraoperative exposure of the neck anastomotic leak position; (C) the position after repair the neck anastomotic leak in the second operation; (D) the state of the neck incision healed after the anastomotic leak repaired; (E) review the postoperative endoscopy after repairing the anastomotic leak; (F) review the postoperative upper gastrointestinal tract after repairing the anastomotic leak. BPP, bovine pericardium patch.

Table 1 Clinical features of patients undergoing BPP repair

Case No.	Patients' characteristics				Esophageal reconstruction		Diagnosis of anastomotic leakage after esophagectomy, days	Bovine pericardial patch repair			
	Age, years	Sex	pTNM	NCT	MIE	Reconstruction route		BPP repair, days	duration of operation, min	Relapse of leakage	Oral intake after repair, days
1	55	Male	IIIA	Yes	TLC	Posterior mediastinal	5	37	63	No	5
2	60	Female	IIIB	Yes	TLC	Posterior mediastinal	4	60	78	No	6
3	59	Female	IIIA	Yes	TLC	Posterior mediastinal	6	42	73	No	5
4	67	Male	IB	No	MLC	Posterior mediastinal	6	35	60	No	7
5	72	Male	IIA	No	TLC	Posterior mediastinal	9	45	78	No	5
6	77	Male	IB	No	MLC	Posterior mediastinal	10	50	90	No	8
7	78	Male	IIA	No	MLC	Posterior mediastinal	7	47	82	No	7

NCT, neoadjuvant chemotherapy; TLC, thoracoscopy combined with laparoscopy; MLC, mediastinoscopy combined with laparoscopy; BPP, bovine pericardium patch; MIE, minimally invasive esophagus.

supply needs to travel for anastomotic healing in the neck than in the intrathoracic region (10). In our department, end-to-side mechanical anastomosis is our first choice, and the embedded cutting edge is then reinforced with an absorbable suture.

In this study, 12.7% of the patients who underwent cervical mechanical anastomosis after esophagectomy developed anastomotic leakage. Leakage was confirmed in these patients by angiography or endoscopy. The three main factors of anastomotic leakage include reduced blood supply, anastomotic tension, and lack of serosa structure (11). Further risk factors are represented by immunosuppression, poor nutrition, and earlier radiation treatment (12). Consistent with most earlier studies, in the end-to-side anastomosis, the blood supply of the gastric stump is damaged in this study.

Once cervical anastomotic leakage occurs after the operation of esophageal squamous cell carcinoma, active anti-infection and drainage treatment is usually given first (13). Leakage is normally healed by granulation tissue filling, and Intractable anastomotic leakage is rare. For intractable cervical anastomotic leakage, active surgical intervention, or interventional treatment often need considering, such as vascularized pedicle tissue flaps, sternocleidomastoid flap repair, and covered stents most commonly used (14). As we know, the treatment of cervical anastomotic fistula with covered stents usually lead to severe swallowing discomfort or stent displacement (15). In clinical practice, vascularized pedicle tissue flaps can be used to repair cervical anastomotic fistula or to reinforce gastrointestinal anastomosis (16). Because of its rich muscle content, pectoralis major muscle is an ideal choice for the repair of anastomotic leakage. The sternocleidomastoid muscle can be transplanted in the same field for the repair of cervical anastomotic fistula. Compared with the pectoralis major muscle flap, the extent of the sternocleidomastoid flap translocation is relatively minimal (17). In contrast, the BPP is used for anastomotic fistula repair, and its operation is minimally invasive. Also, there have been few reports in earlier literature.

BPP is mainly used for repair of cardiovascular surgery. To prevent anastomotic dehiscence, there are reports in the literature where the use of biological materials has been investigated to reinforce an anastomosis (18). In an earlier experimental study in pigs, they conducted a comparative study using BPP embedding anastomosis. The results showed that the anastomotic healing after BPP embedding was better, and it was surprising in the prevention and

treatment of peritonitis caused by anastomotic leakage (19). The knowledge derived from the experimental setting has been applied to esophageal cancer surgery in this study. Independently from the type and the anatomical level of anastomosis, when esophagogastric anastomoses have been wrapped with the patch, neither leak, stenosis, and abscess were seen, nor any cases of displacement and shrinkage of the BPP during follow-up. BPP is a kind of membrane with specific strengths and extensibilities, which is composed of multidirectional fibers and is completely degraded in the host (20). BPP can adequately cover fragile and vulnerable tissue and prevent exosmosis of digestive juice. Based on the previous evidence from animal studies, BPP may have ideal qualities as a tissue to use as anastomotic reinforcement, such as the trend for neoangiogenic function, reduction in adhesion formation, resistance to infection, and biocompatibility (21).

In this study, all leakage sites occurred at the anastomotic site. The debridement of necrotic tissue and the exposure of fistula in the cervical esophagogastric anastomotic area are essential for reliable repair (22). We performed BPP repair in these patients with refractory anastomotic fistula under general anesthesia. With regards to the choice of timing for the repair of anastomotic leakage, Hayashi *et al.* recommended that it be performed four weeks after the first operation because the anastomotic leakage was more likely to recur within three weeks (23). In our study, we recommend early debridement around the anastomotic area. Concerning the radical resection of esophageal squamous cell carcinoma method, double endoscopic esophagectomy with cervical anastomosis was performed. Cervical anastomosis is performed because intrathoracic anastomosis often leads to fatal clinical outcomes (24). Even if these results seem to be encouraging, but the efficacy of BPP for giant anastomotic leakage is unclear. Further investigation of the appropriateness of the BPP for giant anastomotic leakage is needed, and randomized controlled clinical trials are needed to compare the outcomes of anastomosis performed with and without the BPP.

In conclusion, BPP repair is a safe and effective processing scheme for patients with cervical anastomotic fistula after resection of esophageal squamous cell carcinoma. This method may be recommended for appropriate patients with intractable cervical anastomotic fistula.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. In accordance with the requirements of the Helsinki Declaration and relevant laws and regulations, such as the ethical review of biomedical research involving human beings, there is no conflict of interest in the study, which has been examined and approved by the Ethics Committee (Ethics Committee of Henan chest Hospital, 20175021). The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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