Original Article

Alternate approaches for effective reduction in incidence of cervical anastomotic leakage after esophageal cancer resection: a prospective cohort study

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ABSTRACT

Objective: To investigate the method of operation for esophageal cancer to reduce incidence of cervical anastomotic leakage after resection

Design: Prospective study

Setting: Department of Thoracic Surgery, Luoyang Central Hospital Affiliated to Zhengzhou University

Subjects: All esophageal cancer resection patients from August 2009 to August 2014 were included and grouped according to the admission time.

Intervention: Mechanical cervical esophagogastric anastomosis through the highest point of the tubular stomach in addition to embedment and suspension of the anastomosis (group A, from August 2009 to November 2011, n = 37), mechanical cervical esophagus-tubular stomach anastomosis at the plane of the terminal branches of the right gastroepiploic vessels plus embedment and suspension of the anastomosis with redundant tubular stomach removed (group B, from December 2011 to August 2012, n = 39) and without (group C, from September 2012 to August 2014, n = 62).

Main outcome measures: The incidence of cervical anastomotic leakage

Results: All approaches were performed successfully and the anastomoses were tension-free. The incidence of cervical anastomotic leakage was 24.3% (9/32) in group A, 25.6% (10/37) in group B, and 1.6% (1/62) in group C, respectively. There was no statistical difference between groups A and B, while the anastomotic leakage incidence was much lower in group C than the other two groups (P <0.05).

Conclusions: The mechanical cervical esophagus-tubular stomach anastomosis approach without embedment and suspension of the anastomosis may lead to lower cervical anastomotic leakage after esophageal cancer resection.

INTRODUCTION

Esophageal carcinoma is the eighth most common cause of cancer worldwide[1], with surgical resection still considered the gold standard treatment[2]. For middle and upper esophageal carcinoma, surgical approaches include subtotal esophagectomy, cervical esophagus-gastric anastomosis, and thoracolaparoscopic esophagectomy with two-field lymph node dissection. These approaches can effectively reduce the incidence of postoperative recurrence and metastasis. However, a surgical approach involving three incisions of the right thoracic and abdominal portions as well as the cervical anastomosis has a number of disadvantages, including significant surgical trauma, more complications, and lengthy operating times, which are not ideal for either patient or surgeon. Recent studies have shown minimally invasive esophagectomy (MIE) to be safe and effective[3,4]. Continued improvements in endoscopic techniques have resulted in the development of a combined thoracoscopic and laparoscopic esophagectomy approach. However, anastomotic leakage remains a common complication, with an incidence ranging from 3 – 23.5%[5]. Compared with intrathoracic anastomotic leakage, cervical anastomotic leakage is associated with lower mortality rates[6], and healing times can be shortened by opening

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the cervical incision, together with adequate drainage. Nevertheless, this complication still has some adverse effects on patients, such as increased clinical burden and prolonged hospitalization that may lead to anastomotic stenosis, which adversely influences quality of life.

A number of studies have been conducted with the aim of reducing the incidence of cervical anastomotic leakage after surgical resection. Some approaches have included the modification of anastomotic methods, the development of new methods for esophagus reconstruction, and delays in the reintroduction of oral food intake after surgery. However, further improvements to these approaches are required to enhance their efficacy. It is clear, therefore, that further research is required to effectively reduce the incidence of postoperative cervical anastomotic leakage in patients suffering from esophageal carcinoma, which is the rationale of the present research.

Thus, the aim of this study was to investigate approaches to effectively reduce cervical anastomotic leakage after esophageal cancer resection. To meet this goal, we investigated three methods of anastomosis and compared the incidence of anastomotic leakage in a patient population divided into three treatment groups. The most effective method for decreasing the incidence of cervical anastomotic leakage was identified.

**SUBJECTS AND METHODS**

**Patient information**

A total of 138 patients were recruited for this study from August 2009 to August 2014 and combined thoracoscopic and laparoscopic esophagectomy was performed. An endoscopic examination and biopsy was performed on each patient and a diagnosis of esophageal cancer was confirmed by pathology prior to the assigned surgical procedure. Besides regular examinations, all patients underwent chest CT and an upper gastrointestinal radiography test to assess the extent of the lesion and its relationship with the surrounding tissues. Furthermore, the possibilities of surgical resection were evaluated.

**Surgical procedures**

A combined intravenous-inhalational anesthesia was performed on each patient and an artificial pneumothorax was used during surgery. The operational procedures involved positioning the patient in the left lateral decubitus position with the subaxillary lifted by a cushion. The esophagus was isolated under a thoracoscope. The lymph nodes along the esophagus, together with the left and right recurrent laryngeal nerves and the subcarinal nodes, were dissected. An intrathoracic drain was placed. Phlegm was removed under suction before the lungs were inflated. The surgical openings were sewn closed and dressed.

The patient was then placed in a supine position with the head positioned higher than the feet. The patient’s head was turned to the right. Through an incision along the anterior border of the left sternocleidomastoid muscle, the cervical segment of the esophagus was isolated and divided. Then the stomach was isolated using a laparoscope. The incision under the cartilago ensiformis was extended by about 4 cm. The esophagus was amputated and fixed on a traction suture. The stomach and esophagus were pulled out by the traction suture through the abdominal incision. Fragments of the esophagus and lesser curvature were removed using a 75 mm disposable linear stapler (Johnson & Johnson product). The remnant stomach was processed into a tubal form. Suturing was performed at the highest point of the tubular stomach. Once it was confirmed that the stomach was not twisted, it was pulled out from the left cervical incision by the traction suture through the esophageal hiatus and right chest.

Three anastomosis approaches were used based on the order that the patients were admitted to the hospital. Group A included the first 37 patients admitted. The anastomosis approach in this group involved performing a mechanical cervical esophagogastric anastomosis through the highest point of the tubular stomach using a 25 mm disposable circular stapler (Johnson & Johnson product). The anastomosis was embedded and suspended using four silk sutures (Johnson & Johnson product). Group B included the next 39 hospital admissions. The anastomosis approach performed in this group was a mechanical cervical esophagus-tubular stomach anastomosis at the plane of the terminal branches of the right gastroepiploic vessels using a 25 mm disposable circular stapler (Johnson & Johnson product). Then the redundant tubular stomach was resected. The anastomosis was embedded and suspended using four silk sutures (Johnson & Johnson product). Group C included the last 62 patients admitted to hospital during the recruitment period. The anastomosis approach in this group was the same as group B, except that the embedding and suspension process for anastomosis was not carried out. None of the patients received neoadjuvant chemotherapy. The three surgical techniques are shown in Figure 1. All anastomoses were performed successfully and were tension-free. Gastrointestinal decompression and duodenal nutrition tubes were also placed during surgery. A drainage strip was placed in the cervical incision. Cervical and abdominal incisions were then closed using sutures. There were no significant differences.
Alternate approaches for effective reduction in incidence of cervical anastomotic leakage ...

Fig 1: Operation schematic diagram of the three techniques
in gender, age, disease region, nutritional condition, preoperative complications, or the preparation of the tubular stomach among these three groups. The incidence of anastomotic leakage was recorded and analyzed. All operations were performed by the same cohort surgeons.

**Diagnosis of postoperative anastomotic leakage**

 Clinical manifestations of postoperative anastomotic leaks included swelling, heat, pain in cervical incisions, fever, subcutaneous effusion, pneumatosis, and fluctuation of symptoms. Purulent or malodorous secretions, which probably contained gastric juice and food residue, are also seen when the incisions are braced. The complete blood count (CBC) test results may be abnormally high. The esophagogram will show an abnormal flow direction of the contrast agent. When methylene blue is administered orally, the blue liquid flows out from cervical incisions.

Statistical analysis

Statistical analysis was performed using SPSS version 17.0 software. The comparison of the incidence of anastomotic leakage among the three groups was performed using the χ² test. Results were considered statistically significant when p ≤ 0.05. The STROBE checklist was consulted and followed[7].

### RESULTS

Patient characteristics for the three groups are shown in Table 1. The sample patient population consisted of 75 males and 63 females aged from 45 - 78 years (mean age: 64.1 years). Squamous cell carcinoma accounted for 136 cases and two cases were due to adenocarcinoma. From the total 138 patients, the tumors of 40 cases were located in the upper esophagus, 72 were in the middle esophagus, and 26 were in the lower esophagus. In group A, nine patients were diagnosed with anastomotic leakage. In groups B and C, the numbers were ten and one patients, respectively. Thus, the incidence in groups A, B, and C were 24.3%, 25.6%, and 1.6%, respectively. Through opening cervical incisions and adequate drainage, the anastomotic leakages healed after about two weeks for all patients except one, where a small sinus that had not healed developed. During this study, no patients died as a result of surgery. The incidence of anastomotic leakage for the three groups is shown in Table 2. There were no significant differences in incidence of anastomotic leakage between groups A and B (p > 0.05). In contrast, the incidence in group C was significantly lower than that in the other two groups (p < 0.05). There was one patient with postoperative anastomotic stenosis in group B. We treated him with further surgery.

<table>
<thead>
<tr>
<th>Group</th>
<th>Number (n) of operation cases</th>
<th>Number (n) of anastomotic leak cases</th>
<th>Incidence of anastomatic leak (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>37</td>
<td>9</td>
<td>24.3</td>
</tr>
<tr>
<td>B</td>
<td>39</td>
<td>10</td>
<td>25.6</td>
</tr>
<tr>
<td>C</td>
<td>62</td>
<td>1</td>
<td>1.6</td>
</tr>
</tbody>
</table>

**DISCUSSION**

The traditional surgical approaches to the treatment of esophageal carcinoma include cervico-right thoracic-abdominal triple incision, right thoracic-abdominal double incision, and left thoracic single incision[1]. For the middle and upper esophageal carcinoma, subtotal esophagectomy plus cervical esophagus-gastric anastomosis combined with thoracolaparoscopic esophagectomy with two-field lymph node dissection can effectively reduce the incidence of postoperative recurrence and metastasis. This technique is regarded as the ideal surgical method for the treatment of middle and upper esophageal carcinoma. However, the right thoracic approach requires three incisions plus cervical anastomosis and has several disadvantages. These include major surgical trauma, more complications, longer operating times, and higher mortality rates, all of which limit its application in clinical practice. The objective is to develop new surgical methods that can not only remove tumors effectively and dissect associated lymph nodes, but can also reduce surgical trauma and lower the incidence of postoperative complications and mortality.
Recent studies have shown that MIE is both safe and effective\[4-13\]. Compared to traditional open surgical procedures, MIE poses some significant advantages. These include reduced intraoperative hemorrhage\[8-9\], decreased ICU and hospitalization time\[8,10\], fewer perioperative and pulmonary complications, and lower incidences of arrhythmia\[13\] and incision infection rate\[12\] together with decreased postoperative incision pain. Additionally, in terms of postoperative quality of life and functional recovery, MIE is significantly superior to open procedures\[13\]. Minimally invasive esophagectomy can reduce the risk of mortality during surgery\[14\], but is not significantly different from traditional open surgical procedures in terms of total cost of hospitalization and postoperative survival rates\[10\].

There are two types of MIE approaches for the treatment of esophageal carcinoma. A previous study\[15\] suggested that MIE plus mechanical intra-thoracic esophago gastric anastomosis can reduce the possibility of anastomotic leakage and injury of recurrent laryngeal nerves. Unfortunately, the procedures involved in this approach are complicated, costly, and require lengthy operating times. More importantly, however, once the anastomotic leakage develops, mortality is significantly higher than it is for cervical anastomosis. For this reason, this surgical procedure is not typically used in clinical practice. Combined thoracoscopic and laparoscopic esophagectomy plus cervical esophago gastric anastomosis is a more widely adopted approach. Nevertheless, anastomotic leakage remains a common postoperative complication with an incidence of 3 – 23.5\%\[9\], which is not significantly different to the incidence for traditional three-incision open chest surgery. The mortality rates as a result of cervical anastomotic leakage is significantly lower than that of intrathoracic anastomotic leakage\[6\], and type I-II carries a relatively high possibility of death\[16\]. The leakage can heal in a short time through opening the cervical incision and adequate drainage. Nonetheless, complications prolong the length of time patients are required to stay in hospital, together with the associated economic burden. Moreover, it can cause postoperative anastomotic stenosis, which can adversely influence the quality of life of patients.

A number of studies have been conducted to investigate methods that can prevent postoperative cervical anastomotic leakage. Kondra et al\[17\] found that a partially stapled cervical esophagogastric anastomosis (stapled posterior wall and hand-sewn anterior wall) could effectively reduce the leakages. Despite this, 12.7\% of patients who underwent this approach developed an anastomotic leakage. Fang and colleagues\[18\] showed in their study that for patients with a systemic lymph node dissection, a prolonged nasal-gastric drainage of more than seven days could significantly decrease the incidence of leakage to 9.1\%. In another study\[19\], the authors suggested an esophageal-tubular stomach hand-sewn two-layer anastomosis method. This method had a lower incidence of anastomotic leakage than esophageal-whole stomach hand-sewn two-layer anastomosis. However, an incidence of 5.5\% persisted. Further research\[20\] reported end-to-side anastomosis using a circular stapler. The anastomosis and remaining esophagus were embedded into the stomach. This approach reduced the incidence of anastomotic leakage to 3.3\%. However, the incidence of strictures was 11.4\%. Zheng et al suggested that omentoplasty could significantly reduce the incidence of cervical anastomotic leakage down to 3.3\% following esophageal carcinoma surgery\[21\]. Other researchers\[3\] have found that delaying oral consumption of food after esophagectomy (up to 12 days) could reduce the incidence of cervical anastomotic leakage from 14\% to 3\%.

A study conducted by Behzadi and colleagues suggested that for both cervical and intrathoracic anastomosis, the stapled approach was superior to the hand-sewn technique in preventing leakage\[22\]. In our study, we adopted the mechanic anastomotic approach for all patients. The patients in groups A and B underwent mechanical cervical esophagus-tubular stomach end-to-side anastomosis plus embedment and suspension of the anastomosis. The postoperative leakage rates were 24.3\% and 25.6\% respectively, which are consistent with previously published data. The patients in group C underwent mechanical cervical esophagus-tubular stomach end-to-side anastomosis without any treatment of the anastomosis. The leakage rate was reduced to 1.6\%, which was significantly lower than the rates in groups A and B, as well as the rates reported by other studies.

The incidence of anastomotic leakage in groups A and B did not achieve statistical significance. Moreover, embedding of anastomosis can reduce the anastomotic tension. Compared to groups A and B, the incidence of anastomotic leakage in group C was significantly less. The tubular stomach is long enough for three type of anastomosis without tension. There were differences in anastomosis site in terms of anastomotic blood flow for group A compared to groups B and C. In terms of postoperative anastomotic fistula, there was no statistical difference between groups A and B; but there was significant difference for group C compared to groups A and B. These results suggest that there is no significant association between anastomotic leakage and anastomotic tension or local blood supply. The result of upper gastro-enterography for all three groups also showed no significant inter-
group differences in the passage of contrast agent and the shape of the reconstructed esophagus. This finding suggests that there is no significant association between local tension and anastomotic leakage. In addition, there were no significant differences between these three groups in other factors including gender, age, diseased region, nutritional state, preoperative complications, and preparation of the tubular stomach, which excluded the effects of factors such as nutrition and complications. We considered that because the anastomotic leakage was not embedded and suspended, this enhanced the anastomotic patency and reduced the pressure in the upper esophagus. It caused hypertrophy of the anastomotic surrounding tissue and formed a high-pressure area. When patients coughed and swallowed, the esophageal pressure through anastomotic conduction was blocked. This increased the incidence of anastomotic fistula. The mechanism of the approach in group C in reducing the incidence of anastomotic leakage remains unclear at present and is suggested as a topic for future research.

CONCLUSION

Compared with mechanical cervical esophagogastric anastomosis through the highest point of the tubular stomach in addition to embedment and suspension of the anastomosis, there was no improvement on anastomotic leakage occurrence by taking mechanical cervical esophagus-tubular stomach anastomosis at the plane of the terminal branches of the right gastroepiploic vessels plus embedment and suspension of the anastomosis with redundant tubular stomach removed, but has gained a major change with no embedment and suspension of the anastomosis.

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REFERENCES


