Balloon dilatation complications during esophagogastric anastomotic stricture treatment under fluoroscopy: Risk factors, prevention, and management

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Abstract
Background: Balloon dilatation (BD) is a common treatment for esophagogastric anastomotic stricture (EAS), but with complications. This study investigates the risk factors, prevention, and management of BD complications to provide clinical guidance.

Methods: We retrospectively analyzed the clinical data of 378 patients with EAS treated by BD from March 2011 to June 2021. The association between esophagogastric anastomotic rupture outcome and patient and stricture characteristics and treatment were analyzed by logistic regression.

Results: BD was performed 552 times and technical success, 98.0%; overall clinical success, 97.8%; major adverse events, 1.3%; minor adverse events, 9.4%; mortality, 0.3%. Logistic regression showed that age (p = 0.080), sex (p = 0.256), interval from surgery to stricture development (p = 0.817), number of dilatations (p = 0.054), cause of stricture (p ≥ 0.168), and preoperative chemotherapy (p = 0.679) were not associated with anastomotic rupture. Balloon diameter (p < 0.001), preoperative radiotherapy (p = 0.003), and chemoradiotherapy (p = 0.021) were correlated with anastomotic rupture. All patients with type I and II ruptures resumed oral feeding without developing into type III rupture. Type III rupture occurred in six cases, who resumed oral feeding after 7–21 days of nasal feeding and liquid feeding. One patient died of massive bleeding after BD.

Conclusions: Symptomatic treatment for type I and II ruptures and transnasal decompression and jejunal nutrition tubes for type III rupture, are suggested pending rupture healing. Tumor recurrence, preoperative radiotherapy, and balloon diameter affected the anastomotic rupture outcome.

KEYWORDS
balloon dilatation, complications, esophagectomy, esophagogastric anastomotic stricture, interventional radiology

INTRODUCTION

Esophagogastric anastomotic stricture (EAS) after esophagectomy or gastrectomy could be caused by local factors such as tissue ischemia, leakage, infection, anastomotic technique, or tumor recurrence.1 The incidence of EAS after esophagectomy is 10%–43%.2 Dysphagia caused by the stricture seriously affects the patients’ quality of life.

EAS could be divided into malignant recurrent stricture and benign scar stricture. The two types are treated by thoroughly different methods. At present, malignant EAS is managed by placing a nasal feeding tube, a esophageal
stent, or by tumor-directed treatment. Benign EAS is treated by balloon dilatation (BD). BD for EAS has varying degrees of complications such as pain, discomfort, esophagogastric anastomotic rupture (EAR), and bleeding that could lead to death in severe cases. The purpose of this study was to investigate the risk factors, prevention, and management of BD complications associated with EAS treatment to provide clinical guidance.

METHODS

Data on BD under fluoroscopy for EAS were analyzed retrospectively at our center from March 2011 to June 2021 and included medical records, imaging data, and procedure records. Two experienced radiologists evaluated all data. The inclusion criterion was patients with EAS after esophagectomy or gastrectomy treated by BD. The exclusion criteria included: (1) patients with esophageal stricture treated by BD without undergoing esophagectomy. (2) Patients with achalasia treated by BD. (3) Patients with esophageal-jejunal anastomotic stricture after gastrectomy. Patient informed consent was not required because of the retrospective nature of the study.

Procedure

Preoperative preparation

Preoperative investigations included routine blood tests, liver and renal functions, electrolytes, blood glucose, coagulation function, infectious diseases, electrocardiography (ECG), and chest computed tomography (CT). Diazepam (Tianjin Jinyao Pharmaceutical) was used for sedation 30 minutes before the procedure, and oxybuprocaine hydrochloride gel was used for local mucosal anesthesia 10 minutes before the procedure.

Balloon dilatation

BD was used to treat EAS. If the EAS occurred within 3 months after surgery, we usually chose a balloon diameter <25 mm. In such cases, we considered choosing a larger diameter balloon catheter than the one used during the initial treatment. If EAS occurred more than 3 months after surgery, we usually chose a balloon diameter ≥25 mm.

The patients were supine on an operating table, equipped with digital subtraction angiography, oxygen inhalation, ECG monitoring, and sputum aspirator. Esophagography with oral administration of 15 mL ioversol was performed at the normal position and left and right 45° anterior oblique positions to visualize the position, degree, and length of the EAS. The patients were then administered orally with 10 mL of 1 mL (1 mL/mg) adrenaline diluted with 19 mL normal saline. A 5F catheter over a wire was inserted through the mouth into the esophagus, passed beyond the narrow esophagogastric anastomosis and into the stomach under fluoroscopic guidance. The catheter was then withdrawn. An appropriate balloon catheter (the PTA balloon dilatation catheter, Bard peripheral vascular), was introduced along the guidewire to the esophagogastric anastomosis. The balloon was gradually filled with ioversol until a waistband sign disappeared, expansion continued for 1 minute, and the ioversol in the balloon was aspirated for 1 minute. This expansion cycle was repeated three times. The balloon and guidewire were then withdrawn, and 10 mL of the remaining adrenaline preparation was administered orally.

Right and left and right 45° anterior oblique positions esophagography images were used to observe the ioversol patency through the anastomosis and whether there was contrast agent retention or overflow.

Postoperative management and complication treatment

The vital signs of the patients were closely observed after BD, and antibiotics and acid inhibitors were used for 3 days. The patients were asked to drink water after fasting for 4–6 hours. Patients with no obvious pain symptoms or choking in the anastomotic area received a liquid diet for 1 day and solid food the next day. Patients with severe pain or choking continued water fasting and were examined by esophagography for EAR or the presence of a tracheal fistula.

Patients with type I and II ruptures were managed with acid inhibitors, anti-inflammatory drugs, and symptomatic treatment and were given parenteral nutrition. A liquid diet was initiated when the patients showed no apparent pain on drinking water after water fasting for 1–3 days. This was followed by a gradual transition to a semi-liquid diet and then a general diet, encouraging the patients to swallow large food boluses.

Patients with type III rupture were placed on water fasting. Transnasal jejunal nutrition and gastric decompression tubes were inserted under fluoroscopy and the patients received nasal feeding after the procedure. Esophagography was performed again 3–7 days later. The tubes were removed after the rupture had healed, and the patients were encouraged to consume food orally.
Definitions

The esophageal ruptures following BD under fluoroscopy were classified into types I, II, or III according to the contrast agent leakage.\textsuperscript{7,10} Type I rupture is defined as the contrast agent overflowed, but could flow back to the lumen naturally (Figure 1); type II rupture is defined as the contrast agent crossed the anastomotic wall without mediastinal overflow and could not flow back to the lumen naturally (Figure 2); type III rupture is defined as the contrast agent overflowed to the mediastinum or pleura (a transmural type with contrast agent leakage) (Figure 3).

According to the Stooler classification\textsuperscript{11}: grade 0, anastomotic diameter $\geq$9 mm, can eat normal food; grade I, 7 mm $\leq$ anastomotic diameter $<$9 mm, obstruction in the consumption of soft food; grade II, 5 mm $\leq$ anastomotic diameter $<$7 mm, can consume a semi-liquid diet; grade III, 3 mm $\leq$ anastomotic diameter $<$5 mm, can consume a liquid diet; and grade IV, anastomotic diameter $<$3 mm, difficulty or inability in ingesting liquids, clinical success was defined as postoperative dysphagia grade 0–2 and no fatal adverse events. Technical success was the absence of serious adverse events such as death, massive hemorrhage, or rupture and perforation (type III rupture) after BD. The degree of dilation was defined as the difference between the preoperative and postoperative dysphagia grades. The time from surgery to dysphagia was defined as the interval from surgery to stricture development. Major adverse events included death, massive hemorrhage, and type III rupture. Minor adverse events included acid reflux and pain.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows (version 26.0, IBM). Continuous variables are expressed as mean $\pm$ standard deviation. A logistic regression model analyzed the association between the rupture outcome and age, sex, cause of stricture, interval from surgery to stricture development, balloon diameter, number of BD, and preoperative treatment. $p$-Value $<$0.05 was considered statistically significant.

RESULTS

A total of 378 patients with EAS (149 patients were excluded: achalasia in 32 cases, esophageal stricture in 102 cases, esophageal jejunal anastomotic stricture in 9 cases, and pyloric obstruction in 6 cases). A total of 251 males and
127 females, ages 40–89 (63.4 ± 8.1) years, underwent 552 BD procedures. The patient general characteristics are presented in Table 1. The following rates were achieved: technical success, 98.0% (541/552); overall clinical success, 97.8% (540/552); ineffective dilatation 2.2% (12/552; balloon diameter of 12 mm in one case, 14 mm in three cases, 16 mm in seven cases, and 18 mm in one case); death, 0.3% (1/378; a 62-year-old male with esophageal cancer developed massive hematemesis and died after BD). The incidence of major adverse events was 1.3% (7/552), and 9.4% (52/552; all with pain after dilatation) had minor adverse events. No case of type I or II rupture developed into type III.

### Analysis of risk factors of EAR

Among the 552 BD procedures, 82 resulted in EARs (14.9%), of which 10.9% (58/552) were of type I rupture, 2.7% (15/552) of type II rupture, and 1.3% (7/552) of type III rupture. The classifications and distribution frequencies of the 82 EARs are shown in Table 2. There was no significant difference in the total rate of EAR in gender, age, interval from surgery to development of stricture, and balloon diameter. However, the total rate of EAR showed significant differences in the cause of stricture and preoperative treatment. Patients who received preoperative radiotherapy and chemotherapy and patients with anastomotic tumor recurrence showed a higher rupture rate.

Risk factor analysis for EAR outcomes is presented in Table 3. Logistic regression showed that age ($p = 0.080$), sex ($p = 0.256$), interval from surgery to stricture development ($p = 0.817$), number of BD ($p = 0.054$), cause of stricture ($p ≥ 0.168$), and preoperative chemotherapy ($p = 0.679$) were not associated with EAR. Balloon diameter ($p < 0.001$), preoperative radiotherapy ($p = 0.003$), and chemoradiotherapy ($p = 0.021$) were significantly associated with EAR.

### TABLE 1  General characteristics of the patients ($n = 378$)

|                           | n/mean ± SD |
|---------------------------|-------------|
| Age, y                    | 63.4 ± 8.1  |
| Sex                       |             |
| Male                      | 251 (66.4%) |
| Female                    | 127 (33.6%) |
| Cause of stricture        |             |
| Esophagectomy             | 336 (88.9%) |
| Partial gastrectomy       | 36 (9.5%)   |
| Tumor recurrence          | 6 (1.6%)    |
| Number of BD              | 1.46 ± 0.94 |
| Preoperative treatment    |             |
| None                      | 256 (67.7%) |
| Radiotherapy, chemotherapy, or chemoradiotherapy | 122 (32.3%) |

Abbreviations: BD, balloon dilatation; SD, standard deviation.
DISCUSSION

BD under fluoroscopy has been widely used to treat gastrointestinal stenosis such as esophageal stricture, EAS, and Crohn’s disease stricture. BD is suitable for benign stricture, not malignant stricture. On the one hand, because of the rapid growth of tumor tissue, EAS after BD is easy to relapse in a short time; on the other hand, the tumor tissue is brittle and rich in blood supply. BD is easy to cause EAR and even massive bleeding. Moreover, for benign stricture, esophageal stent implantation can relieve the stricture, but the stent is a foreign body. The proliferation of granulation tissue at both ends of the stent for a long time causes restenosis. It is also difficult to remove the seriously embedded esophageal stent. Although the BD technique is mature, it cannot completely avoid the occurrence of complications. We explored the potential risk factors of BD complications and treatment measures to be taken when they occur, striving to provide clinical guidance for EAS treated with BD.

TABLE 2 Classification and distribution of EAR

| Times of BD | Rupture type | I | II | III | Rupture rate (%) |
|-------------|--------------|---|----|----|-----------------|
| Age, y      |              |   |    |    |                 |
| ≤64         | 294          | 24| 9  | 5  | 12.9            |
| >64         | 258          | 36| 6  | 2  | 17.1            |
| Sex         |              |   |    |    |                 |
| Male        | 362          | 33| 8  | 4  | 12.4            |
| Female      | 188          | 27| 7  | 3  | 19.7            |
| Cause of stricture |          |   |    |    |                 |
| Esophagectomy | 493      | 53| 11 | 7  | 14.4            |
| Partial gastrectomy | 53         | 3 | 3  | 0  | 11.3            |
| Tumor recurrence | 6         | 4 | 1  | 0  | 83.3            |
| Interval from surgery to development of stricture (months) |     |   |    |    |                 |
| T ≤3        | 343          | 34| 7  | 3  | 12.8            |
| T >3        | 209          | 26| 8  | 4  | 18.2            |
| Balloon diameter (mm) |          |   |    |    |                 |
| <25 mm      | 346          | 36| 5  | 2  | 12.4            |
| ≥25 mm      | 206          | 24| 10 | 5  | 18.9            |
| Preoperative treatment |          |   |    |    |                 |
| None        | 400          | 27| 7  | 4  | 9.5             |
| Radiotherapy | 139        | 31| 6  | 2  | 28.1            |
| Chemotherapy | 5         | 2 | 0  | 0  | 40              |
| Chemoradiotherapy | 8         | 0 | 2  | 1  | 37.5            |

Abbreviations: BD, balloon dilatation; EAR, esophagogastric anastomotic rupture.

TABLE 3 Risk factors of EAR

|                | p-value |
|----------------|---------|
| Age, y         | 0.080   |
| Sex            | 0.256   |
| Stenosis etiology |       |
| Esophagectomy  | 0.168   |
| Gastrectomy    | 0.189   |
| Tumor recurrence | 0.168   |
| Interval from surgery to development of stricture | 0.817  |
| Balloon diameter | 0.000   |
| Number of BD   | 0.054   |
| Preoperative treatment |       |
| Radiotherapy   | 0.003   |
| Chemotherapy   | 0.679   |
| Chemoradiotherapy | 0.021   |

Abbreviations: BD, balloon dilatation; EAR, esophagogastric anastomotic rupture.

A 62-year-old male patient with esophageal cancer in our study underwent esophagectomy. Lung metastasis was found 12 months later, and the patient was treated with upper mediastinal intensity-modulated radiotherapy (40 Gy, 20 times). The patient was then treated with BD, but died of massive hematemesis after the balloon was withdrawn. The cause of death was adhesion between the thoracic aorta and the anastomotic tissue after radiotherapy. BD caused the tear of the thoracic aorta after radiotherapy increased the fragility of the anastomotic tissue and aortic wall. Type III rupture and
mortality rates of BD under fluoroscopy in this study were 1.3% and 0.3%, respectively, demonstrating the safety and reliability of treating EAS with BD under fluoroscopy. Although the complications were controllable, BD use in patients after radiotherapy in the anastomotic area should be done cautiously.

The occurrence of EAR when treating EAS with BD was associated with various factors. Studies showed that neo-adjuvant radiotherapy could cause mucosal injury, toxicity, and fibrosis, leading to extensive and multi-level stricture that might affect the occurrence of rupture outcome. Furthermore, our study results showed that radiotherapy was significant risk factors for rupture outcome, whereas chemotherapy was not. Therefore, rupture of the esophagogastric anastomosis after BD is likely related to radiotherapy. Our study found that patients with a history of preoperative radiotherapy did not have type III EAR when the balloon diameter was <25 mm. Some patients had type III EAR when the balloon diameter was ≥25 mm. Therefore, we believe that patients with a history of preoperative radiotherapy should be treated carefully when using a BD catheter with a diameter ≥25 mm. Another study showed that myofibrils break when stretched to over 1.3 times their normal length. The incidence of EAR in that study was 21.4% (44/206) in patients treated with a balloon diameter of ≥25 mm and 10.4% (36/346) in patients treated with a balloon diameter of <25 mm. These results showed that the risk of EAR increased with the balloon diameter, possibly because the increased radial tension during dilatation increases the degree of myofibril stretching. However, balloon diameter was not the only factor determining perforation. Our study found that the rupture rate among patients with recurrent tumors was very high, presumably because the tumor tissue in the anastomotic area was more fragile than normal tissue.

We should pay attention to the following aspects to avoid BD complications when treating EAS: (1) perform preoperative CT to evaluate whether the tissue around the esophagogastric anastomotic area is thickened and excludes local recurrence of tumors. (2) Patients with a history of radiotherapy should be treated carefully when using large-diameter balloons. (3) Esophageal stent implantation and arterial infusion chemotherapy rather than BD should be considered in patients with recurrent esophagogastric anastomotic tumors. (4) The appropriate balloon diameter should be selected according to the degree of EAS and the elapsed time since the surgery. It was previously reported that type I and II ruptures did not require any special treatment, whereas surgery could be considered for type III ruptures. Patients with type I and II ruptures in our study cohort were managed with acid inhibitors, anti-inflammatory agents, and symptomatic treatment. Oral water intake could be restored within 3–5 days. Transnasal decompression and jejunal nutrition tubes were placed immediately when type III ruptures occurred. These were removed and oral nutrition was resumed after the anastomosis had healed.

This study was limited by its non-randomized and retrospective nature. We preliminarily found that anastomotic tumor recurrence, preoperative radiotherapy and chemoradiotherapy, and balloon diameter were risk factors of BD-related EAR; however, the quantitative relationship between these factors and EAR needs to be studied further, and an EAR risk prediction model should be established.

In conclusion, BD for EAS under fluoroscopy is safe and effective. The recurrence of esophagogastric anastomotic tumor, preoperative radiotherapy, and balloon diameter affected the anastomotic rupture outcome. Esophageal stent implantation and arterial infusion chemotherapy rather than BD should be considered in patients with recurrent esophagogastric anastomotic tumors. Patients with a history of preoperative radiotherapy should be careful with BD and individualized selection of appropriate balloon catheter. Symptomatic supportive treatment should be given to patients with type I and II ruptures, and transnasal decompression and jejunal nutrition tubes should be inserted during the procedure when type III ruptures occur.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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How to cite this article: Wang S, Li X, Zhang C, Yin M, Ma Y, Tong Y, et al. Balloon dilatation complications during esophagogastric anastomotic stricture treatment under fluoroscopy: Risk factors, prevention, and management. Thorac Cancer. 2022;13:1570–6. https://doi.org/10.1111/1759-7714.14389