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Postoperative Esophageal Leaks in Malignant Pathology – Optimal Management: A Systematic Review

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Rezumat

Fistulele anastomotice postesofagectomie în patologia malignă - managementul optim: revizia literaturii

Introducere: Fistulele esofagiene postoperatorii reprezintă una dintre importantele cauze de mortalitate şi morbiditate postoperatorie. Scopul acestui studiu a fost de a revizui cunoştinţele actuale cu privire la metodele actuale de diagnostic şi management al fistulelor esofagiene postoperatorii
Metodă: O căutare sistematică a literaturii a fost efectuată în baza de date PubMed/Medline folosind termenii „fistule esofagiene postoperatorii" şi „complicaţii postesofagectomie" pentru a identifica articole relevante pentru diagnosticul actual şi tratamentul profilactic şi curativ al fistulelor anastomotice postesofagectomie.
Rezultate: Mai multe lucrări au arătat că incidenţa fistulelor variază şi este dependentă de mai mulţi factori: localizarea anastomozei, tipul de sutură utilizat, condiţia biologică a pacientului. Datorită gravităţii fistulei anastomotice mediastinale se acordă actual o mare importanţă metodelor de prevenire a apariţiei sale prin testarea intraoperatorie sau îmbunătăţirea vascularizaţiei tubului gastric. Cele mai recente articole prezintă metodele endoscopice de tratament al acestei complicaţii prin utilizarea stenturilor esofagiene acoperite şi a terapiei endoluminale cu vacuum.
Concluzii: La pacienţii cu fistule esofagiene postoperatorii mediastinale, diagnosticul şi managementul reprezintă o adevărată provocare pentru echipa chirurg - endoscopist - terapeut. Diagnosticarea precoce şi instituirea unei terapii optime care să se adreseze defectului parietal şi statusului biologic a pacientului sunt condiţii obligatorii pentru rezolvarea acestei complicaţii postoperatorii.

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Cuvinte cheie: fistule esofagiene postoperatorii, complicații postesofagectomie, stenturi esofagiene, cancer esofagian

Abstract

Background and Aims: Postoperative esophageal leaks are one of the major causes of postoperative mortality and morbidity. The purpose of this study was to review current knowledge of current methods of diagnosis and management of postoperative esophageal leaks.

Methods: A systematic literature search was performed in the PubMed/Medline database using the terms "postoperative esophageal leaks" and "postesophagectomy complications" to identify articles relevant to the current diagnostic and prophylactic and curative treatment of post-oesophagectomy anastomotic fistulas.

Results: Several papers have shown that the incidence of fistulas varies and is dependent on several factors: the location of the anastomosis, the type of suture used, the biological condition of the patient. Due to the severity of the mediastinal anastomotic fistula, great importance is being given to the methods of preventing its occurrence by intraoperative testing or improving the gastric tube vascularity. The most recent articles present endoscopic methods of treating this complication by using coated esophageal stents and endoluminal vacuum therapy.

Conclusion: In patients with mediastinal postoperative esophageal fistulas, diagnosis and management represent a real challenge for the surgeon-endoscopist-therapist team. The early diagnosis and the establishment of an optimal therapy to address the parietal defect and the biological status of the patient are mandatory conditions for resolving this postoperative complication.

Key words: esophageal leaks, postesophagectomy complications, esophageal stents, esophageal cancer

Introduction

The post-esophagectomy mortality rate remains high due to procedural complexity. Significant progress has recently been made in surgical techniques, intraoperative fluid administration, and postoperative care. The various forms of neoadjuvant chemoradiotherapy that incorporate minimally invasive esophagectomy procedures, such as McKeown and Ivor Lewis, are one of the most widely accepted current options for esophageal cancer treatment. Patients with a minimally invasive approach had a significantly lower incidence of pulmonary complications, pulmonary embolism, and cardiac arrhythmias, but not for an anastomotic fistula or gastric tube necrosis compering to open approach (1). The most common postoperative complications are pulmonary complications (18.7%), such as empyema and pleural effusion, cardiac arrhythmias (14.1%), anastomotic fistula (14.1%), paralysis of the vocal cords (9.4%), gastric tube stenosis (4.7 %) and acute kidney injury (4.7%). However, despite neoadjuvant radiochemotherapy, the use of minimally invasive techniques and well-controlled anesthesia, the incidence of perioperative complications remains high (2).

Epidemiology of the Postesophagectomy Leaks

The largest of the recent studies on a large number of patients identified a leak rate of 10.6%, and another important study revealed a leak rate after transthoracic esophagectomy of 9.8% and 12% after transhiatal esophagectomy (3,4). Anastomotic leaks increase the length of hospitalization and the costs of medical services and decrease the quality of

life (5). It is associated with high rates of morbidity and mortality; mortality ranges from 17-35% in patients with a leak, compared with 2-3% in patients with intact anastomosis (6,7). There is also evidence that anastomotic fistula affects long-term prognosis, being associated with decreased long-term survival and increased recurrence rates (6).

So far, no esophageal anastomosis technique has been shown to be significantly beneficial. There is some evidence that a mechanical anastomosis using a linear stapler has a low rate of fistula and a reduced rate of stricture compared to a manual anastomosis (9,10). Cervical anastomoses are associated with an increased rate of leaks compared to thoracic anastomoses (11,12).

Definition and Classification of Anastomotic Leak and Gastric Tube Necrosis

In 2015, the Consensual Complications Group for Esophagectomy (ECCG) defined anastomotic leak as total parietal defects involving the esophagus, anastomosis, lining or gastric tube, regardless of presentation or method of identification. In this classification, the fistulas were divided into three types based on the type of management: type 1 - leaks that do not require any modification of the therapy, treated medically or with dietary changes; type 2 - leaks that require interventional but not surgical therapy (radiological drainage, endoscopic stenting, etc.); type 3 - leaks that require surgery. Necrosis of the gastric tube is defined by ischemia and necrosis of the gastric tube. Gastric tube necrosis was further subclassified as type 1 - gastric focal necrosis, endoscopically identified and treated by non-surgical monitoring and therapy; type 2 - focal necrosis of the gastric tube, identified endoscopically without being associated with the anastomotic leak or the gastric tube, treated surgically, but which does not require esophageal diversion; type 3 - extensive gastric tube necrosis, treated with reintervention and resection of the necrotic gastric tube, with various esophageal and cervical esophagostomy (13).

Methods to Prevent the Appearance of Anastomotic Leaks

Due to the high mortality and morbidity associated with anastomotic leaks, several authors have supported the use of prophylactic interventions to reduce the impact and/or incidence of anastomotic leaks. These include ischemic preconditioning of the gastric tube, intraoperative evaluation of gastric tube vascularization, localization (thoracic vs. cervical) and anastomosis type (manual/mechanical suture), anastomotic partner (stomach, jejunum or colon), consolidation of the anastomosis with omental pedicle and intraoperative placement of perianastomotic drainage.

Preoperative laparoscopic gastric devascularization

Some experimental studies from 2012 have shown that the "ischemic conditioning" of the stomach proposed as a technique aimed at improving the microcirculation of the gastric tube prevents the appearance of anastomotic leak. Some authors proposed the preoperative laparoscopic gastric devascularization with left gastric artery, short gastric artery and coronary vein sectioning and esophageal resection and reconstruction after two weeks. The low rate of anastomotic leak (3%) and the absence of anastomotic strictures suggest that this approach may reduce the rate of anastomotic complications (15,16). But recent studies show that there is no evidence that ischemic conditioning influences the anastomotic leak rate. However, it can reduce the severity of this complication. (17)

Intraoperative evaluation of gastric tube vascularization

Infrared fluorescence using Indocyanine Green is a promising system for intraoperative evaluation of blood circulation in the gastric tube. The speed of ICG fluorescence flow in the gastric tube wall may be affected by the capillary vessel network of this tissue. Although

there is no system for intraoperative assessment of adequate blood flow in the gastric tube, ICG fluorescence aims to determine the optimal anastomotic site in the gastric tube and to reduce the risk and degree of anastomotic complications (18-20). Other authors do not have identified these aspects. (21)

Strengthening anastomosis with the omental pedicle

Consolidation of intrathoracic esogastric anastomosis with the omental pedicle has been proposed by several authors as a means of reducing the incidence of anastomotic leak. During the creation of the gastric tube, a segment with 2 or 3 omental vessels is preserved on the great curvature near the site of the future anastomosis. This segment is used to surround the anastomosis, providing reinforcement of the mechanical suture line and endoluminal content in the case of anastomotic dehiscence. Several authors obtained a decrease in the leak rate by using the omental pedicle at 1- 4.7% against 6-14,4% (22-26).

Intraoperative placement of the perianastomotic drainage tube

Perianastomotic drainage is a critical principle that guides the management of anastomotic leaks, with mortality rates of up to 80% being reported in the case of uncontrolled, inappropriately drained leaks. Leaks are identified by detecting the increased volume of drained fluid, odor, turbidity and by the inability to maintain the negative pressure of the suction system. Confirmation of the suspicion of the leak is obtained by ingestion of methylene blue at the patient's bed with an immediate blue coloration of the drainage fluid. Some patients require multiple doses of methylene blue to detect a leak (27-29). Some authors have reported intraluminal migration of drainage tubes after esophagectomy in patients with an anastomotic leak (30).

Methods for Early Identification of the Anastomotic Leak

Prompt recognition of anastomotic leak is critical and may accelerate clinical intervention by improving immediate outcomes. Early signs of anastomotic leaks include: tachycardia, pyrexia, increased neutrophil count, increased C-reactive protein (CRP), delirium, cardiac arrhythmias, especially atrial fibrillation. Late signs include biliary fluid content in thoracic drainage, acidosis, hypotension and septic shock. In patients with recent atrial fibrillation, post-oesophagectomy was associated with infectious complications, is a clinical sign of early warning for the occurrence of anastomotic leaks (31). CRP level on the third postoperative day may be of significant value for early detection of anastomotic leaks after esophagectomy (32). Determination of amylase in the pleural fluid may be useful in assessing the integrity of an esophageal anastomosis, and successive evaluation of amylase on the 5th to the 7th postoperative day may be a method of detecting anastomotic leaks (33). Some authors claim that the anastomotic drain has a limited sensibility in leaks diagnosis and cannot replace the clinical signs and symptoms (34).

A study with the contrast substance was performed on the fifth postoperative day, before resuming oral feeding and had a low sensitivity of 16 %. This attitude we also practice in the 7th postoperative day for checking the integrity of the esophageal anastomosis before resuming the oral feeding (*Fig. 1*).

Another diagnostic method of the anastomotic leak is computed tomography. In the case of clinical suspicion of fistula, some authors recommend computed tomography of the chest and abdomen with oral contrast with a success rate of 41%, followed by endoscopy (35).

Management of Anastomotic Leaks

Historically, the anastomotic leak approach has been to control drainage, nil per os and antibiotic therapy. In the case of mediastinitis or empyema, surgical debridement is used. The current management of leaks is contro-

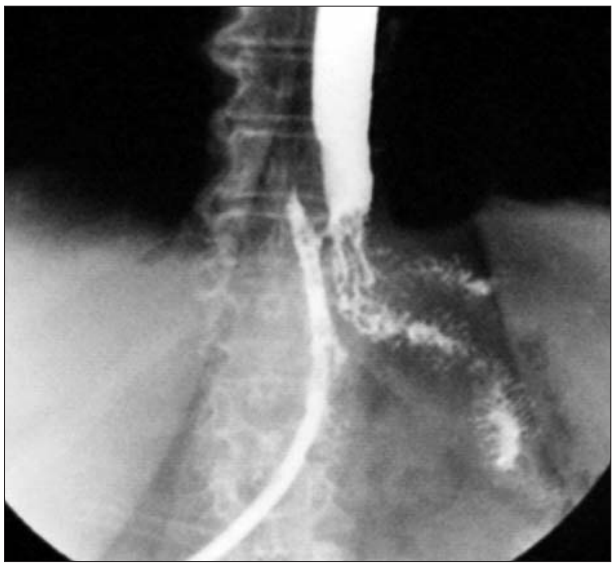

Figure 1. Esojejunal leak externalized on the perianastomotic drainage tube - radiological aspect with contrast substance (Collection of the Surgical Clinic of the "Sf. Maria" Clinical Hospital Bucharest)

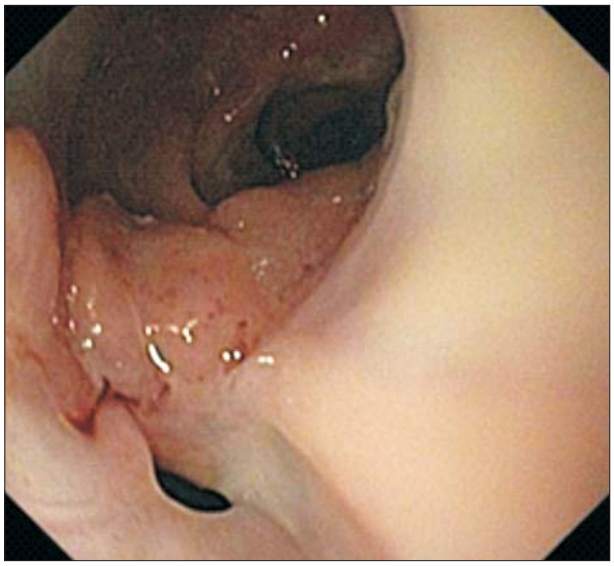

Figure 2. Esojejunal leak - direct endoscopic visualization (Collection of the Surgical Clinic of the "Sf. Maria" Clinical Hospital Bucharest)

versial and depends on the location of the leak, the size of the anastomotic defect, the vascularization of the gastric tube and the clinical status of the patient. Small anastomotic leaks can be treated conservatively, without surgery in young patients, nil per os, antibiotic administration and nasogastric aspiration. Leaks that are not effectively drained or those with systemic impact are those that require active intervention, such as radiologic drainage or endoluminal vacuum therapy, covered esophageal stent or surgical reintervention (36,37). Endoscopic placement of the esophageal stent has been associated with a 72% anastomotic leak treatment efficiency. Vacuum therapy is a useful tool in the treatment of anastomotic leak associated with mediastinitis (22). Extraluminal naso-oesophageal drainage consists in the introduction of a suction tube under endoscopic guidance into the abscess cavity when the percutaneous insertion of a drainage tube into the abscess has been inefficient or technically impossible may be an alternative method of treatment (38). Endoluminal therapy by esophageal stenting has been successfully used for the treatment of intrathoracic anastomotic leaks, being indicated for a defect involving <30% of the anastomotic circumference and without extensive necrosis of the gastric tube. A 2011 study warned that endoscopy may present the risk of exacerbation of anastomotic defect and mediastinal contamination during endoscopy, so it is recommended to mount the esophageal stent at the time of the initial endoscopic diagnosis, attitude that we have adopted (*Figs. 2, 3*).

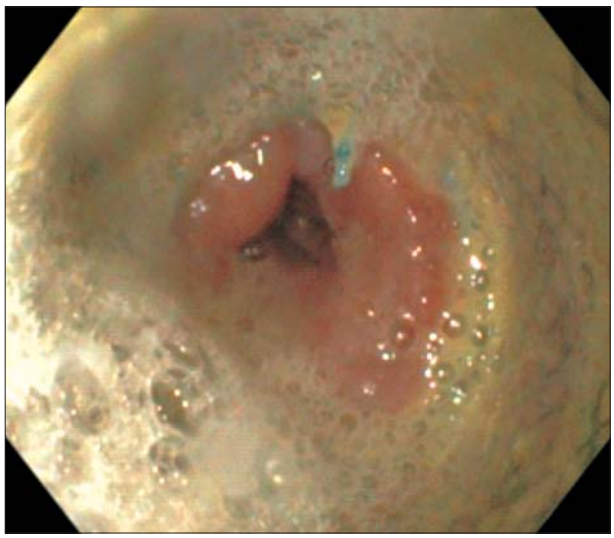

Figure 3. Esojejunal leak – after full covered esophageal stent inserted (Collection of the Surgical Clinic of the "Sf. Maria" Clinical Hospital Bucharest)

The chest x-ray is required to monitor stent position and when migration is detected repeat endoscopy is required to reposition stent or restenture (39). The main advantage of endoscopic stenting is the immediate coverage of the anastomotic defect with the shortening of the time required until oral administration (40).

Another viable option for the treatment of a peripheral abscess is the use of endoscopically positioned transluminal vacuum therapy. Transluminal vacuum therapy involves placing a sponge into the cavity of the suction anastomotic defect provided by a transnasal catheter. Sponges should be changed at different intervals but on average 2 to 3 times a week (41). Patients with extensive devitalization of the esophagus, with large anastomotic fistulas or an unviable gastric tube, are not suitable for endoscopic stenting. If perianastomotic and pleural drainage is inadequate or it was removed before the leakage becomes visible, additional drainage tubes may be required under thoracoscopic or CT guidance (34).

Large anastomotic leaks associated with severe sepsis or gastric tube necrosis, in case of an inefficient stent or vacuum therapy may require reintervention with anastomosis resection and esophageal diversion with cervical esophagostomy. In the case of gastric tube necrosis, there is no documented salvage technique once ischemia has been identified. Treatment for mild cases can be metabolic support and management of anastomotic leaks. Severe necrosis cases require debridement and excision of the tube with proximal esophageal diversion and the feeding jejunostome. Reconstruction can be planned later if possible. Most of the data show that the risk of ischemia is related to the type and length of the gastric tube, comorbidities and operative technique (42,43).

Conclusions

The introduction into the current practice of minimally invasive esophagectomy has led to the decrease of postoperative morbidity, but not the one determined by the anastomotic leaks. In patients with mediastinal post-operative esophageal leaks, diagnosis and management represent a real challenge for the surgeon-endoscopist-therapist team. The early diagnosis and the establishment of an optimal therapy to address the parietal defect and the biological status of the patient are mandatory conditions for resolving this post-operative complication. For most patients endoscopic endoluminal therapy is sufficient, but in case of failure, surgical reintervention is required.

The manuscript has been reviewed and approved by all named authors.

Authors' Contributions

B.R. elaborated the concept and design of this paper; BR and D.D. performed data acquisition and reviewed the literature; H.P. and R.C. revised endoscopic and endoluminal therapeutic technics for anastomotic esophageal leaks; B.R. analyzed the data and drafted the manuscript. C.S revised the manuscript. All authors critically revised the manuscript, approved the final version to be published, and agree to be accountable for all aspects of the work.

Conflict of Interest

The authors declare no conflicts of interests.

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