

Mortality Secondary to Esophageal Anastomotic Leak

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Background: Esophageal anastomotic leak is a potentially life threatening complication of esophagectomy and esophagogastrectomy. We reviewed our experience with this complication and tried to identify factors predictive of mortality after esophageal anastomotic leak.

Methods: Records of patients undergoing esophagectomy and esophagogastrectomy for benign or malignant disease over a 10-year period (1989-1999), who developed esophageal anastomotic leaks, were reviewed.

Results: Three-hundred and seven patients underwent esophagectomy or esophagogastrectomy. Twenty-three (7.5%) developed esophageal anastomotic leaks. Eight of these patients (35%) died. Four of 23 (17%) patients had seemingly normal postoperative contrast studies. Factors potentially predictive of death included age (died, 72.8 ± 8.3 years; survived, 65.3 ± 8.8 years; $p=0.063$), location of anastomosis (cervical, 3/9 died; thoracic, 5/14 died; $p=0.91$), leak presentation (clinical, 6/12 died; contrast study, 2/11 died; $p=0.11$), time of leak (<7 days, 3/5 died; ≥ 7 days, 5/18 died; $p=0.18$), presence of gastric necrosis (necrosis, 3/3 died; no necrosis, 5/20 died; $p=0.019$), and treatment (surgical, 4/4 died; conservative, 4/19 died; $p=0.005$).

Conclusions: Postoperative esophageal anastomotic leaks prove fatal in a significant number of cases. The lethal potential of cervical anastomotic leaks should not be underestimated. Gastric necrosis is an important predictor of subsequent death. Advanced age, early postoperative (<7 days) leakage, and clinically apparent signs of leakage may be predictive of death but these factors did not reach statistical significance in our study. Surgical treatment of esophageal anastomotic leaks is associated with subsequent death, but this relationship is unlikely to be causal; severely ill patients tend to be treated surgically. (*Ann Thorac Cardiovasc Surg* 2004; 10: 71–5)

Key words: esophageal neoplasms/surgery, postoperative complications, esophagectomy/adverse effects, anastomosis/surgical, reconstructive surgical procedures

Introduction

Many patients undergoing esophagectomy and esophagogastrectomy suffer postoperative complications, and these postoperative complications are often life threatening in nature.¹⁻⁴⁾ The anastomosis between the remaining esophagus and its replacement conduit is more likely to leak than most other gastrointestinal anastomoses. Post-

operative esophageal anastomotic leaks range in severity from asymptomatic and minor anastomotic defects that are only apparent on contrast studies, to fulminant leaks with systemic sepsis and multiorgan failure.²⁾ Most esophageal surgery units have noted a favorable trend towards reduced incidence and morbidity of esophageal leaks over the past two decades.¹⁾ Nevertheless, esophageal anastomotic leaks remain an important source of morbidity and mortality after surgery.

We reviewed our experience with esophageal anastomotic leaks. Our goal was to identify factors predictive of mortality. By identifying these factors, we hoped to modify our future management of leaks, and reduce mortality.

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Table 1. Summary data on 23 patients suffering esophageal anastomotic leaks after esophagectomy and esophagogastrectomy

Age	67.9±9.1 years
Sex	Male 18 Female 5
Pathology	Adenocarcinoma 16 Squamous cancer 7
Tumor location	Proximal esophagus 1 Mid esophagus 5 Lower esophagus 4 Gastric cardia 13
Technique of anastomosis	Stapled 7 Hand-sewn 16
Location of anastomosis	Intrathoracic 14 Cervical 9
Presentation of leak - clinical or radiographic	Clinical 12 Radiographic 11
Presentation of leak - time	≤7 days 11 >7 days 12
Gastric necrosis	Necrosis 3 No necrosis 20
Management of leak	Surgical 4 Conservative 19
Length of hospital stay	36.4±19.4 days
Survival	Survived 15 Died 8

Patients and Methods

St. Joseph's Healthcare in Hamilton, Ontario, Canada is a regional thoracic surgical center, and a McMaster University teaching hospital. Records of patients undergoing esophagectomy and esophagogastrectomy for benign or malignant disease over a 10-year period (1989-1999), and developing esophageal anastomotic leaks, were reviewed. Data was collected on age, sex, pathology, operative approach, location and technique of anastomosis, time and presentation of leak, gastric necrosis, treatment, and outcome. Our analysis was designed to identify factors predictive of death.

Continuous data are presented as mean values with standard deviations (mean ± SD). Means were compared with the Mann-Whitney test. Categorical data was compared with a chi-squared test (with Yates correction) or Fisher's exact test. A $p < 0.05$ was considered significant. Statistical analysis was done using Biostat software (Biostat, Englewood, NJ).

Results

Three-hundred and seven patients underwent esophagectomy or esophagogastrectomy. Twenty-three

(7.5%) developed esophageal anastomotic leaks (diagnosed clinically and/or radiographically), and these patients form the basis of this analysis. Twenty-one patients had undergone transthoracic (McKeown, Lewis, or thoracoabdominal) resections, and two had non-thoracic approaches (transhiatal and laparoscopic). Summary data on the patients is presented in Table 1. Four of 23 patients (17%) had seemingly normal postoperative contrast studies. Eight of 23 patients (35%) died.

Factors potentially predictive of death included age (died, 72.8±8.3 years; survived, 65.3±8.8 years; $p=0.063$), location of anastomosis (cervical, 3/9 died; thoracic, 5/14 died; $p=0.91$), technique of anastomosis (stapled, 4/7 died; hand-sewn, 4/16 died; $p=0.14$), leak presentation (clinical, 6/12 died; contrast study, 2/11 died; $p=0.11$), time of leak (<7 days, 3/5 died; ≥7 days, 5/18 died; $p=0.18$), presence of gastric necrosis (necrosis, 3/3 died; no necrosis, 5/20 died; $p=0.019$), and treatment (surgical, 4/4 died; conservative, 4/19 died; $p=0.005$) (Table 2).

Discussion

The etiology of esophageal anastomotic leaks after esophagectomy and esophagogastrectomy is often mul-

Table 2. Variables potentially predictive of death following esophageal anastomotic leak

Variable	Significance
Age	p=0.063
Technique of anastomosis - stapled vs. hand-sewn	p=0.14
Location of anastomosis - thoracic vs. cervical	p=0.91
Presentation of leak - clinical vs. radiographic	p=0.11
Presentation of leak - before vs. after 7 days	p=0.18
Gastric necrosis - present vs. absent	p=0.019
Management - surgical vs. conservative	p=0.005

tifactorial.^{1,2)} However, most leaks can be attributed to conduit ischemia, technical errors, or a combination of the two.^{5,6)} Some anastomotic leaks are clinically asymptomatic (radiographic finding) while others cause fulminant systemic sepsis. Given this spectrum of severity it is not surprising that there is no standard management of esophageal anastomotic leaks. Treatment approaches to leaks are loosely based on the severity, or perceived severity, of the leak. Although treatment results have generally improved over time, esophageal anastomotic leaks remain a major problem after esophageal surgery.¹⁾

Our study was designed to identify factors predictive of death secondary to anastomotic leak. Regrettably, our group of 23 patients with anastomotic leaks is a large series relative to many others in the published literature.^{5,7-10)} Nevertheless, the numbers of patients and events (death) were too small to draw statistically sound conclusions on many issues. That, along with the retrospective nature of our data collection, is the major limitation of our study. We have therefore tried to interpret our findings within the context of existing published data, and then cautiously draw conclusions.

We found cervical esophageal anastomotic leaks to be more lethal than previously appreciated.²⁾ Surprisingly, our cervical leaks were as morbid as those complicating thoracic anastomoses. An anastomosis constructed in the neck does not necessarily leak into the cervical wound; it may leak into the mediastinum or pleural space.^{7,8)}

We noted a trend (not significant) toward greater lethality with leaks that manifest within the first week of surgery, and those that presented with clinical indications of leakage, such as wound drainage or systemic sepsis. This is consistent with current concepts of anastomotic leak pathophysiology.^{2,3)} The earlier an anastomosis fails, the more severe it tends to be; surrounding tissues need time to wall off, or contain, the anastomosis. Similarly, leaks that manifest clinically are less likely to be contained by soft tissues than leaks that are asymptomatic,

and only detectable on contrast studies. We also noted a non-significant (p=0.063) trend towards increasing leak lethality with advancing age, a finding that requires no explanation.

Our study was not designed to analyze diagnostic approaches to possible esophageal leaks, but we were struck by the occurrence (four of 23 patients) of seemingly normal water-soluble contrast studies in patients that later proved to have leaks. Others have reported similar findings.^{2,9)} Although this could be a reflection of the limitations of water-soluble contrast studies relative to barium examinations,¹¹⁾ it could also highlight some fundamental limitations of routine contrast studies after esophageal anastomoses. For example, a fragile and faltering anastomosis on postoperative day 7 may not be leaking when the patient swallows contrast, but its insufficiency may quickly become apparent when the nasogastric tube is removed and the stomach distends.²⁾ The timing of contrast studies is important. The earlier the study is done, the less reassuring it is. Patients destined to develop conduit necrosis, for example, may have an apparently satisfactory contrast radiograph before the necrotic process becomes full-thickness in extent.⁹⁾

We found surgical management of esophageal leaks to be predictive of subsequent death, but this relationship is probably not causal; surgery is a marker for severity of disease. Our four surgically treated patients were extremely ill, and their surgical intervention could be characterized as being "too little too late." This is a recurrent theme in the unsuccessful management of esophageal anastomotic leaks. Most patients do not need formal surgical intervention but those who do need it require early and aggressive operative approaches.^{1,2,5,7,8)} Survival becomes less likely if the septic cascade is allowed to progress to shock and multiple organ failure.⁷⁾

Gastric necrosis was the only unequivocal predictor of mortality secondary to esophageal leaks in our patients. Other surgeons have also emphasized the lethal nature of

this complication.^{2,7-9,12)} Conduit necrosis, at best, produces a large and gaping anastomotic defect that leaks freely. At worst, the entire anastomosis dehisces and the foregut loses continuity. Early recognition of this complication is critical. Otherwise, these patients receive inappropriately conservative treatment. Clinical suspicion and liberal use of flexible endoscopy are the keys to early diagnosis.^{2,9,12)}

Our experience with esophageal anastomotic leaks, together with the published experience of others, has shaped our conceptual framework for leak management. No one standard management strategy is applicable to all situations. Instead, the aggressiveness and invasiveness of treatment should parallel the severity and potential lethality of the leak. We believe that many fatal outcomes are secondary to one of two common mistakes: a failure to adequately diagnose and assess the severity of the leak, and a failure to appropriately match aggressiveness of treatment to leak severity.

Early diagnosis of esophageal anastomotic leaks requires a willingness to liberally investigate patients who show subtle clinical signs of septic illness. Contrast radiography is the diagnostic cornerstone of esophageal leak investigation, but a seemingly normal contrast study, in isolation, may not exclude a leak. Gentle flexible esophagoscopy is critical for assessment of possible conduit necrosis. Computed tomography provides visualization of perianastomotic fluid collections and abscesses. Contrast studies, esophagoscopy, and computed tomography should be considered complimentary in the assessment of esophageal anastomotic leaks. They permit the surgeon to answer these essential questions: is the leak contained, is the conduit viable, and is there an abscess?

Aggressiveness of treatment should parallel the severity of the anastomotic leak. We now try to match treatment and leak pathology by considering three broad treatment goals: adequate drainage of infected fluid collections, resection of necrotic tissue, and prevention of further soilage from the leak. The importance of adequate drainage cannot be over stated.^{2,5,7)} Seemingly innocuous perianastomotic fluid collections can fistulize into the airway or aorta, with catastrophic consequences.^{2,7)} In the past drainage often required an operative approach,²⁾ but percutaneous drainage is now effective for most patients.^{1,13)} The provision of adequate drainage is more important than the specific method by which it is obtained. Surgical drainage is currently reserved for patients with widespread mediastinal and pleural soilage, and those with another indication for surgery, namely tissue resection.

The presence of conduit necrosis should prompt an early and bold return to the operating theater for disconnection of the foregut, resection of nonviable tissue, and creation of an end esophagostomy.^{2,7)} Patients fortunate enough to survive such an illness, and not succumb to cancer recurrence, can be reconstructed secondarily at another time.

The last general management principle, prevention of further soilage from the leak, can be problematic. Eliminating oral intake and decompressing the conduit with a nasogastric tube are basic steps. Many surgeons have attempted secondary surgical repair of anastomotic leaks in an effort to eliminate further soilage. If vascularized tissue is used to reinforce the anastomosis there is some hope for success, and any recurrent leak may be better contained. Secondary repair can therefore be a useful adjunctive strategy if surgical drainage is being done, but secondary repair is not effective enough to warrant surgical intervention for this reason alone. Finally, covered expandable metal stents can occlude anastomotic leaks.¹⁰⁾ Our recent and admittedly limited experience with these stents has been favorable. We foresee increased use of stents in the future, but of course, they only address the issue of prevention of further soilage; drainage is still necessary and the possibility of conduit necrosis must be considered.

References

1. Lerut T, Coosemans W, Decker G, De Leyn P, Naftoux P, van Raemdonck D. Anastomotic complications after esophagectomy. *Dig Surg* 2002; **19**: 92–8.
2. Urschel JD. Esophagogastric anastomotic leaks complicating esophagectomy: a review. *Am J Surg* 1995; **169**: 634–40.
3. Pierie JP, de Graaf PW, van Vroonhoven TJ, Obertop H. Healing of the cervical esophagogastric anastomosis. *J Am Coll Surg* 1999; **188**: 448–54.
4. Urschel JD, Blewett CJ, Bennett WF, Miller JD, Young JE. Handsewn or stapled esophagogastric anastomoses after esophagectomy for cancer: meta-analysis of randomized controlled trials. *Dis Esophagus* 2001; **14**: 212–7.
5. Whooley BP, Law S, Alexandrou A, Murthy SC, Wong J. Critical appraisal of the significance of intrathoracic anastomotic leakage after esophagectomy for cancer. *Am J Surg* 2001; **181**: 198–203.
6. Urschel JD. Esophagogastric anastomotic leaks: the importance of gastric ischemia and therapeutic applications of gastric conditioning. *J Invest Surg* 1998; **11**: 245–50.
7. Iannettoni MD, Whyte RI, Orringer MB. Catastrophic complications of the cervical esophagogastric anastomosis. *J Thorac Cardiovasc Surg* 1995; **110**: 1493–

- 501.
8. Bardini R, Bonavina L, Asolati M, Narne S, Peracchia A. Surgical treatment of cervical anastomotic leaks following esophageal reconstruction. *Int Surg* 1987; **72**: 163–5.
 9. Griffin SM, Lamb PJ, Dresner SM, Richardson DL, Hayes N. Diagnosis and management of a mediastinal leak following radical oesophagectomy. *Br J Surg* 2001; **88**: 1346–51.
 10. Roy-Choudhury SH, Nicholson AA, Wedgwood KR, et al. Symptomatic malignant gastroesophageal anastomotic leak: management with covered metallic esophageal stents. *AJR Am J Roentgenol* 2001; **176**: 161–5.
 11. Gollub MJ, Bains MS. Barium sulfate: a new (old) contrast agent for diagnosis of postoperative esophageal leaks. *Radiology* 1997; **202**: 360–2.
 12. Paterson IM, Wong J. Anastomotic leakage: an avoidable complication of Lewis-Tanner oesophagectomy. *Br J Surg* 1989; **76**: 127–9.
 13. Maher MM, Lucey BC, Boland G, Gervais DA, Mueller PR. The role of interventional radiology in the treatment of mediastinal collections caused by esophageal anastomotic leaks. *AJR Am J Roentgenol* 2002; **178**: 649–53.