Prevalence and Risk Factors for Ischemia, Leak, and Stricture of Esophageal Anastomosis: Gastric Pull-up Versus Colon Interposition

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BACKGROUND: Reports of esophageal anastomotic complications often involve more gastric than colonic reconstructions and are incomplete because of fragmented followup by physicians unfamiliar with the surgical procedure.

STUDY DESIGN: Three hundred ninety-three consecutive esophagectomy patients had prevalence and risk factors determined for graft ischemia and anastomotic leak; 363 of these patients followed for more than 1 month (median 15 months) had prevalence and risk factors determined for anastomotic stricture.

RESULTS: Conduit ischemia occurred in 36 (9.2%) and anastomotic leak in 43 patients (10.9%). Risk factor for ischemia was comorbid conditions requiring therapy (Odds ratio [OR]: 2.2 [95% CI 1.1–4.3]), and for leak were ischemia (OR: 5.5 [95% CI 2.5–12.1]), neoadjuvant therapy (OR: 2.2 [95% CI 1.1–4.5]), and comorbid conditions (OR: 2.1 [95% CI 1.1–3.9]). A stricture developed in 80 patients (22.0%). Risk factors were ischemia (OR: 4.4 [95% CI 2.0–9.6]), anastomotic leak (OR: 3.8 [95% CI 1.9–7.6]), and increasing preoperative weight (p = 0.022). The prevalence of ischemia was similar after gastric (10.4%) versus colonic (7.4%) reconstruction; leak and stricture were more common (14.3% versus 6.1%, p = 0.013, 31.3% versus 8.7%, p < 0.0001, respectively) and strictures were more severe (11.2% versus 2%, p = 0.001) after gastric pull-up. Patients free of ischemia and leak who developed stricture were more likely to have had a gastric pull-up (25% versus 7%, p < 0.0001). Dilatation was effective treatment in 93% of patients.

CONCLUSIONS: After esophagectomy 10% of patients will develop conduit ischemia or an anastomotic leak and 22% will develop anastomotic stricture. Anastomotic leak and strictures are more common and the strictures are more severe after gastric pull-up compared with colon interposition. Dilatation is a safe and effective treatment. (J Am Coll Surg 2004;198:536–542. © 2004 by the American College of Surgeons)

Anastomotic complications of ischemia, leak, or stricture are pivotal to the success or failure of esophagectomy. Reports in the medical literature on the prevalence of these anastomotic complications are variable, and the relationship between them has been poorly studied.1-8 The reasons for this are the lack of a precise definition for recognizing each complication and fragmented followup by endoscopists or physicians unfamiliar with the details of the surgical procedure and the immediate postoperative period. Additionally, the reports often consist of small numbers of patients and have a predominance of gastric versus colonic reconstructions.

The purpose of this study was to determine the prevalence, risk factors, and inter-relationships of the anastomotic complications of ischemia, leak, and stricture in a large group of consecutive patients followed by the operating surgeon after esophagectomy reconstructed with stomach or colon.
METHODS
Between January 1996 and July 2002, 404 patients had esophageal resection and primary reconstruction at the University of Southern California. Followup records were not available for review in 11 patients (2.7%) who survived the operation. This resulted in a study population of 363 (404 – 41 = 363) patients: 214 with gastric pull-up (n = 230) or colon interposition (n = 163). The stomach or colon was anastomosed to the cervical esophagus in the neck using a hand-sewn technique with interrupted sutures. Reconstruction after esophagectomy was with a gastric pull-up (n = 230) or colon interposition (n = 163). The stomach or colon was anastomosed to the cervical esophagus in the neck using a hand-sewn technique with interrupted sutures.

Fourteen patients died within 30 days of the operation (operative mortality, 14/404 = 3.5%), 5 patients died in hospital (overall hospital mortality: 19/404 = 4.7%), the records of 11 patients were not available for review and an additional 11 patients were followed for less than 1 month. Together these 41 patients had insufficient followup to determine the prevalence of a stricture. This resulted in a study population of 363 (404 – 41 = 363) patients: 214 with gastric pull-up and 149 with colon interposition, to determine the prevalence of a stricture, the risk factors leading to anastomotic stricture, and the inter-relationship between ischemia, leak, and stricture.

Patients received daily care after surgery and were followed by the operating surgeon on a regular basis after discharge from the hospital. Median followup time of the 363 patients was 15 months (interquartile range 8 to 34 months). All patients had a gastrografin swallow before discharge, and endoscopy was used liberally to evaluate the symptoms of ischemia in the hospital and dysphagia after discharge. Conduit ischemia was defined by blue to black discolorization of the mucosa, adherence of a green or silver-metallic mucus to the mucosa that could not be removed by irrigation, or a clearly demarcated nonedematous mucosa with ulceration. Anastomotic leak was defined by extravasation of contrast material during gastrografin swallow or visualization of a breakdown of an anastomosis on endoscopy. A benign anastomotic stricture was defined as a stenosis that precluded passage of a 9-mm endoscope in the absence of recurrent cancer. The time of onset of the stricture was defined by the date of the initial endoscopic recognition of a stricture. Severity of the stricture was graded by the number of dilatations needed to relieve dysphagia (mild: 1–2, severe: ≥3). Dilatations were performed using a pneumatic balloon dilator passed through an endoscope or an orally passed bougie.

Variables evaluated as potential risk factors for the occurrence of ischemia, leak, and stricture are listed in Table 1. Comorbid conditions included diabetes, cardiovascular conditions, and pulmonary diseases that required medical therapy.

Statistical analysis
Student’s t-test was used for comparison of continuous variables between groups using the SPSS package for Windows (release 10.1.0; SPSS Inc). Categorical variables were compared using chi-square analysis. Multivariable logistic regression (backward stepwise) was used for risk factor assessment. Odds ratios were calculated for each risk factor, expressed with 95% confidence intervals. A p value of 0.05 was considered significant.

### Table 1. Multivariable Analysis of Risk Factors for Ischemia, Leak, and Stricture

<table>
<thead>
<tr>
<th>Variables</th>
<th>Ischemia OR (95% CI) p Value*</th>
<th>Leak OR (95% CI) p Value*</th>
<th>Stricture OR (95% CI) p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Gender</td>
<td>1.1(0.5–2.5) p=NS</td>
<td>0.9(0.4–1.7) p=NS</td>
<td>1.1(0.6–1.9) p=NS</td>
</tr>
<tr>
<td>Preoperative weight</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Comorbid conditions</td>
<td>2.2(1.1–4.3) p=0.023</td>
<td>2.1(1.1–3.9) p=0.044</td>
<td>1.5(0.9–2.5) p=NS</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.9(0.8–4.5) p=NS</td>
<td>1.0(0.4–2.4) p=NS</td>
<td>0.9(0.4–1.9) p=NS</td>
</tr>
<tr>
<td>Neoadjuvant therapy</td>
<td>2.0(0.9–4.4) p=NS</td>
<td>2.2(1.1–4.5) p=0.037</td>
<td>1.6(0.9–2.9) p=NS</td>
</tr>
<tr>
<td>Manubrium resection</td>
<td>1.7(0.6–4.7) p=NS</td>
<td>1.0(0.3–2.9) p=NS</td>
<td>0.8(0.3–2.1) p=NS</td>
</tr>
<tr>
<td>Conduit ischemia</td>
<td>N/A</td>
<td>5.5(2.5–12.1) p &lt; 0.0001</td>
<td>4.4(2.0–9.6) p=0.003</td>
</tr>
<tr>
<td>Anastomotic leak</td>
<td>N/A</td>
<td>N/A</td>
<td>3.8(1.9–7.6) p=0.001</td>
</tr>
</tbody>
</table>

A p value of 0.05 was considered significant.

*Logistic regression analysis (backward stepwise) OR, odds ratio.
RESULTS

Conduit ischemia occurred in 36 of the 393 patients (9.2%) after esophagectomy. Three died within 30 days of the operation, and two died while in the hospital. The mortality rate for conduit ischemia was 13.9% (5 of 36). The 31 patients who survived were at risk for additional complications of their anastomosis. The only risk factor for developing conduit ischemia was the presence of co-morbid conditions (odds ratio [OR]: 2.2 [95% CI 1.1–4.3], Table 1).

Anastomotic leak occurred in 43 of the 393 patients (10.9%) after esophagectomy. Three died within 30 days of the operation, and two died while in the hospital. Three of the five patients who died also had ischemia. The mortality rate for anastomotic leak was 11.6% (5 of 43). The 38 patients who survived were at risk for more complications of their anastomosis. Risk factors for developing an anastomotic leak were ischemia (OR: 5.5 [95% CI 2.5–12.1]), neoadjuvant therapy (OR: 2.2 [95% CI 1.1–4.5]), and comorbid conditions (OR: 2.1 [95% CI 1.1–3.9], Table 1).

Seven (37%) of the 19 hospital deaths after esophagectomy resulted from sepsis caused by anastomotic complications: 2 from ischemia alone, 2 from anastomotic leak alone, and 3 from a combination of ischemia and leak.

A stricture occurred in 80 of the 363 patients (22.0%) who were discharged from the hospital and were followed for 1 month or more after esophagectomy. Multivariable analysis identified three risk factors for development of a stricture (Table 1). A stricture developed in 15 of the 31 patients (48%) who had an ischemic conduit. The odds ratio for development of a stricture in a patient with an ischemic conduit was 4.4 (95% CI 2.0–9.6). As would be expected, no ischemic strictures occurred 6 months after operations. A stricture developed in 18 of the 38 patients (47%) who had an anastomotic leak. The odds ratio for development of a stricture in a patient with an anastomotic leak was 3.8 (95% CI 1.9–7.6). The risk of stricture rose with increasing weight as a continuous variable (p = 0.015, Fig. 1). Thirty-four percent of the strictures were severe (≥ 3 dilatations) (27/80) and characteristically developed early (1 to 3 months, p < 0.001, Fig. 2). Risk factors for development of a severe stricture were ischemia (OR: 5.6 [95% CI 1.7–18.9]), comorbid conditions (OR: 3.3 [95% CI 1.2–8.7]), and preoperative weight (p = 0.033, Fig. 1).

A Venn diagram (Fig. 3) shows the inter-relationship of the anastomotic complications: ischemia, leak, and stricture.
stricture. Ischemia or leak alone led to a stricture in 48% (10 of 21) and 46% (13 of 28) of patients, respectively. The combination of ischemia and leak led to stricture in 50% (5 of 10) of the patients. Fifty-two percent (11 of 21) of patients with only ischemia and 54% (15 of 28) with only a leak recovered from their ischemia or healed their leak without developing a stricture. Of the 80 patients who developed a stricture, 52 (65%) did not have evidence of conduit ischemia or anastomotic leak.

The prevalence of ischemia was similar with gastric and colonic reconstructions: 10.4% (24 of 230) versus 7.4% (12 of 163), respectively (p = 0.375, Fig. 4). In contrast, anastomotic leak was more common after gastric (14.3%, 33 of 230) than colonic (6.1%, 10 of 163) reconstruction (p = 0.013, Fig. 4). The prevalence of a stricture was more common after gastric (31.3%) than colonic (8.7%) reconstruction (p < 0.0001, Fig. 5). Similarly, severe strictures were also more likely to occur after gastric (11.2%) than colonic (2.0%) reconstruction (p = 0.001).

Clinical evidence of ischemia or a leak did not develop in 304 of the 363 patients, 167 of whom had reconstruction with the stomach and 137 with the colon. In patients who did not have ischemia or leak, using the stomach was more likely to result in a stricture (25%) than using the colon was (7%, p < 0.0001, Fig. 6). Fourteen of the 52 patients who developed a stricture without obvious clinical conduit ischemia or anastomotic leak had endoscopic esophagitis, and with one exception, the esophagitis occurred in patients with gastric reconstructions.

All anastomotic strictures were able to be dilated, and none required surgical repair. Dysphagia was relieved effectively by dilatation in 93% of patients. Fifty per cent of patients required one, 16% two, and 34% three or more dilatations for relief. One perforation occurred in a total of 223 dilatations (0.45%), and was managed conservatively by a covered esophageal stent. Eleven of the 27 patients with a severe stricture (≥3 dilatations) were managed by self-performed home dilatations, the frequency of which was gradually reduced over time.
Dysphagia persisted in six patients, four of whom died of systemic recurrence during treatment, and two who are still under treatment.

**DISCUSSION**

Occurrence of early complications of conduit ischemia and anastomotic leak had a major impact on the outcomes of esophagectomy. Together, they account for 37% (7 of 19) of hospital deaths after esophagectomy, and each are risk factors for development of the late complication of anastomotic stricture. Development of new techniques that would protect against conduit ischemia and prevent anastomotic leak would have a significant impact on the mortality and morbidity of esophagectomy and is a fruitful area for future investigation. Conduit ischemia was more likely to occur in the presence of comorbid conditions that require therapy: namely diabetes, cardiovascular disorders such as hypertension, arrhythmia, and reduced cardiac contractility, and chronic obstructive pulmonary disease. These conditions are known to compromise tissue perfusion and oxygenation. Anastomotic leaks are more likely to occur in patients with conditions known to affect healing. Consequently, the risk factors include conduit ischemia, administration of neoadjuvant therapy, and comorbid conditions.

Although others have reported the importance of conduit ischemia and anastomotic leak in stricture development, the relationship of these complications to one another has not been well studied. This relationship is shown schematically in Figure 7 and is useful in clinical management. For example, in patients who develop clinical ischemia, one-third will heal without complication, one-third will develop a stricture without a leak, and one-third will develop an anastomotic leak, with half going on to develop a stricture. Consequently, the combination of ischemia and an anastomotic leak is particularly apt to result in a stricture. In patients who develop an anastomotic leak without associated ischemia, about half will develop a stricture and half will heal without complication.

In addition to conduit ischemia and anastomotic leak, increasing patient weight was associated with the occurrence of stricture. Interestingly, weight was not a risk factor for conduit ischemia and anastomotic leak. This suggests that the additional fat on the graft in heavier patients may lead to compression of the conduit by the confined space of the posterior mediastinum and the thoracic inlet. This may result in localized vascular insufficiency and stricture. In addition, body habitus in heavier patients may contribute to technical difficulties with the anastomosis that lead to stricture.

Both early and late anastomotic complications are more common after gastric than after colonic reconstruction. After gastric pull-up, leaks are more common, and strictures are both more common and severe. Strictures are also more common after gastric reconstruction in the group of patients without clinical evidence of conduit ischemia or leak. The fact that esophagitis in the

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**Figure 7.** Summary of the risk factors and interrelationships of ischemia, leak, and stricture. OR, odds ratio.
cervical esophagus was seen almost exclusively in those who had a gastric pull-up suggests that reflux of gastric juices may contribute to stricture formation. The observation that late strictures (more than 1 year) occurred only in patients with gastric pull-up additionally supports a reflux etiology.

Although the presence of a stricture is disruptive to the patient’s quality of life, its treatment is relatively straightforward. Half of the patients require only a single dilatation, and an additional 16% require only two. Those with more severe strictures eventually respond to dilatation, with only a small minority requiring home dilatations. No patient required surgical correction.

In summary, approximately 10% of patients who undergo esophagectomy will develop conduit ischemia or an anastomotic leak, with mortality rates of 14% and 12%, respectively. Comorbid conditions are the only risk factors for conduit ischemia. Risk factors for anastomotic leak are conduit ischemia, neoadjuvant therapy, and comorbid conditions. Anastomotic strictures occur after esophagectomy in 22% of patients. Risk factors for stricture are conduit ischemia, anastomotic leak, and increasing weight. The highest prevalence of stricture occurs in patients with both ischemia and leak. Anastomotic leak and strictures are more common and the strictures are more severe after gastric pull-up than after colon interposition. Dilatation is a safe and effective treatment.

**Author Contributions**

Study conception and design: Briel, Johansson, Bremner DeMeester, Choustoulakis, Peters, TR DeMeester

Analysis and interpretation of data: Briel, Hagen

Drafting of manuscript: Briel, TR DeMeester

Critical revision: Briel, TR DeMeester

Statistical expertise: Hagen

Supervision: TR DeMeester

**REFERENCES**


**Invited Commentary**

David R Jones, MD, FACS

Charlottesville, VA

I wish to congratulate the authors on this scholarly piece of work and Dr Briel for his fine presentation of the data. This study is another in a long line of similar investigations on management of benign and malignant esophageal disorders by Dr DeMeester and his group at the University of Southern California. I have had an opportunity to review the article and I have several questions for the authors.

1) Were the esophagogastric and esophagocolonic groups matched with respect to comorbid conditions, induction therapies, and so on?

2) Did you examine whether the indication for the esophagectomy played any role in the likelihood of developing an anastomotic complication? That is to say, were patients with cancer more likely to develop these problems than patients with end-stage benign esophageal disease?

3) Did you look at the patient’s preoperative nutritional status as a predictor of the development of ischemia, anastomotic leak, or both? Literature has suggested that a low serum albumin may be a predictor for gastrointestinal anastomotic leaks.

4) I always teach my residents and fellows that conduit ischemia is the primary reason for the majority of anastomotic leaks. In your series, ischemia rates were nearly identical between esophagogastric and esophagocolonic anastomoses. Despite similar rates of ischemia, the anastomotic leak rate and the development of a stricture were significantly higher in the esophagogastric anastomoses than in the esophagocolonic anastomoses. How do you explain this apparent disparity? In the article you suggest that patients who underwent neoadjuvant therapy were more likely to have an esophagogastric reconstruction. Does this mean that the type of anastomosis...