

Role of Barium Swallow in Diagnosing Clinically Significant Anastomotic Leak following Esophagectomy

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Background: Barium swallow is performed following esophagectomy to evaluate the anastomosis for detection of leaks and to assess the emptying of the gastric conduit. The aim of this study was to evaluate the reliability of the barium swallow study in diagnosing anastomotic leaks following esophagectomy. **Methods:** Patients who underwent esophagectomy from January 2000 to December 2013 at our institution were investigated. Barium swallow was routinely done between days 5–7 to detect a leak. These results were compared to clinically determined leaks (defined by neck wound infection requiring jejunal feeds and or parenteral nutrition) during the postoperative period. The sensitivity and specificity of barium swallow in diagnosing clinically significant anastomotic leaks was determined. **Results:** A total of 395 esophagectomies were performed (mean age, 62.2 years). The indications for the esophagectomy were as follows: malignancy (n=320), high-grade dysplasia (n=14), perforation (n=27), benign stricture (n=7), achalasia (n=16), and other (n=11). A variety of techniques were used including transhiatal (n=351), McKeown (n=35), and Ivor Lewis (n=9) esophagectomies. Operative mortality was 2.8% (n=11). Three hundred and sixty-eight patients (93%) underwent barium swallow study after esophagectomy. Clinically significant anastomotic leak was identified in 36 patients (9.8%). Barium swallow was able to detect only 13/36 clinically significant leaks. The sensitivity of the swallow in diagnosing a leak was 36% and specificity was 97%. The positive and negative predictive values of barium swallow study in detecting leaks were 59% and 93%, respectively. **Conclusion:** Barium swallow is an insensitive but specific test for detecting leaks at the cervical anastomotic site after esophagectomy.

Key words: 1. Esophagectomy
2. Anastomotic leak
3. Barium
4. Esophagus

INTRODUCTION

Esophagectomy is a major operation with significant morbidity and is performed for a variety of conditions; however, the main indication for the procedure is an esophageal malignancy [1-7]. It is also a treatment option for certain pre-ma-

lignant diseases such as high-grade dysplasias, but with the advent of endoscopic mucosal resection, esophagectomy is offered only to selected cases with high risk factors, unless there is invasive esophageal cancer on histology. In addition, the procedure can be a treatment option for some end-stage benign diseases such as strictures, traumatic rupture, and ia-

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trogenic injuries.

Depending on institutional preferences and expertise, various techniques for performing open esophagectomies are utilized including the Ivor Lewis, McKeown, and transhiatal approaches. In recent times, minimally invasive esophagectomy using laparoscopy and thoracoscopy is also an alternative approach that is increasingly being utilized [8-11]. Transhiatal esophagectomy with cervical anastomosis is the predominant approach used at our institution, as its advantages include ease of treatment at the anastomotic site in case of a leak as well as lower pulmonary morbidity [2,4,12-15]. A major criticism against the transhiatal approach for oncologic operations is that mediastinal lymph node dissection is inadequate relative to the transthoracic approach [3,13,15,16]; however, long term survival is no different than with the transthoracic approach, and transhiatal esophagectomy may be more cost effective [17]. Furthermore, higher rates of anastomotic leaks have been reported with cervical compared to mediastinal anastomosis [6,18].

Although it has become controversial in recent years, many hospitals continue the routine practice of assessing for anastomotic leaks with the use of contrast swallow studies [19]. Recent experience has shown the false negative rate of water-soluble contrast swallow studies to be unacceptably high [5,19-21]. Barium contrast has also been used to check for anastomotic leaks in the gastrointestinal tract. The theory that barium leakage may cause mediastinitis has prevented more widespread usage of the contrast material. The sensitivity for detecting anastomotic leaks with barium may be higher than with water-soluble contrast given the greater affinity of barium to the gastrointestinal mucosa as well as its higher density [22-24]. Prior studies have used aqueous solution as the initial contrast material in detecting leaks, with select studies using barium for a subsequent verification swallow test if the initial aqueous solution did not show a leak [5,19-21,25-30]. This paper reports on the measurement of the sensitivity and specificity of a screening swallow study after esophagectomy using barium as the initial contrast agent.

METHODS

1) Patient population

The present study was granted approval by the University of Iowa institutional review board (200703773). This was a retrospective review of a prospectively collected database of medical records. The University of Iowa institutional review board waived the need for patient consent for the study. All patients who underwent esophagectomy during the period of January 2000 to December 2013 were analyzed for the study. A total of 395 patients met criteria for inclusion in the study. Of these, 320 esophagectomies were performed for malignancy and 75 for benign disease (high grade dysplasia [n=14], perforation [n=27], benign stricture [n=7], achalasia [n=16], dysphagia [n=4], esophageal fistula [n=4], severe reflux status post-Nissen [n=1], esophagogastric leak [n=1], and schwannoma [n=1]). As 27 patients were unable to undergo a postoperative barium swallow due to their clinical condition, 368 screening barium swallow studies were performed.

2) Barium esophagram

Patients were routinely scheduled to undergo a screening barium swallow study on postoperative day 5, using 70% (weight to volume) barium during the entire study period. Results of the barium swallow study were compared to clinical signs of an anastomotic leak. The relevant standard for detection of an anastomotic leak was through clinical evaluation. A clinical leak was defined as any cervical or thoracic anastomosis that required drainage and/or enteral tube feeding. When clinical evaluation showed signs of a leak, the barium swallow was categorized as a true positive when a leak was seen and a false negative when a leak was not seen on the barium swallow. When clinical evaluation did not show signs of a leak, the barium swallow was categorized as a true negative when a leak was not seen and a false positive when a leak was seen. Additional information, including the gastric or colonic conduit emptying rate and signs of aspiration were routinely assessed during the barium swallow study.

3) Clinical condition

Various clinical factors were analyzed to determine whether

the presence of a clinical condition affected postoperative leak rates. Patients with anastomotic leaks were compared to those without anastomotic leaks, and the statistical significance of the clinical parameters was calculated.

4) Statistical analysis

Associations between categorical variables were determined using a chi-square test or Fisher's exact test as appropriate. Associations between continuous variables were determined using a 2 sample t-test or Mann-Whitney U-test as appropriate. All $p \leq 0.05$ were considered statistically significant. All data analyses were performed using Stata ver. 13.0 software (Stata Co., College Station, TX, USA).

RESULTS

During the period of January 2000 to December 2013, 395 patients underwent esophagectomies. Sex, smoking status, existing medical comorbidities, history of prior operations, weight loss status, length of stay, and age at the time of surgery are listed in Table 1.

Esophagectomy procedures consisted of a variety of techniques including transhiatal (n=351), McKeown (n=35), and Ivor Lewis (n=9) approaches. A screening barium swallow study was performed in 368 patients. Fifteen patients were clinically unable to perform a swallow study. Nine patients did not undergo cervical esophagogastric anastomosis due to tenuous blood supply to the gastric or colonic conduit; therefore, an esophageal spit fistula was created with the intention of performing the anastomosis at a later date. Three patients were noted to have a cervical anastomotic leak prior to postoperative day 4. In those cases, the cervical incisions were opened and packed at the bedside. These patients were not scheduled to undergo the routine swallow study.

Although patients were routinely scheduled to undergo a barium swallow study on postoperative day 5, due to clinical factors, some underwent the study outside of the scheduled time, at mean postoperative day 6.4 (range, 3 to 75 day). The median time for undergoing the barium swallow was postoperative day 5. All patients underwent a barium swallow study within 20 days except for one patient for whom the study was performed on day 75 due to prolonged respiratory

Table 1. Patient co-morbidities and postoperative length of stay among all 395 patients undergoing esophagectomy at our institution

Variable	Value
Age at surgery (yr)	62.2±11.4 (range, 21–88)
Gender (male)	316 (80)
Never smoker	103 (26)
Ever smoker	292 (74)
Current smoker	88 (22)
Previous smoker	204 (52)
Diabetes	68 (17)
Chronic obstructive pulmonary disease	49 (12)
Coronary artery disease	76 (19)
Renal failure	9 (2)
Hypertension	191 (48)
Previous abdominal surgery	174 (44)
Previous thoracic surgery	47 (12)
Previous esophageal surgery	43 (11)
Previous coronary artery bypass	30 (8)
Weight loss >4.535924 kg	188 (48)
Length of stay (day)	
Median	7
25th–75th percentile	Range, 5–12
Min–max	Range, 1–148

Values are presented as mean±standard deviation or number (%), unless otherwise stated. The median length of stay for the entire cohort was 7 days (range, 1–148 days). Operative mortality occurred on postoperative day 1 in one patient.

failure and intensive care unit stay.

Among the 368 patients who underwent a barium swallow, clinically significant anastomotic leaks were identified in 36 patients (9.8%) (malignancy 83% [n=30], high grade dysplasia 11% [n=4], stricture/dysphagia 6% [n=2]). The anastomotic leaks were graded based on the criteria defined by the Esophagectomy Complications Consensus Group [31]. The types of leaks based on these criteria were as follows: type 1 (n=1), type 2 (n=25), and type 3 (n=10). Barium swallow was able to pick up only 13/36 clinically significant leaks. Among these 13 patients, 5 did not have any clinical symptoms prior to the swallow study. In addition, 9 patients that were thought to have a leak as shown by the barium swallow had no clinical signs of a leak and had an uneventful course following the surgery (Fig. 1). Thus in our cohort, the sensitivity of the swallow in diagnosing a leak was 36% and specificity was 97%. The positive and negative predictive values

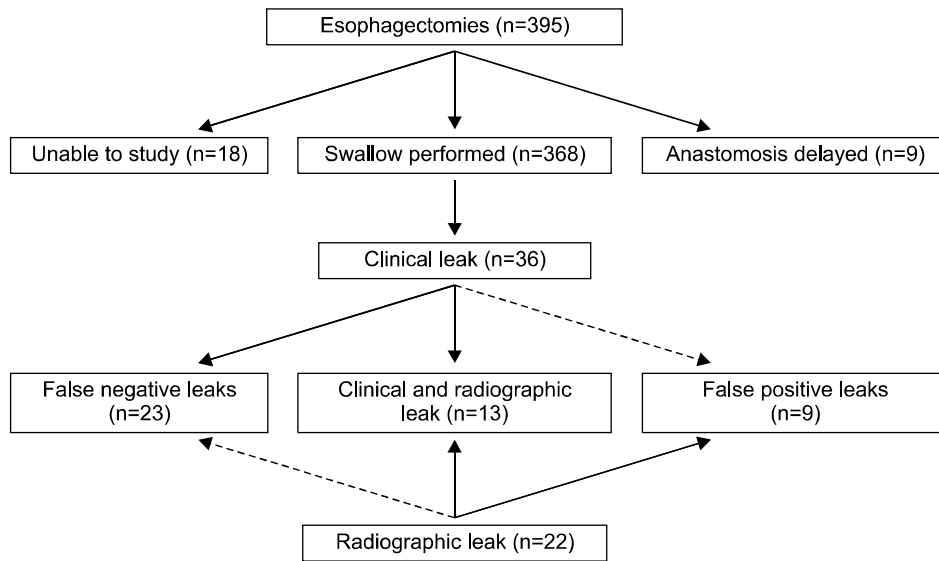


Fig. 1. Flow diagram showing the distribution of patients who underwent esophagectomy at our institution. Between 2000–2013, 395 patients underwent esophagectomy and 368 were studied with a postoperative barium swallow to detect an anastomotic leak. There were 36 (9.8%) clinically significant leaks in the cohort. Barium swallow picked up only 13 (36%) of these clinically significant leaks. There were 9 false positive leaks on the swallow and 23 false negative leaks. The sensitivity of the barium swallow in detecting a leak was 36%, and the specificity was 97%. The positive predictive value was 59%, and the negative predictive value was 93%.

of the barium swallow study in detecting leaks were 59% and 93%, respectively.

A sub-group analysis was performed analyzing patients who underwent the barium swallow study at greater than postoperative day 5. In these 166 patients, the barium swallow had been performed on median postoperative day 7 (range, 6 to 75 day). In this sub-group, the sensitivity was 52%, specificity 95%, positive predictive value 61%, and negative predictive value 93%.

Delayed emptying of contrast was noted in 78 patients (21.2%) and aspiration was noted in 60 patients (16.3%) undergoing a barium swallow study. Twenty-six percent (6/23) of patients with a false negative barium swallow showed signs of aspiration as compared to 16% (54/345) of patients without a false negative barium swallow ($p=0.19$).

Of all the risk factors for a leak that we analyzed, previous history of coronary artery bypass surgery was the only risk factor that significantly increased the risk of development of anastomotic leaks in our patient population. Once the leak developed, the length of stay in the hospital also increased significantly (Table 2).

A subgroup analysis was performed on patients treated

with esophagectomy for esophageal cancer. Out of 395 patients, 302 underwent a barium swallow test after undergoing esophagectomy for malignancy. No significant difference was seen in the leak rate between the patients who had received neoadjuvant therapy, 9.0% (18/199 patients), compared to patients who did not receive neoadjuvant therapy, 11.7% (12/103 patients) ($p=0.47$). The median length of hospital stay for patients receiving neoadjuvant therapy was 6 days (25th–75th percentile, 1 to 10 days) and patients not receiving neoadjuvant therapy was 9 days (25th–75th percentile, 3 to 15.5 days; $p<0.001$).

DISCUSSION

Recent papers recommend against routine contrast swallow studies after an esophagectomy to assess the integrity of the esophagogastric anastomosis [5,20]. Many high-volume centers have stopped performing routine swallow examinations after esophagectomy [6]; however, this practice continues in a large number of hospitals [19]. Barium is thought to be more sensitive in the detection of leaks compared to water-soluble contrast, as barium coats the mucosal lining with greater af-

Table 2. Patient characteristics and outcomes among 368 patients undergoing a barium swallow study after esophagectomy

Variable	With anastomotic leak (N=36)	No anastomotic leak (N=332)	p-value ^{a)}
Age at surgery (yr)	60.9±9.5 (range, 45–78)	61.9±11.5 (range, 21–88)	0.632 ^{b)}
Gender (male)	29 (81)	267 (80)	0.985
Never smoker	7 (19)	87 (26)	0.377
Ever smoker	29 (81)	245 (74)	0.246
Current smoker	12 (33)	71 (21)	
Previous smoker	17 (47)	174 (52)	
Diabetes	6 (17)	57 (17)	0.940
Chronic obstructive pulmonary disease	5 (14)	39 (12)	0.707
Coronary artery disease	10 (28)	60 (18)	0.159
Renal failure	0	8 (2)	1.0 ^{c)}
Hypertension	18 (50)	160 (48)	0.837
Previous abdominal surgery	12 (33)	146 (44)	0.221
Previous thoracic surgery	3 (8)	40 (12)	0.784 ^{c)}
Previous esophageal surgery	3 (8)	37 (11)	0.782 ^{c)}
Coronary artery bypass	7 (19)	20 (6)	0.003
No neoadjuvant treatment	14 (39)	143 (43)	0.630
Weight loss >4.535924 kg	15 (42)	160 (48)	0.456
Delayed emptying on barium swallow	9 (25)	69 (21)	0.557
Aspiration during barium swallow	10 (28)	50 (15)	0.050
Length of stay (day)			
Median	21	7	<0.001
25th–75th percentile ^{d)}	Range, 9.8–35	Range, 5–10	
Min–max	Range, 5–82	Range, 4–121	
Operative mortality	2 (5.6)	3 (0.9)	0.077 ^{c)}

Values are presented as mean±standard deviation or number (%), unless otherwise stated. Patients who developed anastomotic leaks were compared to the group that did not develop a leak. Operative mortality was defined as death within 30 days after surgery during the same hospitalization. Previous history of coronary artery disease requiring a bypass surgery was the most significant risk factor that predicted the development of an anastomotic leak.

^{a)}By chi-square test. ^{b)}By Student t-test. ^{c)}By Fisher's exact test. ^{d)}By Mann-Whitney U-test.

finity and has a higher density [22-24,27,29].

The sensitivity of the barium swallow was only 36% for the entire cohort in our study when the median time of performing the test was 5 days postoperatively. A sub-group analysis showed that at 7 days postoperatively, the sensitivity of the test did increase to 52%. This increase in the sensitivity may be explained partially because most of the leaks happen around day 5–7 and they may be easier to detect at a later point in time. Our results show that the barium swallow is a test with low sensitivity but good specificity for detecting leaks at the cervical anastomotic site after esophagectomy. Other research has shown unacceptably low rates of sensitivity of the contrast swallow study in detecting leaks after esophagectomy [5,19-21,27,28,30]. These studies used either water-soluble contrast as the sole contrast agent, or both

water-soluble and barium contrast. If barium contrast was utilized, it was only after the initial water-soluble contrast swallow showed no evidence of a leak.

Our protocol is to perform swallow studies using barium as the initial contrast agent. Patients that are noted to have a large leak through the cervical anastomosis are taken to the operating room for re-exploration and drainage or revision of the anastomosis. Therefore, the concern about a barium leak causing mediastinitis is eliminated. Our study included a small number of patients with mediastinal esophagogastric anastomosis. Clinical detection of an intrathoracic leak includes septic deterioration or shock and foul chest tube drainage containing gastrointestinal contents [12]. Only one out of the nine patients in our study who had an intrathoracic anastomosis had a clinically significant leak and was taken to the

operating room for re-exploration.

It is possible that some patients categorized into the false positive swallow study may have had a small subclinical leakage. Under these circumstances, it is nearly impossible to determine whether a small leak on barium swallow was a false positive or a true positive as patients will not have clinical symptoms. The gold standard for detection of a small subclinical leakage is unknown, as these patients will remain asymptomatic.

Cervical anastomosis is routinely used at our institution in esophagogastric anastomosis, as it has shown to decrease the morbidity in case of an anastomotic leak [2,4,12-15]. Patients with clinical evidence of minor cervical anastomotic leaks undergo opening of their cervical incisions at the bedside. However, in cases of major anastomotic leaks, patients can be more optimally managed by re-exploring the wound in the operating room as major leaks have been associated with significant complications [1,12,20,32-34].

Contrast swallow studies are routinely scheduled on postoperative day 5 at our institution. This can vary, as other institutions perform the test at up to postoperative day 10 [5,19,20]. Given the unpredictable clinical downturn in some patients, the swallow study may be delayed significantly. No literature is available on when the optimum timing is for obtaining a contrast swallow study after esophagectomy.

Schaible et al. [27] performed the contrast swallow at postoperative days 5 to 7 and reported a sensitivity of 20%. Several other studies that performed the contrast swallow on median postoperative days 6 to 10 showed slightly higher sensitivities ranging from 40.4% to 67% [5,19,28,30]. Our study showed a sensitivity of 36% when all 368 patients were included, with the barium swallow study being performed on median postoperative day 5. However, when analyzing only the patients undergoing the swallow study at greater than 5 days (166 patients; median postoperative day=7; range, 6 to 75 days), the sensitivity increases to 52%. However, even at day 7, with only 50% accuracy, it is still not a sensitive test.

As our experiences have shown, the barium swallow has a low sensitivity and is not reliable in diagnosing clinically significant anastomotic leaks following esophagectomy. Therefore, our practice has evolved to resume oral intake three weeks

after the surgery even in the case that the barium swallow is negative for a leak. Delaying oral intake was shown to decrease the rate of cervical anastomotic leaks [35]. Tomaszek et al. [6] showed that delaying oral intake up to four weeks postoperatively with the use of a jejunostomy tube and not routinely obtaining a barium swallow study was shown to result in a shorter hospital stay with no additional risks for complications after discharge. The best route of early enteral feeding after esophagectomy remains unclear [36].

Another possible method of postoperative management of patients suspected to have a cervical anastomotic leak would be to obtain a computed tomography (CT) of the chest along with a contrast swallow study, as this has been shown to increase the sensitivity and negative predictive value of a leak [26,28,30]. The comparison of a water-soluble contrast swallow study with CT showed CT to have mixed results in terms of having better specificity in detection of anastomotic leaks [25,30].

Routine postoperative endoscopy has been proposed to detect anastomotic leaks [37]. Schaible et al. [27] proposed abandoning routine use of contrast swallow studies after esophagectomy entirely in favor of routine endoscopy, as the latter was significantly more sensitive in detecting pathological findings. Novel techniques have recently been investigated for detection of anastomotic leaks, including measuring electrical changes induced by electrolyte extravasation at the site of the leak [38], monitoring local metabolism through the use of mediastinal microdialysis [39], and measuring cervical drain amylase levels [40]. These methods have not yet gained widespread adoption. Most of the esophagogastric anastomotic leaks are presumed to have developed as a result of the tissue hypoxia in the gastric conduit. Servais et al. [41] have developed a wireless pulse oximetry device, which measures tissue oxygen saturation to identify the ideal sites for anastomosis.

Barium contrast swallow studies continue to be scheduled at our institution on day 5 following an esophagectomy, given that the studies provide additional useful information such as signs of aspiration and the gastric or colonic conduit emptying rate. In spite of an increase in the sensitivity at day 7, we have not withheld patient discharge just to perform a barium swallow on day 7 for a test that is only accurate 50%

of the time. Our practice allows for early discharge on enteral tube feedings; however, oral feeding is delayed to 3 weeks after the operation.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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