Chest *vs.* neck anastomotic leak post esophagectomy for malignancy: rate, predictors, and outcomes

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Background: Anastomotic leak is a major contributor to comorbidity and mortality following esophagectomy. We sought to assess rate and predictors of leak after esophagectomy and compare outcomes of chest versus neck anastomotic leaks.

Methods: A retrospective review was performed utilizing National-Surgical-Quality-Improvement-Program data from 2016–2019 for patients undergoing esophagectomy for malignancy. Preoperative characteristics and postoperative outcomes were compared. Patients were classified into two groups: Ivor Lewis esophagectomy [ILE, chest leak (CL)] and transhiatal esophagectomy (THE)/McKeown esophagectomy [ME, neck leak (NL)]. Multivariable regression models were constructed to determine predictors of each type of leak and postoperative complications.

Results: A total of 1,665 patients underwent esophagectomy with 14.1% reported post-operative leak, 61% of patients underwent ILE while 39% underwent THE or ME. Of patients who underwent ILE, 13.8% had CL with complications including significantly higher length of stay and mortality compared to patients without leak. Independent predictors of CL included: diabetes, hypertension, advanced disease stage, chronic steroid use, and operative time. Ninety-five patients (14.6%) who underwent either THE or ME had NL with similar complications. Diabetes, pre-operative white blood cell (WBC), and operative time were independent predictors for NL. On multivariable regression, CL was associated with greater odds of requiring intervention compared with NL.

Conclusions: Post-esophagectomy CL and NL are associated with higher morbidity and mortality. Diabetes and operative time were independent predictors for both leaks while steroid use, hypertension, and advanced disease stage predicted CL. CL was associated with greater odds of needing an intervention, but contrary to conventional wisdom, was not associated with higher morbidity or mortality.

Keywords: Esophagus; esophagectomy; esophageal cancer; anastomotic leak

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Introduction

Esophageal cancer is one of the most common cancers worldwide and continues to remain associated with a poor prognosis. The incidence of esophageal adenocarcinoma in the United States has recently begun to decline while the incidence of esophageal squamous cell carcinoma has been decreasing since 1986 (1,2). Esophagectomy continues to remain the mainstay of treatment in cases of certain early stage and locally advanced esophageal cancer.

Esophagectomy continues to carry a significant risk of associated morbidity and mortality. An anastomotic leak is one of the most feared complications with esophagectomies and has been associated with an increased morbidity and a reduction in overall survival (3). The surgical approach is dependent on multiple factors, including tumor location, extent of desired lymphadenectomy, and surgeon expertise and preference (4). Numerous studies and meta-analyses have been conducted, evaluating oncologic outcomes between the different surgical approaches for esophagectomy. Data from these studies have indicated that surgical approach has no significant influence on oncologic outcomes (5-8). Although there is significant variance in current literature, anastomotic leaks following esophagectomy are reported between 10–25% for cervical

anastomoses and 3–25% for intrathoracic anastomoses (9,10). Prior studies have hypothesized a difference in complication rates by whether the anastomosis was made in the neck versus the chest (11,12).

There is a gap in the literature regarding a multicenter study assessing the contemporary practice of different esophagectomy techniques with a focus on the evaluation of morbidity and mortality associated with anastomotic leaks in the chest versus in the neck. Using a large national surgical database, we aim to investigate the rate and predictors of anastomotic leak following esophagectomy and compare outcomes of chest versus neck anastomotic leaks. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-37/rc).

Methods

Database and patient population

The American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database including targeted files for esophagectomy was queried for patients who underwent esophagectomy for esophageal cancer between 2015 and 2019. The ACS-NSQIP contains over 135 variables captured from de-identified surgical cases performed in participating hospitals. These variables include preoperative characteristics, intraoperative events, and postoperative outcomes within 30 days of the operation.

The Current Procedural Terminology (CPT) codes 43107, 43117, 43112 were used to identify patients who underwent esophagectomy with Transhiatal, Ivor Lewis, and McKeown approach, respectively. Only patients with the following International Classification of Diseases (ICD) codes for malignant esophageal cancer diagnosis were included: ICD-9 codes: 150 Malignant neoplasm of esophagus, 150.0 Malignant neoplasm of cervical esophagus, 150.1 Malignant neoplasm of thoracic esophagus, 150.2 Malignant neoplasm of abdominal esophagus, 150.3 Malignant neoplasm of upper third of esophagus, 150.4 Malignant neoplasm of middle third of esophagus, 150.5 Malignant neoplasm of lower third of esophagus, 150.8 Malignant neoplasm of other specified part of esophagus, and 150.9 Malignant neoplasm of esophagus, unspecified site. ICD-10 codes included were C15 Malignant neoplasm of esophagus, C15.3 Malignant neoplasm of upper third of esophagus, C15.4 Malignant neoplasm of middle third of esophagus, C15.5 Malignant neoplasm of lower third of

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Highlight box

Key findings
- Intrathoracic anastomotic leaks, following esophagectomy for malignancy, were associated with greater odds of needing an intervention but were not associated with higher morbidity or mortality, when compared with cervical anastomotic leaks.

What is known and what is new?
- Some surgeons avoid performing Ivor-Lewis esophagectomies due to the belief that an anastomotic leak in the chest is associated with increased morbidity and mortality.
- With the utilization of the most contemporary National Surgical Quality Improvement Project data, our study has compared the outcomes of Ivor-Lewis esophagectomies with McKeown and Transhiatal esophagectomies.

What is the implication, and what should change now?
- As surgeons continue to perform esophagectomies for esophageal cancer, we must continue to evaluate outcomes data to ensure patients continue to receive the best care. This study demonstrates similar outcomes in patients who develop an anastomotic leak postoperatively, whether the anastomosis was made in the chest or in the neck.

esophagus, C15.8 Malignant neoplasm of overlapping sites of esophagus, and C15.9 Malignant neoplasm of esophagus, unspecified.

Those with metastatic disease, the American Society of Anesthesiologists Physical Status Classification (ASA Class) of five, and cases done in emergent settings were excluded from the study. Patients who underwent esophagectomy for benign pathologies were not included given the heterogenicity in outcomes in these cases. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Given the de-identified nature of the data, this study was deemed exempt by the institutional review board at Virginia Commonwealth University, and individual consent for this retrospective analysis was waived.

Patient demographics and clinical characteristics, and study outcomes

The patients were classified into two groups; patients who underwent Ivor Lewis esophagectomy [ILE, chest leak (CL)] and patients who underwent transhiatal esophagectomy (THE) or McKeown esophagectomy [ME, neck leak (NL)]. The following preoperative variables were studied: demographic and anthropomorphic information [age, gender, body mass index (BMI)], ASA class, lab values (pre-operative white blood cell (WBC) count, creatinine, and albumin), smoking (within the last year), history of comorbid conditions (diabetes mellitus, hypertension, chronic obstructive pulmonary disease (COPD), congestive heart failure, and chronic renal failure requiring dialysis). The primary surgeon specialty: thoracic surgery or general surgery were compared. Oncological data included tumor size (T), nodal involvement (N), staging, pathology (adenocarcinoma, squamous cell carcinoma, others), and positive resection margin in addition to perioperative chemotherapy and radiation were recorded.

Patients who had leak were reported by ACS-NSQIP and were classified whether interventional means were required. Postoperative adverse outcomes included: pneumonia, pulmonary embolism (PE), prolonged intubation (>48 hours), unplanned re-intubation, wound infection, urinary tract infection (UTI), acute renal failure, myocardial infarction (MI), bleeding requiring transfusion, stroke, sepsis, numeric length of stay (truncated to the nearest day), extended length of hospital stay (>6 days), and 30-day mortality. Other postoperative outcomes included: rates of discharge to a facility, reoperation, and readmission.

Within the group of patients with chest anastomoses,

patients with leak were compared to patients without leak and the same comparison was performed within the neck anastomoses patients. Separate analyses were performed to determine the predictors of each type of leak. An adjusted analysis was then performed to determine if the outcomes of patients with chest leaks differed from those with neck leaks. The outcomes investigated were pneumonia, unplanned intubation, sepsis, a leak requiring intervention, any postoperative complication, and 30-day mortality.

Statistical analyses

Continuous variables were presented as mean ± standard deviation (SD) or median and IQR and compared between the surgical groups using Wilcoxon signed-rank test, whereas categorical variables were summarized via frequency and percentage and compared using Pearson's Chi-squared or Fisher's exact test. For the adjusted analysis, multivariable linear or logistic regression models with a backward selection procedure via Akaike information criterion (AIC) were constructed to determine predictors of each type of leak and postoperative complications associated with each leak type. Covariates considered in the model building process were preoperative demographics, comorbidities, oncological characteristics, surgical approach, and surgeon specialty. Differences or odds ratios along with 95% confidence intervals were computed for each of the estimated parameters in the model. IBM SPSS Statistics for Windows, Version 27 (IBM Corp., Armonk, NY, USA) and SAS V9.4 (SAS Institute, Cary, NC, USA) were used for all analyses and statistical significance was determined if $P<0.05$.

Results

Throughout the study time period, 1,665 patients underwent esophagectomy for esophageal malignancy with 235 (14.1%) reported post-operative leak. One thousand and fourteen patients (61%) underwent ILE, of which 140 patients (13.8%) experienced a chest leak. Six hundred and fifty-one patients (39%) underwent THE or ME, of which 95 (14.6%) experienced a neck leak (*Figure 1*).

Chest leak: pre-operative characteristics, comorbidities, and cancer staging

The mean age of patients who underwent an ILE was 65.0 years old and 85.2% (n=864) of these patients were
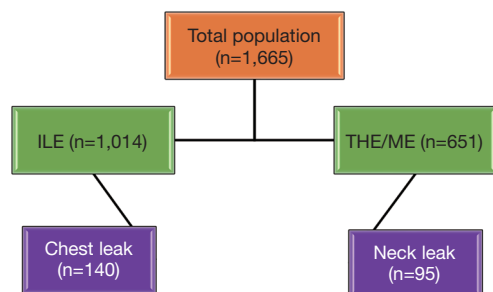
Figure 1 Study population breakdown into chest leak and neck leak cohorts. ILE, Ivor Lewis esophagectomy; THE, transhiatal esophagectomy; ME, McKeown esophagectomy.

males, 28.3% (n=287) of patients had a history of smoking and 25.9% (n=263) had >10% weight loss prior to surgery. Eight hundred and sixty-eight patients (85.6%) had an ASA classification of three or four. Patients who experienced a chest leak had significantly higher rates of diabetes and a significantly higher BMI compared to patients without leak. Oncological data are demonstrated in *Table 1*. Adenocarcinoma was the most common pathological cause of malignancy detected (n=888).

Chest leak: complications, outcomes, and independent predictors

Thirty-day postoperative complications and outcomes following ILE are presented in *Table 2*. Patients who experienced a chest leak had significantly higher rates of pneumonia, prolonged intubation >48 hours, reintubation, sepsis, cardiac arrest, and bleeding requiring transfusions than patients who did not experience a chest leak. Length of stay was significantly longer in patients who experienced a chest leak (16 *vs.* 9 days, P<0.001) and a significantly larger number of patients remained the hospital over 30 days (20.00% *vs.* 2.75%, P<0.001). There were also higher rates of reoperation, readmission, and 30-day mortality in patients who experienced a chest leak.

Neck leak: pre-operative characteristics, comorbidities, and cancer staging

The mean age of patients who underwent a THE or ME was 65.0 years old and 83.9% (n=546) of these patients were males, 24.0% (n=156) of patients had a history of smoking and 21.0% (n=137) had >10% weight loss prior to surgery. Five hundred and forty-eight (84.2%) of patients

undergoing THE or ME had an ASA classification of three or four (*Table 3*). Adenocarcinoma was the most common pathological cause of malignancy detected (n=539).

Neck leak: complications, outcomes, and independent predictors

Thirty-day postoperative complications and outcomes following THE and ME are presented in *Table 4*. Bleeding requiring transfusion, pneumonia, and reintubation were the three most common complications. Patients who experienced a neck leak had significantly higher rates of pneumonia, prolonged intubation >48 hours, reintubation, sepsis, cardiac arrest, and acute renal failure than patients who did not experience a neck leak. Length of stay was significantly longer in patients who experienced a neck leak (15 *vs.* 8 days, P<0.001). There was a significantly larger number of patients who remained the hospital over 30 days if postoperative course was complicated by a neck leak (15.79% *vs.* 3.24%, P<0.001). There were also higher rates of reoperation, readmission, and 30-day mortality in patients who experienced a neck leak.

Comparing chest leak vs. neck leak

Preoperatively, the patients had comparable comorbidities and oncological characteristics (Table S1). *Table 5* demonstrates the comparison of complications and outcomes with chest leaks and neck leaks. The only significant complication that was seen in the chest leak group when compared with the neck leak group was pneumonia (35.00% *vs.* 22.11%, P=0.034). Rates of PE, prolonged intubation, reintubation, UTI, sepsis, MI, acute renal failure, and bleeding requiring transfusion were similar between the chest leak and neck leak groups. Additionally, a significant association between the type of anastomotic leak and the management was identified, although there was no difference in reoperation rates between chest and neck leaks. The length of stay, discharge destination, mortality rate, and readmission rate were similar between the chest leak and neck leak groups.

Independent predictors and outcomes associated with anastomotic leak

An adjusted analysis looking into predictors of post esophagectomy anastomotic leak can be seen in *Table 6*. The use of chronic steroids, diabetes mellitus, hypertension,

Table 1 Comparison of demographics, preoperative clinical, and oncological characteristics among the Ivor Lewis esophagectomy group

Variables	No leak (N=874)	Leak (N=140)	P value
Age (years)	65.00 (58.00–71.00)	65.00 (59.50–71.00)	0.407
Male gender	747 (85.47)	117 (83.57)	0.557
BMI (Kg/m^2)	26.62 (23.11–30.18)	27.98 (24.82–31.94)	0.008
Pre-operative serum creatinine (mg/dL)	0.81 (0.70–0.97)	0.88 (0.75–1.03)	0.016
Pre-operative serum albumin (g/dL)	3.90 (3.60–4.20)	3.90 (3.60–4.10)	0.335
Diabetes	50 (5.72)	21 (15.00)	<0.001
Smoking (within one year)	242 (27.69)	45 (32.14)	0.277
COPD	79 (9.04)	8 (5.71)	0.192
CHF (30 days before surgery)	4 (0.46)	0 (0.00)	0.423
Hypertension (on medications)	403 (46.11)	87 (62.14)	<0.001
Weight loss (>10% last 6 months)	239 (27.35)	24 (17.14)	0.011
Steroid use for chronic condition	17 (1.95)	2 (1.43)	0.610
ASA classification			0.034
ASA Class 1 & 2	134 (15.23)	12 (8.57)	
ASA Class 3 & 4	740 (84.77)	128 (91.43)	
Total operative time (minutes)	340.00 (271.00–438.00)	396.00 (311.00–484.00)	<0.001
Surgeon specialty			0.079
Thoracic surgery	617 (70.92)	89 (63.57)	
General surgery	253 (29.08)	51 (36.43)	
T (tumor) stage			0.675
T0/Tis	84 (10.05)	16 (12.21)	
T1	199 (23.80)	36 (27.48)	
T2	168 (20.10)	21 (16.03)	
T3	375 (44.86)	57 (43.51)	
T4	10 (1.20)	1 (0.76)	
N (node) stage			0.477
N0	467 (55.93)	71 (53.38)	
N1	207 (24.79)	31 (23.31)	
N2	109 (13.05)	24 (18.05)	
N3	52 (6.23)	7 (5.26)	
Pathology			0.164
Adenocarcinoma	760 (87.06)	128 (91.43)	
Squamous cell	71 (8.13)	5 (3.57)	
Other malignancy	42 (4.81)	7 (5.00)	
Perioperative chemotherapy[†]	628 (71.85)	90 (64.29)	0.100
Perioperative radiotherapy[†]	528 (60.41)	78 (55.71)	0.404

Continuous variables are presented as median (range) and categorical variables as number (percentage). [†], within 90 days of surgery. BMI, body mass index; COPD, chronic obstructive pulmonary disease; CHF, congestive heart failure; ASA, American Society of Anesthesiologists.

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Table 2 Comparison of perioperative outcomes and complication among patients undergoing Ivor Lewis esophagectomy for malignancy

Complications	No leak (N=874)	Leak (N=140)	P value
Pneumonia	109 (12.47)	49 (35.00)	<0.001
Prolonged intubation >48 hours	65 (7.44)	38 (27.14)	<0.001
Unplanned intubation	76 (8.70)	34 (24.29)	<0.001
Urinary tract infection	17 (1.95)	3 (2.14)	0.876
Sepsis	28 (3.20)	24 (17.14)	<0.001
Cardiac arrest requiring CPR	9 (1.03)	5 (3.57)	0.017
Myocardial infarction	7 (0.80)	1 (0.71)	0.914
Acute renal failure	10 (1.14)	4 (2.86)	0.107
Bleeding requiring transfusion	87 (9.95)	24 (17.14)	0.011
Reoperation	88 (10.07)	85 (60.71)	<0.001
Length of stay (days)	9.00 (7.00–12.00)	16.00 (9.00–24.00)	<0.001
Length of stay >6 days	770 (88.10)	119 (85.00)	0.300
Length of stay >30 days	24 (2.75)	28 (20.00)	<0.001
30-day operative mortality	22 (2.52)	9 (6.43)	0.013
Discharge destination			<0.001
Death	19 (2.19)	13 (10.40)	
Home	751 (86.52)	98 (78.40)	
Other facility	98 (11.29)	14 (11.20)	
Readmission	73 (8.35)	34 (24.29)	<0.001

Continuous variables are presented as median (range) and categorical variables as number (percentage). CPR, Cardiopulmonary resuscitation.

esophageal cancer (stage N2 *vs.* N0), and operative time were all significantly associated with chest leak. When evaluating factors independently associated with neck leaks, diabetes mellitus and operative time were significant positive predictors.

Of all post-operative outcomes examined, there was significantly greater odds of a patient with an intrathoracic leak requiring an intervention (OR: 0.166, P=0.001), however, the anastomosis site did not correlate with an increase in morbidities (*Table 7*).

Discussion

Esophagectomy techniques have progressed over time, but complications are still seen in over one-third of cases (13). Anastomotic leak continues to be a feared and costly complication following esophagectomy as it has a significant impact on patient morbidity and mortality (14). Prior

studies have demonstrated an increased risk for leak with cervical anastomosis due to the need for a gastric conduit to be placed higher which can place increased tension on the anastomosis and compromise the vascular supply (15,16). Some surgeons continue to advocate for a cervical anastomosis, with knowledge of this increased risk, due to the thought that the sequelae of a cervical anastomotic leak are less severe, as the leak can drain from the cervical wound (17). We found there to be a lack of contemporary research comparing the risk factors, complications, and outcomes of chest anastomotic leaks with neck anastomotic leaks. In our study, we demonstrated a lack of statistical difference in many complications and outcomes in patients with a chest anastomotic leak compared with a neck leak.

Although chronic steroid use was not significantly associated with chest or neck leak in the preoperative characteristics of the study, after multivariate analysis, it was found to be an independent predictor of chest leaks

Table 3 Comparison of demographics, preoperative clinical and oncological characteristics among the Transhiatal and McKeown esophagectomy group

Variables	No leak (N=556)	Leak (N=95)	P value
Age (years)	66.00 (58.00–71.00)	65.00 (58.00–71.00)	0.937
Male gender	470 (84.53)	76 (80.00)	0.267
BMI (kg/m^2)	26.92 (23.86–30.45)	27.24 (24.63–32.14)	0.203
Pre-operative serum creatinine	0.83 (0.70–0.98)	0.87 (0.70–1.10)	0.260
Pre-operative serum albumin	3.80 (3.50–4.10)	3.90 (3.50–4.20)	0.900
Diabetes	26 (4.68)	16 (16.84)	<.001
Smoking (within one year)	131 (23.56)	25 (26.32)	0.561
COPD	39 (7.01)	10 (10.53)	0.231
CHF (30 days before surgery)	3 (0.54)	0 (0.00)	0.473
Hypertension (on medications)	268 (48.20)	50 (52.63)	0.425
Weight loss (>10% last 6 months)	117 (21.04)	20 (21.05)	0.998
Steroid use for chronic condition	17 (3.06)	2 (2.11)	0.610
ASA classification			0.233
ASA Class 1 & 2	91 (16.40)	11 (11.58)	
ASA Class 3 & 4	464 (83.60)	84 (88.42)	
Total operative time (minutes)	302.00 (228.50–420.00)	370.00 (243.00–445.00)	0.020
Surgeon specialty			0.426
Thoracic surgery	223 (40.11)	34 (35.79)	
General surgery	333 (59.89)	61 (64.21)	
T (tumor) stage			0.426
T0/Tis	63 (12.19)	14 (15.73)	
T1	165 (31.91)	25 (28.09)	
T2	88 (17.02)	20 (22.47)	
T3	195 (37.72)	28 (31.46)	
T4	6 (1.16)	2 (2.25)	
N (node) stage			0.520
N0	323 (61.17)	48 (53.93)	
N1	114 (21.59)	24 (26.97)	
N2	61 (11.55)	10 (11.24)	
N3	30 (5.68)	7 (7.87)	
Pathology			0.378
Adenocarcinoma	457 (82.34)	82 (88.17)	
Squamous cell	73 (13.15)	8 (8.60)	
Other malignancy	25 (4.50)	3 (8.60)	
Perioperative chemotherapy[†]	384 (69.69)	64 (68.09)	0.755
Perioperative radiotherapy[†]	343 (62.25)	58 (61.70)	0.919

Continuous variables are presented as mean ± SD and categorical variables as number (percentage). [†], within 90 days of surgery. BMI, body mass index; COPD, chronic obstructive pulmonary disease; CHF, congestive heart failure; ASA, American Society of Anesthesiologists; SD, standard deviation.

Table 4 Comparison of perioperative outcomes and complication among patients undergoing Transhiatal and McKeown esophagectomy for malignancy

Complications	No leak (N=556)	Leak (N=95)	P value
Pneumonia	61 (10.97)	21 (22.11)	0.003
Prolonged Intubation >48 hours	36 (6.47)	20 (21.05)	<0.001
Unplanned intubation	46 (8.27)	29 (30.53)	<0.001
Urinary tract infection	8 (1.44)	1 (1.05)	0.766
Sepsis	14 (2.52)	22 (23.16)	<0.001
Cardiac arrest requiring CPR	10 (1.80)	5 (5.26)	0.038
Myocardial infarction	6 (1.08)	2 (2.11)	0.402
Acute renal failure	2 (0.36)	3 (3.16)	0.004
Bleeding requiring transfusion	67 (12.05)	16 (16.84)	0.196
Reoperation	63 (11.33)	51 (53.68)	<0.001
Length of stay (days)	8.00 (7.00–11.00)	15.00 (10.00–22.00)	<0.001
Length of stay >6 days	438 (78.78)	81 (85.26)	0.146
Length of stay >30 days	18 (3.24)	15 (15.79)	<0.001
30-day operative mortality	11 (1.98)	7 (7.37)	0.003
Discharge destination			<0.001
Mortality	11 (2.01)	8 (9.09)	
Home	491 (89.76)	59 (67.05)	
Other facility	45 (8.23)	21 (23.86)	
Readmission	48 (8.71)	22 (23.16)	<0.001

Continuous variables are presented as mean ± SD and categorical variables as number (percentage). CPR, cardiopulmonary resuscitation; SD, standard deviation.

following an ILE. Chronic steroid use suppresses the immune system which has been shown to delay wound and intestinal healing (18). With this finding, surgeons may consider substituting/weaning of steroids or a cervical anastomosis in patients who cannot be weaned off steroids prior to their esophagectomy.

Additionally, hypertension was found to be a predictor of a chest anastomotic leak in patients with an intrathoracic anastomosis. Uncontrolled hypertension is known to contribute to macrovascular disease and affects the microvasculature of the gastrointestinal tract, mainly in the serosal layer. Although the submucosal layer is believed to be the most important layer in anastomotic healing, the submucosa receives its blood supply from the serosal plexus. Diseased vasculature in the proximal serosal vessels, may lead to decreased blood flow and healing of the submucosal layer in patients with hypertension (19,20).

In our study, we found multiple complications that were significantly associated with an anastomotic leak, whether in the chest or in the neck. Pulmonary complications, including pneumonia, prolonged intubation (>48 hours), and reintubation, were higher. Patients undergoing esophagectomy regardless of experiencing an anastomotic leak are at increased risk of postoperative aspiration pneumonia due to the loss of the lower esophageal sphincter and distension of the gastric conduit in the thoracic cavity (21). When comparing pneumonia occurrence between intrathoracic and cervical leaks, the was no significant difference in the odds of one type of leak versus the other. Sepsis was higher in patients who experienced leak compared to patients without leak but was not more prevalent in the chest leak group which contradicts the belief that performing a cervical anastomosis would decrease the risk of sepsis. During this investigation, we found that

Table 5 Comparison of perioperative outcomes and complications among patients who sustained leak after esophagectomy

Complications	Chest leak (N=140)	Neck leak (N=95)	P value
Pneumonia	49 (35.00)	21 (22.11)	0.034
Prolonged intubation >48 hours	38 (27.14)	20 (21.05)	0.288
Unplanned intubation	34 (24.29)	29 (30.53)	0.289
Urinary tract infection	3 (2.14)	1 (1.05)	0.526
Sepsis	24 (17.14)	22 (23.16)	0.254
Cardiac arrest requiring CPR	5 (3.57)	5 (5.26)	0.528
Myocardial infarction	1 (0.71)	2 (2.11)	0.351
Acute renal failure	4 (2.86)	3 (3.16)	0.894
Bleeding requiring transfusion	24 (17.14)	16 (16.84)	0.952
Reoperation	85 (60.71)	51 (53.68)	0.284
Management			0.021
Non-interventional means	15 (10.71)	20 (21.05)	
Interventional means	57 (40.71)	30 (31.58)	
Length of stay (days)	16.00 (9.00–24.00)	15.00 (10.00–22.00)	0.599
Length of stay >6 days	119 (85.00)	81 (85.26)	0.956
Length of stay >30 days	28 (20.00)	15 (15.79)	0.413
30-day operative mortality	9 (6.43)	7 (7.37)	0.779
Discharge destination			0.049
Expired	13 (10.40)	8 (9.09)	
Home	98 (78.40)	59 (67.05)	
Other facility	14 (11.20)	21 (23.86)	
Readmission	34 (24.29)	22 (23.16)	0.842

Continuous variables are presented as mean ± SD and categorical variables as number (percentage). CPR, cardiopulmonary resuscitation; SD, standard deviation.

Table 6 Independent predictors of esophagectomy anastomotic leak

Chest leak	OR/estimate	OR (95% CI)	P value
Chronic steroids use	2.547	1.069–6.068	0.034
Thoracic vs. general surgeon specialty	0.676	0.448–1.019	0.061
Diabetes mellitus	2.347	1.269–4.343	0.006
Hypertension on medications	2.021	1.352–3.022	<0.001
Esophageal cancer stage N2 vs. N0	1.916	1.112–3.303	0.019
Operative time (per 30 minutes increase)	1.062	1.014–1.113	0.011
Neck leak			
Pre-operative WBC	1.101	0.996–1.216	0.059
Diabetes mellitus	3.587	1.745–7.372	<0.001
Operative time (per 30 minutes increase)	1.059	1.003–1.117	0.037

OR, odds ratio; CI, confidence interval; WBC, white blood cell.

Table 7 Post-operative complications associated with anastomotic leak type (NL *vs.* CL)

Independent outcomes	OR/estimate	OR (95% CI)	P value
Pneumonia	0.563	0.298–1.064	0.077
Unplanned Intubation	1.148	0.608–1.064	0.670
Sepsis	1.917	0.948–3.877	0.070
Leak requiring intervention	0.166	0.056–0.494	0.001
Any complications	0.880	0.489–1.584	0.670
Mortality	0.884	0.273–2.870	0.838

NL, neck leak; CL, chest leak; OR, odds ratio; CI, confidence interval.

overall hospital length of stay, prolonged admission, and 30-day mortality rate were all significantly increased in patients experiencing anastomotic leaks, whether chest or neck secondary to aforementioned complications. Higher rates of sepsis, pneumonia, reintubation, and cardiac arrest have been associated with prolonged length of stay and increased mortality rates (22,23).

Through multivariable regression, we identified a lack of differences in outcomes between chest and neck leaks, although chest leaks were found to have greater odds of requiring an intervention, A possible explanation for the lack of differences between chest and neck anastomotic leaks could be due to the implementation of interventional techniques that are currently used for intrathoracic leaks. Kauer *et al.* demonstrated that covered metal stents are an effective treatment option for intrathoracic anastomotic leaks (24). Stenting across a cervical anastomosis has been studied and found to be technically challenging and resulted in the development of new problems, including migration, overgrowth, and major erosive complications (25). Although the placement of an esophageal stent across an intrathoracic anastomosis requires additional procedures to place and remove the stent, the feared complication of an uncontrolled chest leak can be controlled, further reducing morbidity and mortality. To avoid the risk of stent migration, endoluminal vacuum (EndoVAC) therapy has recently become increasingly utilized for intrathoracic anastomotic leaks following esophagectomy (26). Similar to the esophageal stent, EndoVAC therapy cannot be easily performed for cervical leaks, as EndoVAC therapy requires the use of a sponge on a tube which is redirected through the nose (26). These interventions can potentially explain the significantly greater odds of chest leaks requiring interventions while nullifying other differences in outcomes.

There were limitations to this study that were inherent to the use of the ACS-NSQIP database, and the variable collected in it. ACS-NSQIP does not track any morbidities or mortalities after 30 days, which does not allow for any long-term data to be followed. Additionally, the data is deidentified which does not allow for comparisons between surgeon and hospital volume. Also, ACS-NSQIP does not report the esophagectomy reconstruction substitute, preventing patients who had a colonic reconstruction substitute from being excluded from our analysis. Furthermore, the lack of leak severity data in the ACS-NSQIP database provides an additional limitation, as we cannot discern mild anastomotic leaks from severe anastomotic leaks. Another limitation that is included with the use of a national database is the underestimated errors in coding which can result in reporting bias. However, we elected to use ACS-NSQIP database because it is a large national database, derived from over 700 hospitals throughout the United States. This database is collected directly from patients' charts, and it is risk-adjusted (to account for differences in risk factors between patients), and case-mix-adjusted (to account for difference between hospitals) (27). These qualities made ACS-NSQIP database particularly suitable to answer our questions regarding the preoperative characteristics and post-operative complications in patients undergoing esophagectomy who experience an anastomotic leak. In addition to the relatively large sample size, an adjusted statistical analysis was utilized to assess independent predictors of post-operative leak in esophagectomy patients.

Conclusions

Post-esophagectomy chest and neck leak are associated

with higher mortality and significantly increased post-operative complications. Diabetes and operative time were independent predictors for both leaks while steroid use, hypertension and advanced disease stage predicted intrathoracic leak. Intrathoracic leaks were associated with greater odds of needing an intervention but, contrary to conventional wisdom, were not associated with higher morbidity or mortality.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-37/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-37/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-37/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Given the de-identified nature of the data, this study was deemed exempt by the institutional review board at Virginia Commonwealth University, and individual consent for this retrospective analysis was waived.

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