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Oesophagectomy with *en bloc* resection of the thoracic duct: risk factors for post-operative chyle leak and current management

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Background: Routine ligation of the thoracic duct during oesophagectomy has been reported to reduce the rate of chyle leak (CL) following oesophagectomy. This study aims to identify risk factors for developing a CL with this approach and review current management.

Methods: All patients who underwent transthoracic oesophagectomy over a 3-year period were identified from a prospectively collected database and their medical records reviewed.

Results: A total of 147 oesophagectomies were performed in the period January 2012–December 2014. Eighteen patients with anastomotic leak were excluded. Eleven (8.5%) of the remaining 129 patients developed a CL. Statistically significant predictive factors for CL were squamous cell carcinoma (6/16, 37.5% vs. 5/113, 4.4% in other tumour types, $P=0.0005$) and high total chest drain volumes on day 2 post operatively measured prior to commencing enteric feeding. Using a threshold of 600 mL on day 2, the sensitivity and specificity for predicting CL are 92% and 82% respectively. Low BMI (mean 24.1 with CL vs. 27.5 without CL) was also associated with a CL, but was not statistically significant. Neither the extent of lymphadenectomy nor the extent of lymph node involvement (N stage) were associated with CL. Six patients with a low volume CL (<600 mL/day) were successfully managed conservatively. The main thoracic duct was never the source of leakage in the 5 patients requiring re-thoracotomy. All 11 patients were successfully discharged home.

Conclusions: This study demonstrates squamous cell carcinoma remains a significant risk factor for the development of post-oesophagectomy chylothorax despite the routine ligation of the thoracic duct. In the knowledge that with this approach the main thoracic duct is never the source of CL, patients with a chest drainage of <600 mL/24 h can be successfully treated conservatively. Patients with a chest drain volume of >600 mL/24 h despite conservative management should undergo re-thoracotomy at an early stage.

Keywords: Oesophagectomy; chyle leak; risk factors

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Introduction

Chylothorax following oesophagectomy for cancer is reported to occur in 0–11% of patients (1,2). The development of a chyle leak (CL) has a detrimental impact on survival, disease recurrence, length of hospital stays and

postoperative quality of life (3–9). There are 2 arguments for routine ligation and resection of the thoracic duct. Firstly, on an oncological basis, *en bloc* resection of the thoracic duct during oesophagectomy for oesophageal cancer has been reported to increase the number of resected mediastinal lymph nodes and ensures removal of potentially involved

Table 1 Patient demographics

Demographics	Control (N=118)	Chyle leak (N=11)	P value
Median age in yrs [IQR]	65 [58–72]	67 [61–77]	0.24
M:F	96:22	7:4	0.76
ASA [IQR]	2 [2–3]	2 [2–2]	
BMI, mean (range)	27.5 (24.0–30.3)	24.1 (23.0–28.5)	0.098
CL (%)			
CL in smokers	4/25 (16.0)		0.22
CL in non-smokers	7/104 (6.7)		
CL with neoadj chemo	7/62 (11.3)		0.35
CL without neoadj chemo	4/67 (6.0)		

Neoadj chemo, neoadjuvant chemotherapy; ASA, American Society of Anesthesiologists; CL, chyle leak.

nodes adjacent to the duct (10). Secondly, to prevent development of a chylothorax, the prophylactic mass ligation of the thoracic duct has been recommended with a randomized trial of 653 patients undergoing oesophageal resection reporting a chylothorax rate of 0.3% with ligation of the duct and 2.1% in patients with duct preservation (11). However, 2 recent systematic reviews and meta-analysis have reached different conclusions (12,13). Crucitti *et al.* reported a significant reduction in chylothorax rates with prophylactic ligation of the thoracic duct while Lei *et al.* found no evidence to support such an approach. Current practice in our unit is to routinely ligate the thoracic duct and remove all surrounding tissue *en bloc*.

The aim of this study was to determine the rate of chylothorax within the unit and to identify patient, disease and surgical risk factors which predispose to CL following oesophagectomy.

Methods

All patients who underwent subtotal oesophagectomy with formation of a gastric conduit and oesophago-gastric anastomosis were included in a 3-year study period (January 2012–December 2014). Patients were identified from a prospectively collected database in a single tertiary referral centre. All operations were performed or supervised by 5 consultant specialist oesophago-gastric surgeons. Patients who underwent transhiatal and left thoraco-abdominal procedures were excluded. Patients who

developed anastomotic leak were excluded. Case notes were individually retrieved and reviewed retrospectively. All patients had placement of a feeding jejunostomy and feeding was commenced at 48 hours postoperatively at 10 mL per hour then increased incrementally over the next few days using a standard protocol.

CL was diagnosed clinically in the majority of cases by the appearance of creamy hydrophobic fluid in the chest drain in the post-operative period on commencing enteral feeding. If confirmation was required drain fluid was tested for the presence of chylomicrons or for a triglyceride level greater than 100 mg/dL.

Statistical analysis was undertaken using SPSS version 21 and STATA version 13.1. Fisher's exact test was used to determine the association between outcome and categorical variables. Continuous variables were assessed for *t*-test assumptions, equal variance between groups, normal distribution, no significant outliers, by graphing and calculating descriptive statistics. If violations were identified data were log transformed to fit a normal distribution and/or an unequal variance design used. If non-normal distribution Mann-Whitney U test was used as a non-parametric test. P values of less than 0.05 was considered statistically significant.

Ethical approval was granted by the local Caldicott Guardian Council prior to data collection. All participants gave informed consent for anonymised data to be used for clinical research purposes at the time of surgery.

Results

During the 36-month study period 147 oesophagectomies were performed. Eighteen patients with anastomotic leak were excluded. Of the remaining 129 patients, 11 developed a CL (8.5%). A total of 10 patients underwent thoracoscopic-assisted oesophagectomy with a cervical anastomosis and 119 an Ivor-Lewis 2-phase oesophagectomy with anastomosis in the upper thorax. The patient demographics are described in *Table 1*.

Patients with squamous cell carcinoma had a significantly increased risk of CL (6/16, 37.5%) when compared to patients with other tumour types (5/113, 4.4%, $P=0.0005$, *Table 2*). Patients with low BMI were more likely to develop a CL although this was not statistically significant (*Table 1*). Neither the extent of lymphadenectomy nor the extent of lymph node involvement (N stage) were associated with CL (*Table 2*).

Patients who developed a CL had both a prolonged ICU stay compared to those without a CL [8.3 days (5–16 days)

Table 2 Disease demographics

Demographics	Control (N=118) (%)	Chyle leak (N=11) (%)	P value
Tumour location			
Middle third	10/118 (8.5)	1/11 (9.1)	
Lower third	81/118 (68.6)	10/11(90.9)	–
OGJ 1	13/118 (11.0)	0/11 (0)	
OGJ 2	14/118 (11.9)	0/11 (0)	
Pathology			
Adenocarcinoma	96/118 (81.4)	5/11 (45.5)	
Squamous	10/118 (8.5)	6/11 (54.5)	0.0005
Other	12/118 (10.2)	0/11 (0)	
Staging			
Tx	1/118 (0.8)	0/11 (0)	
T1	36/118 (30.5)	0/11 (0)	
T2	14/118 (11.9)	1/11 (9.1)	–
T3	61/118 (51.7)	9/11 (81.8)	
T4	5/118 (4.2)	1/11 (9.1)	
Melanoma	1/118 (0.8)	0/11 (0)	
Nodal stage			
N0	51/118 (43.2)	4/18 (22.2)	
N1	31/118 (26.3)	5/18 (27.8)	
N2	23/118 (19.5)	5/18 (27.8)	–
N3	12/118 (10.2)	4/18 (22.2)	
Melanoma	1/118 (0.8)	0/18 (0)	
Neurovascular invasion (yes)	74/118 (62.7)	9/11 (81.8)	–
Mean No. of LNs examined, [range]	20.9 [5–50]	25 [9–40]	0.17
Mean No. of LNs positive, [range]	2.3 [0–18]	4.9 [0–23]	0.18

OGJ, oesophagogastric junction.

vs. 5.8 days (2–19 days), $P=0.01$] and a prolonged total inpatient stay [24.5 days (14–62 days) *vs.* 18.2 days (9–84 days), $P=0.01$] (*Table 3*).

On day 1 post-operatively both groups of patients had similar median chest drain volumes, median volume 715.5 mL (200–1,550 mL) in patients who subsequently developed a CL and 532.1 mL (25–1,025 mL) in patients who did not ($P=0.08$) (*Table 4*). In comparison on day 2, prior to commencing enteral feeding, patients who subsequently developed a CL had a significantly higher chest drain volume compared to those who did not, 970.5 mL (100–

2,000 mL) *vs.* 541.2 mL (125–4,225 mL), $P=0.003$. Using a chest drain volume threshold of 600 mL on day 2, prior to commencing enteral feeding or the appearance of chyle, the sensitivity and specificity for predicting a CL was 92% and 82% respectively.

Six of the 11 (54.5%) patients with a CL had a reduction in chest drainage to <600 mL/24 h after introduction of conservative measures (*Table 5*). All were successfully managed with non-operative treatment. Five patients with high volume CL (>600 mL/24 h despite conservative management) underwent re-thoracotomy. At the time of

Table 3 Procedural demographics

Demographics	Control (N=118) (%)	Chyle leak (N=11) (%)	P value
Mean total intraoperative blood loss [range], mL	560.2 [50–3,900]	399.1 [200–700]	0.30
Mean total operating time [range], min	391.2 [380–540]	367.7 [300–500]	0.91
Stapled anastomosis (yes)	74/118 (62.7)	8/11 (72.7)	0.76
Lap gastric mobilisation (yes)	14/118 (11.9)	2/11 (18.2)	–
Lap oesophageal mobilisation (yes)	10/118 (8.5)	0/11 (0)	–
Abdo phase performed by trainee (yes)	64/118 (54.2)	4/11 (36.4)	–
Chest phase performed by trainee (yes)	53/118 (44.9)	6/11 (54.5)	–
Mean ICU stay ventilated [range], days	1.8 [0–55]	0 [0–0]	0.23
Mean ICU stay unventilated [range], days	5.8 [2–19]	8.3 [5–16]	0.01
Mean duration of admission [range], days	18.2 [9–84]	24.5 [14–62]	0.01
New AF (yes)	15/118 (12.7)	–	–

AF, atrial fibrillation.

Table 4 Daily total chest drain volumes (in mL, median)

Day	Control (N=118)	Chyle leak (N=11)	P value
Day 0	532.1 [25–1,025]	715.5 [200–1,550]	0.08
Day 1	541.2 [125–4,225]	970.5 [100–2,000]	0.003
Day 2	364.0 [25–1,225]	907.3 [300–1,800]	<0.0001
Day 3	286.7 [25–825]	944.6 [150–2,275]	0.0001
Day 4	195.9 [0–700]	724.1 [235–1,575]	<0.0001
Day 5	126.1 [0–565]	627.3 [175–1,500]	<0.0001
Day 6	93.1 [0–400]	509.1 [25–1,625]	<0.0001
Day 7	69.1 [0–350]	425.0 [0–1,900]	0.0003
Day 8	53.7 [0–350]	400.0 [30–1,020]	0.0001
Day 9	38.2 [0–225]	320.0 [0–725]	<0.0001
Day 10	37.3 [0–200]	430.6 [0–925]	<0.0001

re-operation, the main thoracic duct was never the source of leakage with numerous lymphatic channels throughout the mediastinal region of dissection the source. These were controlled with insertion of sutures at multiple levels. This achieved control in 4 cases with 1 patient subsequently requiring the insertion of a pleura-peritoneal shunt.

Discussion

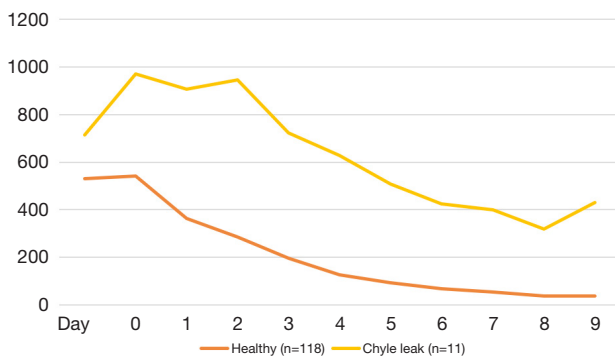
The routine practice of ligation of the thoracic duct has not

prevented the development of chylothorax post-operatively in our unit. While the leak rate is 8.5% overall, the risk of developing a leak is greatly increased in patients with squamous cell carcinoma. The reason for this is unclear but may relate to lymphatic changes occurring in squamous cell carcinoma that increase the likelihood of a CL. The knowledge that at the time of re-operation the source of the leak was never the main thoracic duct encourages a conservative approach to CL in low volume cases, taken as <600 mL/24 h in our unit. This includes initially changing from a standard enteral feed to a medium-chain triglyceride (MCT) feed and then to total parenteral nutrition (TPN) if chest drain volumes do not decrease quickly. Based on these criteria all patients selected for conservative management were successfully treated. A chest drainage of >600 mL/24 h despite appropriate conservative measures is best treated with a re-thoracotomy at an early stage. The mediastinal lymphatic channels causing the CL are often sizeable and can be successfully controlled with additional sutures in the majority of cases. Fifty mL of cream is administered via the jejunostomy just prior to surgery to aid the identification of the lymphatic channels.

In post oesophagectomy patients the daily chest drainage volume is reported to be highest on the first post-operative day and then reduces daily over time (14). This is similar in our study with patients who did not develop either a chyle or anastomotic leak (N=118) (*Figure 1*). In contrast, patients who developed a CL had higher chest drain volumes on day 1 and the volumes remained high on the

Table 5 Management of chyle leak

Patients	Chyle volume	Modality of treatment	Intraoperative findings	Resolution
1	Low	Conservative	N/A	Yes
2	Low	Conservative	N/A	Yes
3	Low	Conservative	N/A	Yes
4	Low	Conservative	N/A	Yes
5	Low	Conservative	N/A	Yes
6	Low	Conservative	N/A	Yes
7	High	Re-thoracotomy	Leaks at multiple levels	Yes
8	High	Re-thoracotomy	Leaks at multiple levels	Yes
9	High	Re-thoracotomy	Leaks at multiple levels	Yes
10	High	Re-thoracotomy	Leaks at multiple levels	Yes
11	High	Re-thoracotomy	Leaks at multiple levels. Pleuroperitoneal shunt	Yes

**Figure 1** Trends in median 24 h total chest drain volumes (mL).

second post-operative day prior to starting enteral feeding or the appearance of chyle. This should raise a high level of suspicion particularly in those with squamous cell cancer of a possible impending problem.

Previous studies have shown that patients with low BMI, squamous cell carcinoma and advanced nodal disease (high number of positive lymph nodes) predispose to a CL (15-17). The results of this study would suggest that neither the radicality of lymph node dissection nor extent of lymph node involvement increased the risk of CL.

In conclusion, this study demonstrates squamous cell carcinoma remains a significant risk factor for the development of post-oesophagectomy chylothorax despite the routine ligation of the thoracic duct. In the knowledge that with this approach the main thoracic duct is never the source of CL, patients with a chest drainage of <600 mL/24 h can be

successfully treated conservatively. Patients with a chest drain volume of >600 mL/24 h despite conservative management should under re-thoracotomy at an early stage.

Acknowledgments

None.

Footnote

Conflict of Interest: 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. Ethical approval was granted by the local Caldicott Guardian Council prior to data collection. All participants gave informed consent for anonymised data to be used for clinical research purposes at the time of surgery.

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