Diseases of the Esophagus (2023), **36**, 1–7
https://doi.org/10.1093/dote/doac047

DISEASES OF THE ESOPHAGUS

ISDE The International Society for Diseases of the Esophagus

Original Article

Clinical implications of chyle leakage following esophagectomy

Pascale J.M. Schafrat,[1,2,3,†] Sofie P.G. Henckens,[1,2,3,†] Eliza R.C. Hagens,[1,2,3] Wietse J. Eshuis,[1,2,3] Suzanne S. Gisbertz,[1,2,3] Wytze Laméris,[1,2,3] Mark I. van Berge Henegouwen,[1,2,3]

[1]*Amsterdam UMC, location University of Amsterdam, Department of Surgery, Meibergdreef 9, Amsterdam, The Netherlands,* [2]*Cancer Center Amsterdam, Cancer Treatment and Quality of Life, Amsterdam, The Netherlands, and* [3]*Amsterdam UMC, location University of Amsterdam, Department of Gastroenterology and Hepatology, Amsterdam Gastroenterology Endocrinology Metabolism, Meibergdreef 9, Amsterdam, The Netherlands*

SUMMARY. **The clinical consequences of chyle leakage following esophagectomy are underexposed. The aim of this study was to investigate the clinical implications of chyle leakage following esophagectomy. This retrospective study of prospectively collected data included patients who underwent transthoracic esophagectomy in 2017–2020. Routinely, the thoracic duct was resected en bloc as part of the mediastinal lymphadenectomy. Chyle leakage was defined as milky drain fluid for which specific treatment was initiated and/or a triglyceride level in drain fluid of ≥1.13 mmol/L, according to the Esophagectomy Complications Consensus Group (ECCG) classification. Primary endpoints were the clinical characteristics of chyle leakage (type, severity and treatment). Secondary endpoints were the impact of chyle leakage on duration of thoracic drainage and hospital stay. Chyle leakage was present in 43/314 patients (14%), of whom 24 (56%) were classified as severity A and 19 (44%) as severity B. All patients were successfully treated with either medium chain triglyceride diet (98%) or total parental nutrition (2%). There were no re-interventions for chyle leakage during initial admission, although one patient needed additional pleural drainage during readmission. Patients with chyle leakage had 3 days longer duration of thoracic drainage (bias corrected accelerated (BCa) 95%CI:0.46–0.76) and 3 days longer hospital stay (BCa 95%CI:0.07–0.36), independently of the presence of other complications. Chyle leakage is a relatively frequent complication following esophagectomy. Postoperative chyle leakage was associated with a significant longer duration of thoracic drainage and hospital admission. Nonsurgical treatment was successful in all patients with chyle leakage.**

KEY WORDS: **chylothorax, complications, esophagectomy, lymphadenectomy.**

INTRODUCTION

Esophagectomy is a technically challenging surgical procedure, causing high morbidity rates.[1,2] Sixty-six percent of patients that underwent esophagectomy for cancer in the Netherlands in 2017–2018 developed any postoperative complication, and 30% had a severe complication (Clavien Dindo ≥III).[2]

One of the common complications after esophagectomy is chyle leakage, the incidence of which widely ranges in current literature from 2 to 21%.[1,3–6] This range may be due to the use of different definitions, but also due to large variety in surgical technique and lymphadenectomy. For esophageal malignancies, leading oncological centers advocate transthoracic esophagectomy, including routine en bloc resection of the thoracic duct for adequate mediastinal lymphadenectomy.[7] However, resection of the thoracic duct is previously thought to increase the incidence of chyle leakage, as a result of injury to the main thoracic duct or its collateral branches during resection.[8,9] Therefore, not all surgeons perform resection of the thoracic duct.[4,5] Additionally, several other factors have shown to be independent risk factors for chyle leakage after esophagectomy, such as squamous cell carcinoma, neoadjuvant chemoradiotherapy, preoperative body mass index and a transthoracic approach.[4,5,10]

Persisting chyle leakage can lead to nutritional and immunological deficits and re-interventions such as pleural drainage or even reoperation.[11–13] Approximately 10% of patients with chyle leakage need to undergo a reoperation, as a result of failed nonsurgical treatment.[5] Recent studies have also shown that

Address correspondence to: Professor Dr. M. I. van Berge Henegouwen, Amsterdam UMC, location University of Amsterdam, Department of Surgery, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands. Email: m.i.vanbergehenegouwen@amsterdamumc.nl
[†]Shared first authorship: both authors contributed equally to this article

chyle leakage after esophagectomy for cancer was associated with decreased long-term survival.[14]

The short-term clinical consequences of chyle leakage have not often been quantified, resulting in underexposure of this frequent complication. The present study describes the clinical characteristics of patients with chyle leakage following esophagectomy and quantifies the impact of chyle leakage on postoperative outcomes in a large cohort of patients in a tertiary referral center.

METHODS

Most data used in this study were prospectively recorded as part of the database with all patients who underwent esophageal surgery in the Amsterdam UMC from January 2017 until December 2020. Additional data on daily production and duration of thoracic drainage, triglyceride (TG) levels, initiated treatment and duration of hospital admission were retrospectively collected. Patients were given the opportunity to opt out if they did not agree with the usage of their medical data for research. The STROBE guidelines were used to ensure correct reporting of study results.[15]

Patients

Patients were included if they underwent open, hybrid or minimally invasive transthoracic esophagectomy for adenocarcinoma, squamous cell carcinoma, high grade dysplasia of the esophagus, or for other conditions (inconclusive preoperative histology or neuroendocrine tumors). Patients were excluded if nonelective surgery, esophagectomy via thoracophrenicolaparotomy or transhiatal approach was performed.

Surgery

A dedicated upper gastrointestinal surgical team performed all procedures. Routinely, the thoracic duct was resected en bloc as part of the mediastinal lymphadenectomy. Mediastinal dissection was done using a Maryland dissector, diathermic hook and LigaSure Blunt Tip laparoscopic sealer (Medtronic). Approximately 2–3 cm above the diaphragm and at the level of the arc of the azygos vein, the thoracic duct was double clipped using metal clips and transected. At the end of the procedure, a right-sided silicone 27French chest tube was placed in the right pleural cavity. In patients undergoing salvage procedures, an additional chest tube was placed in the left pleural cavity.

Postoperative protocol

All patients received a feeding jejunostomy and enteral tube feeding was routinely started at 6:00 AM on the first postoperative day (POD). Several hours postoperatively, a chest radiograph was routinely performed to detect persistent pneumothorax and evaluate nasogastric tube position. In the absence of a pneumothorax, the drain was immediately put on water seal without active suction. On daily basis, the thoracic drain fluid output was evaluated.

Chyle leakage definition and treatment

In Supplementary A, the adhered protocol on diagnostics and treatment of chyle leakage after esophagectomy with gastric conduit reconstruction is described. In case of suspected chyle leakage (either high volume [>400 mL/24 hours] output of the thoracic drain or milky aspect of the drain fluid), TG-levels were measured. According to the Esophagectomy Complications Consensus Group (ECCG), chyle leakage was defined as a milky aspect of drain fluid for which medium chain triglyceride (MCT) diet or total parenteral nutrition (TPN) was initiated, or a TG-level in the drain fluid of ≥100 mg/dL (equals ≥1.13 mmol/L).[1,16] Chyle leaks were classified as type 1 when treated by MCT diet, as type 2 when TPN was required and as type 3 when interventional or surgical treatment was required. Severity level A was defined as an output <1 L/day and severity level B as an output >1 L/day.[16] Patients with chyle leakage were initially treated with an MCT diet, which was continued until 2 weeks after thoracic drain removal. If thoracic drain production did not reduce >50% in response to MCT diet after 48 hours, TPN was initiated. In case of persistent high thoracic drain production during TPN (<50% decrease in thoracic drain production after 48–72 hours), re-intervention or surgical treatment was indicated. The thoracic drain was removed if production had a clear aspect and was less than 200 mL/24 hours in patients with and without chyle leakage. TG-level measurement was not repeated in drain fluid before drain removal.

Outcomes

The primary endpoints were the clinical characteristics of chyle leakage after esophagectomy (type, severity, daily thoracic drain production, TG-level and initiated treatment). The secondary endpoints were the impact of chyle leakage on the duration of thoracic drainage and the duration of hospital stay.

Statistical analysis

Variables were presented as number (percentage), mean (standard deviation) and median (interquartile range) when appropriate. Categorical variables were compared with Chi^2 test or Fisher's Exact test. Continuous variables were compared using independent sample T-test (normal distribution) or Mann–Whitney U test (non-normally distribution).

Linear regression analysis was performed to investigate the effect of the presence of chyle leakage on the duration of thoracic drainage and hospital stay. Dependent variables duration of thoracic drainage and hospital stay did not meet the assumptions for

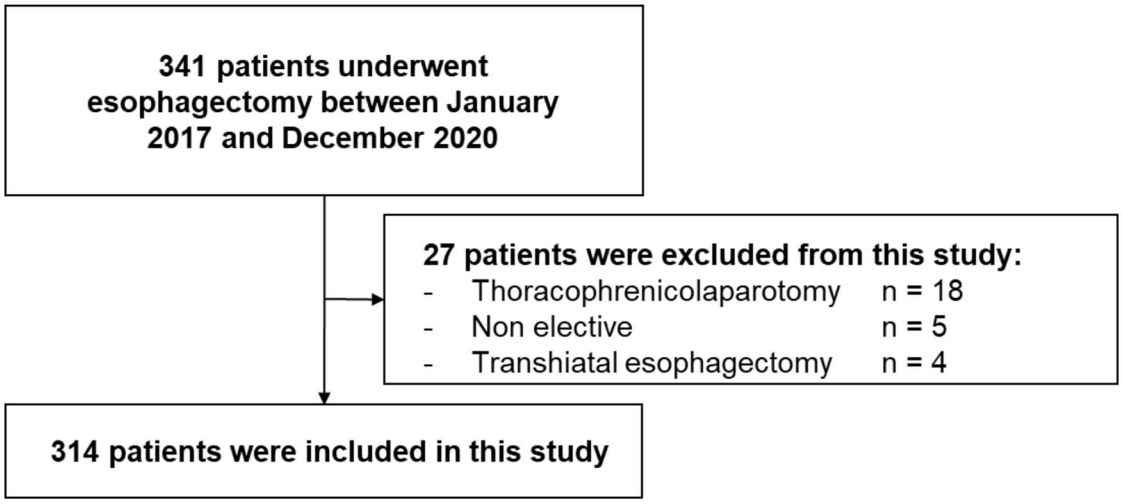

Fig. 1 Study flowchart.

linear regression as they were non-normally distributed and were therefore logarithmically transformed using the natural log (ln). Subsequently, transformed regression coefficients were used to calculate the natural logarithm (ln) of the dependent variables for patients with and without chyle leakage, using the following regression equation: ln(Y) = a + bX. Into this equation, Y is the logarithmically transformed dependent variable, a is the constant coefficient (Intercept), b is the coefficient associated with the independent variable (presence of chyle leakage) and X is the independent variable (presence of chyle leakage: absent = 0, present = 1). (exp(Y)) was subsequently interpreted since exponentiation is the inversion of lgarithm function. Because both dependent variables did not meet the assumption of homoscedasticity, *P*-values and 95% confidence intervals (CI) were calculated based on 1000 bootstrap samples.[17] Results of the linear regression analyses were reported as B (regression coefficient) with corresponding bias corrected accelerated (BCa) and 95%CI. Possible predictors of the duration of thoracic drainage and hospital stay that were included in the models were sex, age, BMI, ASA score, histology, surgical approach and the presence of postoperative pneumonia, anastomotic leakage and atrial fibrillation. Potential predictors were excluded by backward selection until only significant variables remained in the model.[18,19] All statistical analyses were performed using IBM SPSS Statistics 26.0 (SPSS Inc., Chicago, IL). For all analyses, a *P*-value <0.05 was considered to be statistically significant.

RESULTS

Patients

In total, 341 patients underwent esophagectomy between January 2017 and December 2020. A total of 27 patients were excluded because they did not meet the inclusion criteria, leaving 314 patients eligible for inclusion (Fig. 1). The majority was male (79%) and mean age at surgery was 65 (SD 9.3). Most patients had an adenocarcinoma (77%), located at the distal esophagus (66%). Nine patients (3%) underwent open esophagectomy, 300 patients (96%) underwent minimally invasive esophagectomy and five patients (2%) underwent hybrid esophagectomy (Table 1). Median lymph node yield was 37 (IQR: 30–45). For variables in our analyses, missing data percentages varied from 0 to 3%.

Patients with chyle leakage

A total of 43 patients out of 341 (14%) developed postoperative chyle leakage. Of these 43 patients, 42 had a type 1 leak (98%) and one patient had a type 2 leak (2%). Severity of the leak was grade A in 24 patients (56%) and grade B in 19 patients (44%). There were no significant differences between both groups. The median day at which chyle leakage was diagnosed was POD 3 (IQR 2–4).

From POD 1–3, and POD 5 and 6, the thoracic drain output was significantly higher in patients with chyle leakage, compared with patients without (Table 2). The difference in thoracic drain output did not reach significance on POD 4, although the output was 57 mL higher in patients with chyle leakage compared with patients without chyle leakage during these 24 hours (*P* = 0.052). Median level of TGs measured in drain fluid in 41 patients with chyle leakage (not determined in two) was 2.1 mmol/L (IQR 1.4–3.2).

Chyle leakage was successfully treated with an MCT diet in 42 of 43 patients (98%). One patient was successfully treated with TPN (2%). None of these patients needed additional pleural drainage or another re-intervention for chyle leakage during initial admission. In only one patient, chyle leakage was diagnosed later in the postoperative period and after thoracic drain removal. This patient needed pleural drainage during readmission 40 days after surgery.

Table 1 Baseline characteristics

	All patients ***N*** **= 314 (100%)** ***N*** **(%)**	**Without chyle leakage** ***N*** **= 271 (86%)** ***N*** **(%)**	**With chyle leakage** ***N*** **= 43 (14%)** ***N*** **(%)**	***P*-value**
Gender				0.419
Male	249 (79)	217 (80)	32 (74)	
Age *(mean, SD)*	64.6 (9.3)	64.4 (9.4)	66.1 (8.5)	0.286
BMI *(mean, SD)*	25.6 (4.3)	25.6 (4.2)	25.7 (4.9)	0.841
ASA score				0.355
I	39 (12)	36 (13)	3 (7)	
II	195 (62)	169 (63)	26 (61)	
III	80 (26)	66 (24)	14 (33)	
WHO performance status				0.555
0	223 (71)	193 (71)	30 (70)	
I	74 (24)	64 (24)	10 (23)	
II	6 (2)	6 (2)	-	
III	3 (1)	2 (1)	1 (2)	
Missing	*8 (3)*	*6 (2)*	*2 (5)*	
cT-stage				0.466
T0	1 (0)	1 (0)	-	
T1	16 (10)	15 (6)	1 (2)	
T2	49 (16)	43 (16)	6 (14)	
T3	236 (75)	202 (75)	34 (79)	
T4	2 (1)	1 (0)	1 (2)	
Missing	*10 (3)*	*9 (3)*	*1 (2)*	
cN-stage				0.157
N0	111 (35)	95 (35)	16 (37)	
N1	119 (38)	108 (40)	11 (26)	
N2	72 (23)	57 (21)	15 (35)	
N3	3 (1)	3 (1)	-	
Missing	*9 (3)*	*8 (3)*	*1 (2)*	
Tumor localization				0.958
Proximal	6 (2)	5 (2)	1 (2)	
Mid	42 (13)	37 (14)	5 (12)	
Distal	206 (66)	179 (66)	27 (63)	
GEJ	53 (17)	44 (16)	9 (21)	
Cardia (Siewert type III)	7 (2)	6 (2)	1 (2)	
Preoperative histology				0.919
Adenocarcinoma	241 (77)	208 (77)	33 (77)	
Squamous cell carcinoma	64 (20)	54 (20)	10 (23)	
High-grade dysplasia	4 (1)	4 (2)	-	
Other*	5 (2)	5 (2)	-	
Neoadjuvant/previous therapy				0.732
None	23 (7)	20 (7)	3 (7)	
Chemoradiotherapy	262 (83)	227 (84)	35 (81)	
Chemotherapy	25 (8)	20 (7)	5 (12)	
Radiotherapy	1 (0)	1 (0)	-	
Definite chemoradiotherapy	2 (1)	2 (1)	-	
Missing	*1 (0)*	*1 (0)*	-	
Surgical procedure				0.549
Minimal invasive	300 (96)	259 (96)	41 (95)	
Open	9 (3)	7 (3)	2 (5)	
Hybrid	5 (2)	5 (2)	-	
Reconstruction type				0.447
Gastric conduit	310 (99)	268 (99)	42 (98)	
Colon interposition	1 (0)	1 (0)	-	
No reconstruction	3 (1)	2 (1)	1 (2)	
Location anastomosis				
No anastomosis	2 (1)	2 (1)	-	0.053
Cervical	51 (16)	49 (18)	2 (5)	
Intrathoracic	260 (83)	220 (81)	40 (93)	
Missing	*1 (0)*	-	*1 (2)*	
Lymph node yield *(median, IQR)*	37 (30–45)	37 (29–45)	38 (32–45)	0.478

SD = standard deviation, CI = confidence interval, ASA = American society of anesthesiologists, WHO = world health organization, GEJ = gastro esophageal junction, * = other histology included inconclusive preoperative histology or neuroendocrine tumors.

Clinical implications of chyle leakage

Patients with chyle leakage did not have more other postoperative complications compared with patients without chyle leakage (pneumonia 23% vs. 17%, $P = 0.286$; anastomotic leakage 16% vs. 12%, $P = 0.409$; atrial fibrillation 16% vs. 17%, $P = 0.864$ for patients with and without chyle leakage, respectively).

The median duration of thoracic drainage was 4 days (IQR: 2–6) for patients without chyle leakage,

Table 2 Postoperative baseline characteristics

	All patients *N* **= 314 (100%)** *N* **(%)**	**Without chyle leakage** *N* **= 271 (86%)** *N* **(%)**	**With chyle leakage** *N* **= 43 (14%)** *N* **(%)**	***P*-value**
Daily thoracic drain production in mL *(median, IQR)*				
Day 1	200 (75–338)	180 (70–315)	295 (121–438)	**0.008**
Day 2	323 (169–550)	300 (155–530)	540 (290–900)	**<0.001**
Day 3	410 (250–640)	383 (235–603)	570 (380–940)	**0.002**
Day 4	400 (220–600)	393 (210–555)	450 (300–815)	0.052
Day 5	370 (255–528)	350 (200–515)	460 (310–710)	**0.015**
Day 6	320 (180–491)	293 (160–453)	400 (250–600)	**0.042**
Day 7	410 (170–570)	395 (170–595)	445 (193–546)	0.875
Hospital admission in days *(median, IQR)*	11 (8–16)	10 (8–15)	14 (9–20)	**0.007**
Thoracic drainage in days *(median, IQR)*	5 (3–7)	4 (2–6)	7 (6–11)	**<0.001**

IQR = inter quartile range

Table 3 Influence of chyle leakage on duration of thoracic drainage

	All patients (*n* = 313*)		
	B^	**BCa 95%CI**	***P*-value**
Univariable analysis			
Intercept	1.410	1.344–1.472	**<0.001**
Chyle leakage			
No	*Reference*		
Yes	0.622	0.471–0.778	**<0.001**
Multivariable analysis**			
Intercept	1.376	1.307–1.445	**<0.001**
Chyle leakage			
No	*Reference*		
Yes	0.609	0.456–0.759	**<0.001**
Anastomotic leakage			
No	*Reference*		
Yes	0.284	0.080–0.480	**0.008**

B = regression coefficient, BCa = bias corrected accelerated, CI = confidence interval, * = duration of thoracic drainage was unknown for one patient, ** = corrected for the presence of anastomotic leakage, ^= the dependent variable was logarithmically transformed using the natural log (ln). Logarithmically transformed regression coefficients from the table were used to calculate the natural logarithm (ln) of the duration of thoracic drainage for patients with and without chyle leakage, using the following regression equation: $\ln(Y) = a + bX$. Into this equation, Y is the logarithmically transformed dependent variable (duration of drainage), a is the constant coefficient (Intercept), b is the coefficient associated with the independent variable (presence of chyle leakage) and X is the independent variable (presence of chyle leakage: absent = 0, present = 1). (exp(Y)) was subsequently interpreted since exponentiation is the inversion of logarithm function.

Table 4 Influence of chyle leakage on duration of hospital admission

	All patients (*n* = 314)		
	B**	**BCa 95%CI**	***P*-value**
Univariable analysis			
Intercept	2.507	2.444–2.569	**<0.001**
Chyle leakage			
No	*Reference*		
Yes	0.296	0.079–0.537	**0.011**
Multivariable analysis*			
Intercept	2.320	2.270–2.373	**0.001**
Chyle leakage			
No	*Reference*		
Yes	0.224	0.071–0.360	**0.004**
Pneumonia			
No	*Reference*		
Yes	0.392	0.220–0.565	**0.001**
Anastomotic leakage			
No	*Reference*		
Yes	1.039	0.798–1.259	**0.001**

B = regression coefficient, BCa = bias corrected accelerated, CI = confidence interval, * = corrected for the presence of postoperative pneumonia and anastomotic leakage, ** = the dependent variable was logarithmically transformed using the natural log (ln). Logarithmically transformed regression coefficients from the table were used to calculate the natural logarithm (ln) of the duration of hospital admission for patients with and without chyle leakage, using the following regression equation: $\ln(Y) = a + bX$. Into this equation, Y is the logarithmically transformed dependent variable (duration of hospital admission), a is the constant coefficient (Intercept), b is the coefficient associated with the independent variable (presence of chyle leakage) and X is the independent variable (presence of chyle leakage: absent = 0, present = 1). (exp(Y)) was subsequently interpreted since exponentiation is the inversion of logarithm function.

compared with 7 days (IQR: 6–11) for patients with chyle leakage ($P < 0.001$). When adjusted for the presence of anastomotic leakage, chyle leakage was associated with a 3 day (BCa 95% CI 0.456–0.759, $P < 0.001$) longer duration of thoracic drainage compared with having no chyle leakage. The results of both uni- and multivariable linear regression analyses regarding thoracic drainage are presented in Table 3.

Median hospital stay was 10 days (IQR: 8–15) for patients without chyle leakage versus 14 days (IQR: 9–20) for patients with chyle leakage ($P = 0.007$). The presence of chyle leakage was associated with an increase in hospital stay of 3 days (BCa 95% CI 0.071–0.360, $P = 0.004$), independently of the presence of pneumonia and anastomotic leakage (Table 4).

DISCUSSION

This study investigated the clinical characteristics of patients with chyle leakage after esophagectomy and the impact of chyle leakage on short-term postoperative outcomes. Despite the relatively high incidence of chyle leakage of 14%, and in contrast to

previous studies, the severity of the chyle leakages was mild, with almost only type 1 leakages in this series. The success rate of nonsurgical management of chyle leakage was 100%.

The incidence of chyle leakage was comparable high (21%) in a paper that also adhered to the strict ECCG definition for chyle leakage.[1,5] In other papers, the incidence is lower (range 2–8%). However, these papers used different definitions and diagnosed chyle leakage only in case of elevated TG-levels (>89/mg/dL i.e. 1 mmol/L) in intrathoracic fluid, not in case of milky aspect of drain fluid.[3,4,6] The incidence of 14% in this tertiary referral center over the past 4 years is furthermore likely to be explained by the fact that the majority of patients routinely underwent transthoracic esophagectomy after neoadjuvant chemoradiotherapy, both previously found as independent risk factors for chyle leakage after esophagectomy.[4,5,20] Transthoracic esophagectomy was routinely performed combined with extensive paratracheal lymphadenectomy and dissection and transection of the thoracic duct, which is known to be associated with damage to collateral lymphatic vessels.[21] Besides, enteral tube feeding was routinely started POD 1, facilitating a higher caloric and therewith fat intake, which may expose small chyle leakages that might not be detected in case of direct oral feeding. The NUTRIENT-II trial indeed showed that tube feeding leads to a significant higher median intake of calories in the first days after surgery and a higher incidence of chyle leakage, when compared with direct oral feeding (10.4% vs. 1.5%).[22]

No surgical interventions were performed for chyle leakage during initial admission, although one patient required pleural drainage during readmission. This is in contrast with previous studies, in which the reoperation rates vary from 4 to 32%.[5,6,23] The authors expect this to be due to the performed surgical techniques and severity of leakages in this series. The thoracic duct was routinely resected after selective clipping at the level of the arc of the azygos vein and several centimeters above the diaphragm. This approach probably prevented main duct leakage and chyle leakages were more likely to originate from collateral lymphatic branches rather than the main thoracic duct, requiring TPN or surgical treatment less frequently.[24] As recommended in the guidelines, a step-up treatment strategy was adhered for the treatment of chyle leakage. Primarily MCT diet was initiated in all patients, independently of the volume of leakage. This differs from the approach described in other papers, in which high volume leakages were initially treated with TPN for 7 days.[5] Our preference for restraint with initial treatment with TPN is substantiated by the fact that MCT diet can, in contrast to TPN, be continued at home, leading to a less prolonged length of stay for the patient.

Despite successful nonsurgical treatment in all patients, chyle leakage had a significant effect on the duration of thoracic drainage and hospital stay. Independent of the presence of other complications, duration of thoracic drainage and hospital stay was 3 days longer for patients with chyle leakage. These results confirm the findings of previous literature.[5] The consequences of this increase in duration of thoracic drainage and hospital admission are substantial. Patients experience pain from a thoracic drain, which can affect postoperative mobilization and recovery. A study by Goense *et al*.[25] found chyle leakage to be independently associated with an increase in hospital stay, associated with an increased cost of around €6.000. Although a cost analysis was beyond the scope of this study, it seems clear that chyle leakage after esophagectomy results in increased utilization of resources and increasing costs, increasing the burden on the health care system.

Some limitations to this study should be noted. First, this study was based on data from a single, high volume institution, which may limit the generalizability of the results. The number of patients with chyle leakage available for analysis was too small for reliable analysis of predictive factors for postoperative chyle leakage. Although our study population seems comparable to the general esophagectomy population, the success rate of conservative treatment of chyle leakage differs from previous literature. It would be helpful for the interpretation of the current results if more large-volume esophagectomy centers present recent data on surgical technique in relation to the occurrence and treatment of chyle leakage. It is unlikely that the current results are incidentally positive, as they reflect clinical practice over a 4-year period. Secondly, in addition to the prospective collected data from the local upper gastrointestinal surgery database, additional variables were retrospectively extracted from electronic patient files. Despite partly retrospective data collection, missing data were limited to max. 3%.

Future research should focus on the prevention and early detection of chyle leakage, leading to limited thoracic drainage and hospital admission, better clinical outcomes and longer survival.[14,26] Intraoperative detection of chyle leakage is difficult, since patients are starved before and during surgery, leading to limited flow of chyle in the lymphatic vessels. There are some indications that intraoperative administration of high TG containing fluids such as oral cream or oil is successful in the stimulation of chyle flow, and therefore detection of chyle leakage during esophagectomy.[27] Also the use of intraoperative fluorescent lymphography might be helpful in visualizing the thoracic duct and its branches.[28]

In conclusion, chyle leakage is a frequently occurring complication after esophagectomy with resection of the thoracic duct and extensive lymphadenectomy, with substantial clinical consequences (increased

postoperative drainage and hospital stay). Even though all leakages in this series could be successfully managed by nonsurgical treatment, chyle leakage impedes postoperative recovery. Future research should therefore focus on reducing the incidence of chyle leakage after esophageal surgery.

SUPPLEMENTARY DATA

Supplementary data mentioned in the text are available to subscribers in DOTESO online.

ACKNOWLEDGMENTS

The authors would like to express their gratitude to Dr. Susan van Dieren (Epidemiologist, Amsterdam UMC, location University of Amsterdam) for her assistance with statistical analysis.

DISCLOSURES

M.I.B.H. is consultant for Mylan, Johnson & Johnson, Alesi Surgical, BBraun and Medtronic, and received research/travel grants from Olympus and Stryker. None of these companies were involved in the design, conduct, or analysis of this study. For the remaining authors none were declared.

CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

References

1. Low D E, Kuppusamy M K, Alderson D *et al.* Benchmarking complications associated with esophagectomy. Ann Surg 2019; 269(2): 291–8.
2. Voeten D M, Busweiler L A D, van der Werf L R *et al.* Outcomes of Esophagogastric cancer surgery during eight years of surgical auditing by the Dutch upper gastrointestinal cancer audit (DUCA). Ann Surg 2021; 274(5): 866–73.
3. Nederlof N, Slaman A E, van Hagen P *et al.* Using the comprehensive complication index to assess the impact of neoadjuvant Chemoradiotherapy on complication severity after Esophagectomy for cancer. Ann Surg Oncol 2016; 23(12): 3964–71.
4. Kranzfelder M, Gertler R, Hapfelmeier A, Friess H, Feith M. Chylothorax after esophagectomy for cancer: impact of the surgical approach and neoadjuvant treatment: systematic review and institutional analysis. Surg Endosc 2013; 27(10): 3530–8.
5. Weijs T J, Ruurda J P, Broekhuizen M E, Bracco Gartner T C L, van Hillegersberg R. Outcome of a step-up treatment strategy for Chyle leakage after Esophagectomy. Ann Thorac Surg 2017; 104(2): 477–84.
6. Miao L, Zhang Y, Hu H *et al.* Incidence and management of chylothorax after esophagectomy. Thorac Cancer 2015; 6(3): 354–8.
7. Udagawa H, Ueno M, Shinohara H *et al.* Should lymph nodes along the thoracic duct be dissected routinely in radical esophagectomy? Esophagus 2014; 11(3): 204–10.
8. Oshikiri T, Takiguchi G, Miura S *et al.* Thoracic duct resection during Esophagectomy does not contribute to improved prognosis in Esophageal squamous cell carcinoma: a propensity score matched-cohort study. Ann Surg Oncol 2019; 26(12): 4053–61.
9. van Rijswijk A S, Hagens E R C, van der Peet D L, van Berge Henegouwen M I, Gisbertz S S. Differences in Esophageal cancer surgery in terms of surgical approach and extent of lymphadenectomy: findings of an international survey. Ann Surg Oncol 2019; 26(7): 2063–72.
10. Mertens A C, Kalff M C, Eshuis W J, Van Gulik T M, Van Berge Henegouwen M I, Gisbertz S S. Transthoracic versus Transhiatal Esophagectomy for Esophageal cancer: a Nationwide propensity score-matched cohort analysis. Ann Surg Oncol 2021; 28(1): 175–83.
11. Lagarde S M, Omloo J M T, De Jong K, Busch O R C, Obertop H, Van Lanschot J J B. Incidence and management of chyle leakage after esophagectomy. Ann Thorac Surg 2005; 80(2): 449–54.
12. Shah R, Luketich J, Schuchert M *et al.* Postesophagectomy chylothorax: incidence, risk factors and outcomes. Ann Thorac Surg 2012; 93(3): 897–904.
13. Nair S K, Petko M, Hayward M P. Aetiology and management of chylothorax in adults. Eur J Cardio-thoracic Surg 2007; 32(2): 362–9.
14. Hagens E R C, Feenstra M L, Eshuis W J *et al.* Conditional survival after neoadjuvant chemoradiotherapy and surgery for oesophageal cancer. Br J Surg 2020; 107(8): 1053–61.
15. Pocock SJ, Vandenbroucke JP. Strengthening the reporting of observational studies in epidemiology (StroBE) statement: guidelines for reporting observational studies. www.strobe-statement.org.
16. Low D E, Alderson D, Cecconello I *et al.* International consensus on standardization of data collection for complications associated with esophagectomy: Esophagectomy Complications Consensus Group (ECCG). Ann Surg 2015; 262(2): 286–94.
17. Field A. Discovering Statistics Using IBM SPSS Statistics. 2000.
18. Maldonado G. Simulation study of confounder-selection strategies. Am J Epidemiol 1993; 138(11): 923–36.
19. Vittinghoff E, Glidden D V, Shiboski S C, McCulloch C E. Regression Methods in biostatistics. Linear, Logistic, Survival, and Repeated Measures Models 2004.
20. Lagarde S M, Omloo J M T, Ubbink D T, Busch O R C, Obertop H, van Lanschot J J B. Predictive factors associated with prolonged chest drain production after esophagectomy. Dis Esophagus 2007; 20(1): 24–8.
21. Kutlu C A, Sayar A, Olgac G *et al.* Chylothorax: a complication following lung resection in patients with NSCLC - Chylothorax following lung resection. Thorac Cardiovasc Surg 2003; 51(6): 342–5.
22. Berkelmans G H K, Fransen L F C, Dolmans-Zwartjes A C P *et al.* Direct oral feeding following minimally invasive Esophagectomy (NUTRIENT II trial): an international, Multicenter. Open-label Randomized Controlled Trial Ann Surg 2020; 271(1): 41–7.
23. Lin Y, Li Z, Li G *et al.* Selective En masse ligation of the thoracic duct to prevent Chyle leak after Esophagectomy. Ann Thorac Surg 2017; 103(6): 1802–7.
24. Defize I L, Schurink B, Weijs T J *et al.* The anatomy of the thoracic duct at the level of the diaphragm: a cadaver study. Ann Anat 2018; 217: 47–53.
25. Goense L, van Dijk W A, Govaert J A, van Rossum P S N, Ruurda J P, van Hillegersberg R. Hospital costs of complications after esophagectomy for cancer. Eur J Surg Oncol 2017; 43(4): 696–702.
26. Baba Y, Yoshida N, Shigaki H *et al.* Prognostic impact of postoperative complications in 502 patients with surgically resected Esophageal squamous cell carcinoma: a retrospective single-institution study. Ann Surg 2016; 264(2): 305–11.
27. Shen Y, Feng M, Khan M A, Wang H, Tan L, Wang Q. A simple method minimizes chylothorax after minimally invasive esophagectomy. J Am Coll Surg 2014; 218(1): 108–12.
28. Vecchiato M, Martino A, Sponza M *et al.* Thoracic duct identification with indocyanine green fluorescence during minimally invasive esophagectomy with patient in prone position. Dis Esophagus 2020; 33(12): 1–6.