Original Article

Influence of body composition measures on chyle leak after oesophagectomy

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Background: Chyle leak (CL) is an infrequent but potentially serious complication of oesophagectomy. Sarcopenia is an increasingly recognised prognostic factor in oesophageal cancer surgery. The aim of this study was to identify the influence of body composition measures on CL following oesophagectomy.

Methods: Patients who developed CL after oesophagectomy between January 2006–December 2020 were identified retrospectively from a prospectively maintained dataset. A control group of patients undergoing oesophagectomy, who did not experience chyle leak during the same time period, was also collected. Relationships between CL and demographics, operative factors and body composition measures were investigated as primary outcomes. Risk factors for severe CL were evaluated as a secondary outcome.

Results: There were 26 patients who developed a CL following an oesophagectomy. On univariate analysis, preoperative body mass index (BMI) (P=0.001), subcutaneous fat index (P=0.001) and total fat index (P=0.004) were significantly associated with CL. On multivariate analysis, a lower preoperative subcutaneous fat index was a significant independent predictor of CL (P=0.003). Sarcopenia, as an overall measure, was not found to be a significant predictor of developing CLs. No significant predictors of severe CL were identified.

Conclusions: A reduced preoperative BMI and body fat composition are risk factors for CL after oesophagectomy. Sarcopenia does not predict either the occurrence or severity of CL. This presents potentially modifiable risk factors for CL after oesophagectomy and emphasises the importance of physiological and nutritional optimisation before oesophagectomy.

Keywords: Chyle leak (CL); sarcopenia; body mass index (BMI); oesophagectomy

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Introduction

With a reported incidence between 1.1–3.8%, chyle leak (CL) is an infrequent but potentially serious complication of oesophagectomy (1-5). Whilst mild CL may be managed conservatively, surgical management is often required (5,6), for example in high output leaks (7). It is therefore desirable to identify any preoperative factors that increase the risk of CL after oesophagectomy, to improve individualised preoperative counselling and risk stratification.

Preoperative nutritional status has been shown to be significantly related to risk of complications after oesophagectomy (8-10). Given that nutritional status can be accurately assessed using preoperative cross-sectional imaging (11), body composition measures such as sarcopenia are increasingly being used as preoperative risk assessment tools for major surgery such as oesophagectomy (12-15).

However, the interaction between CL and body composition is not known. Therefore, the aim of this study was to identify the influence of body composition and related factors on CL following oesophagectomy. We present the following article in accordance with the STARD reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-21-1580/rc).

Methods

A prospectively collected and maintained departmental database of oesophageal cancer resections between January 2006–December 2020 was reviewed retrospectively to identify patients who developed CL after oesophageal cancer resection. A control group of patients who underwent oesophagectomy, who did not experience CL, for cancer during the same time period was also collected from the same departmental database to allow for investigation of risk factors. Oesophagectomy was performed in accordance with the operating surgeon's expertise and case. If the thoracic duct is visualized intraoperatively it was ligated with ties or clips.

Relationships between CL and demographics, operative factors and body composition measures were investigated as primary outcomes. Risk factors for severe CL, defined as need for reintervention or greater than 1 litre of output per day, were evaluated as a secondary outcome.

Sarcopenia and myosteatosis evaluation

Computed tomography (CT) scan has proven to be accurate for measuring human body composition (11). Regional muscle tissue was measured on CT scans performed on diagnosis as part of the staging process preoperatively.

Preoperative CT scans, that were previously used in the staging process, were reviewed to evaluate body composition measures such as sarcopenia and myosteatosis. A transverse CT image from L3 was assessed from each scan. Images were analysed with SliceOmatic V4.3 software (Tomovision, Montreal, QB, Canada), which enables specific tissue demarcation using previously reported Hounsfield unit (HU) thresholds (11). Skeletal muscle is identified and quantified by HU thresholds of −29 to +150. Muscles in the L3 region encompass psoas, erector spinae, quadratus lumborum, transversus abdominus, external and internal obliques, and rectus abdominus. The following HU thresholds were used for adipose tissues: −190 to −30 for subcutaneous and intermuscular adipose tissues and −150 to −50 for visceral adipose tissues (16). Cross-sectional areas (cm^2) were automatically computed by summing tissue pixels and multiplying by pixel surface area. Cross-sectional area of muscle and adipose tissue was normalized for stature (cm^2/m^2) as reported elsewhere (17), and this value is referred to as the L3 (Skeletal Muscle Index) SMI. Cut-offs for sarcopenia were based on a CT-based study in patients with solid tumours using optimal stratification, a statistical method similar to receiver operator curve analysis, to solve specific threshold values for L3 SMI in relation to an outcome (death) (L3 SMI: ≤ 41 cm^2/m^2 for women and ≤ 53 cm^2/m^2 for men with BMI ≥ 25 and ≤ 43 cm^2/m^2 in patients with BMI <25) (16). Muscle attenuation indirectly measures fat infiltration in muscles. Mean muscle attenuation in HU was reported for the entire muscle area at the third lumbar vertebra. We also, used previous cut-off values for muscle attenuation previously associated with mortality, specifically <41HU in patients with a BMI up to 24.9, and <33 in those with a BMI ≥ 25 (16). Sarcopenic obesity was defined as those patients with concurrent sarcopenia and overweight or obesity (BMI >25 kg/m^2).

Statistical analyses

Comparisons were initially made between the CL and no CL groups. Univariate analyses were performed using Chi-Squared test for categorical variables and Mann-Whitney U test for continuous variables. Multivariate analyses were then performed, to identify independent predictors of CL, using multivariable cox regression modelling with a forward stepwise approach. Receiver operating characteristic (ROC) curves were then used to quantify the relationship of body composition measures to the development of CL. All analyses were performed using IBM SPSS Statistics 26 (IBM Corp. Armonk, NY, USA), with P<0.05 deemed to be indicative of statistical significance.

Institutional approval

This was a retrospective human study so individual patient consent was not required for this study. Institutional approval for this study was acquired from the local Clinical Audit Registration and Management System (No. CARMS-16870). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Table 1 Baseline characteristics of chyle leak and no chyle leak cohort

Factor	Chyle leak (n=26)	No chyle leak (n=60)	P
Age	71 [62–76]	66 [59–70]	0.085
Gender, male	22 [85]	48 [80]	0.767
BMI	24 [22–27]	27 [25–32]	0.001
Neoadjuvant chemotherapy	20 [77]	49 [82]	0.769

Given as n (%) or median (Q1–Q3). Univariate analyses performed using Chi-Squared test (categorical variables) and Mann-Whitney U test (continuous variables). BMI, body mass index.

Table 2 Relationship between body composition measures and chyle leak after oesophagectomy

Factor	Chyle leak (n=26)	No chyle leak (n=60)	P
Preoperative sarcopenia	10 [46]	36 [60]	0.316
Preoperative myosteatosis	13 [59]	33 [56]	1
Preoperative BMI	24 [22–27]	27 [25–32]	0.001
Preoperative subcutaneous fat index	34 [25–47]	71 [42–103]	0.001
Preoperative visceral fat index	54 [39–92]	68 [48–96]	0.135
Preoperative total fat index	95 [71–136]	148 [103–184]	0.004
Preoperative muscle HU	36 [32–41]	34 [29–38]	0.072

Given as n (%) or median (Q1–Q3). Fat indices calculated by diving fat area by height in metres squared. (cross-sectional area of skeletal muscle was normalized for stature (cm^2/m^2) as reported elsewhere (17). Univariate analyses performed using Chi-Squared test (categorical variables) and Mann-Whitney U test (continuous variables). BMI, body mass index; HU, Hounsfield units.

Table 3 Multivariate analysis to determine independent predictors of chyle leak after oesophagectomy

Factor	Odds ratio (95% CI)	P
Preoperative BMI	–	0.214
Preoperative subcutaneous fat index	1.026 (1.009–1.043)	0.003
Preoperative total fat index	–	0.925

Multivariate analyses performed using multivariable cox regression modelling with forwards stepwise approach. CI, confidence interval; BMI, body mass index.

Results

There were 26 patients who developed a CL following an oesophagectomy during the study period and 60 patients were included in the control group (*Table 1*). Age and gender were similar between the CL and no CL cohorts whilst preoperative body mass index (BMI) (P=0.001), subcutaneous fat index (P=0.001) and total fat index (P=0.004) were significantly associated with CL (*Table 2*).

On multivariate analysis, a lower preoperative subcutaneous fat index was a significant independent predictor of CL (P=0.003). Sarcopenia was not found to be a significant predictor of developing CL (*Table 3*).

The relationship between body composition measures and CL were further investigated with ROC curves. Decreasing preoperative subcutaneous fat index [area under the receiver operating characteristic curve (AUROC) 0.744, P=0.001] and BMI (AUROC 0.728, P=0.001) were significantly associated with CL (*Figure 1A,1B*).

There were 10 (38%) patients who developed a severe CL but no significant predictors of severe CL were identified (*Table 4*).

Discussion

This retrospective descriptive study sought to investigate the aetiology of CL after oesophagectomy using body composition measures. The main finding is that a reduced preoperative body fat composition is a risk factor for

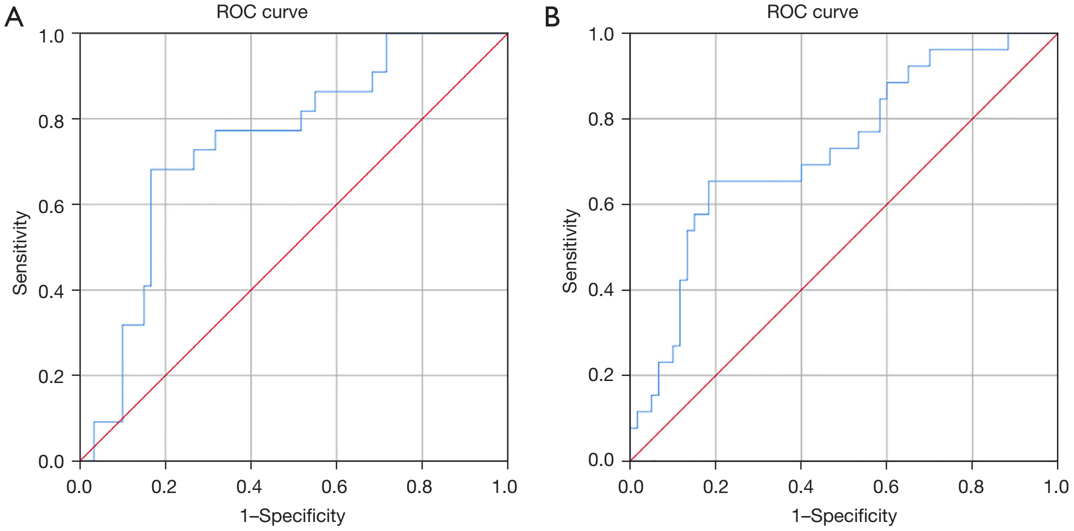

Figure 1 ROC curves generated using SPSS Statistics 26 (IBM Corp. Armonk, NY, USA). The AUROC for A =0.744 (P=0.001) and B =0.728 (P=0.001). (A) ROC curve demonstrating the relationship between subcutaneous fat index and chyle leak after oesophagectomy. (B) ROC curve demonstrating the relationship between body mass index and chyle leak after oesophagectomy. ROC, receiver operating characteristic; AUROC, area under the receiver operating characteristic curve.

CL after oesophagectomy. This is similar to previous studies which have reported a reduced incidence of CL after oesophagectomy amongst those with a higher BMI (18-21). CL seems to be anomalous in this regard, as other complications after oesophagectomy such as anastomotic leakage have been shown to be increased amongst those with a higher BMI (20,22-24).

Sarcopenia did not influence either the occurrence or severity of CL. Given that sarcopenia has frequently been shown to increase prevalence of complications after oesophagectomy (21,25), it was surprising that was not related to the prevalence of CL in this study. Rather, it seems that body fat is the most important factor influencing CL, opposed to muscle mass. Given this important finding and the fact that preoperative CT scans are readily available, clinicians could certainly consider routine preoperative measurement of body fat indices as this may allow some individualised risk stratification.

The mechanism for increased CL rate amongst those with a lower BMI and in this study, specifically a reduced body fat composition, is unclear and previous cohort studies and meta-analyses have also struggled to explain this finding (22). Reviewing the physiology, it is possible to suggest some potential causes. For instance, it is known that fasting can dramatically reduce flow through the thoracic duct, down to 1 mL/minute, which is in contrast to the physiological norm of approximately 200 mL/minute with normal diet (26-28). A reduction in flow could make the thoracic duct and its tributaries more difficult to identify intraoperatively, leading to an increase in iatrogenic injury. Furthermore, it is known that lymph flow is increased with hypertension (26,29). This then may explain why those with a higher BMI, who are more likely to be hypertensive, have a lower incidence of CL.

Previously published evidence indicates that nutritional status may not only be important preoperatively, but also play a vital role in patients' recovery from CL (30-32). It is likely that this is related to both the loss of plasma proteins, such as albumin, and immune cells, such as lymphocytes. Combined, these will lead to impairment of the patient's tissue healing and immune function. This emphasises the importance of physiological and nutritional optimisation before oesophagectomy to both reduce the likelihood of CL and to promote its recovery in the event it does occur.

Limitations of this study include its retrospective nature and the fact that CL is a relatively uncommon complication, so the number of patients are small and cases that are included in this study are spread over a large time period of time. Furthermore, in this study sarcopenia was assessed purely on a radiological basis, whereas the European Working Group on Sarcopenia in Older People (EWGSOP) does recommend the use of both low muscle mass and low muscle function to diagnose sarcopenia (33). In this study

Table 4 Factors affecting severity of chyle leak

Factor	Mild chyle leak (n=16)	Severe chyle leak (n=10)	P
Demographics			
Age	69 [63–77]	73 [62–73]	0.816
Male	14 [88]	8 [80]	0.625
BMI	23 [22–25]	25 [23–28]	0.310
Oesophagectomy type			0.723
Open	3 [19]	3 [30]	
Hybrid	6 [38]	4 [40]	
MIO	7 [44]	3 [30]	
Neoadjuvant Therapy			
Neoadjuvant Chemotherapy	14 [88]	6 [60]	0.163
Neoadjuvant Chemoradiotherapy	0 (0)	2 [20]	0.138
Preoperative Bloods			
Albumin	41 [35–46]	44 [37–46]	0.484
CRP	5 [3–7]	8 [3–14]	0.464
NLR	3.0 (2.6–3.7)	2.7 (2.1–4.2)	0.938
Preoperative sarcopenia	5 [31]	5 [50]	0.378
Preoperative myosteatosis	8 [50]	5 [50]	1.000
Preoperative subcutaneous fat index	34 [25–38]	39 [26–58]	0.616
Preoperative visceral fat index	54 [39–73]	68 [36–100]	0.714
Preoperative total fat index	95 [66–136]	103 [75–139]	0.570
Preoperative Mus HU	35 [33–41]	38 [32–41]	0.920
Preoperative SMI	49 [44–53]	43 [40–46]	0.145

Given as n (%) or median (Q1-Q3). Fat indices calculated by diving fat area by height in metres squared. HU, Hounsfield units. SMI, skeletal muscle index [cross-sectional area of skeletal muscle was normalized for stature (cm^2/m^2) as reported elsewhere (17)]. Univariate analyses performed using Chi-Squared test (categorical variables) and Mann-Whitney U test (continuous variables). MIO, minimally invasive oesophagectomy; BMI, body mass index; NLR, neutrophil:lymphocyte ratio; CRP, C-reactive protein.

muscle function was not used but this is certainly an area of development for future studies.

The knowledge that reduced preoperative body fat increases the risk of CL presents a potentially modifiable risk factor for CL after oesophagectomy. Preoperative nutritional and physical optimisation could help to reduce CL rates after oesophagectomy.

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Footnote

Reporting Checklist: The authors have completed the STARD reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-21-1580/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-21-1580/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-21-1580/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. This was a retrospective human study so individual patient consent was not required for this study. Institutional approval for this study was acquired from the local Clinical Audit Registration and Management System (No. CARMS-16870). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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