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A systematic review of the nutritional consequences of esophagectomy

Melanie Baker[a], **Vanessa Halliday**[b], **Robert N. Williams**[a], and **David J. Bowrey**[a,*]

[a]Dept of Surgery, Leicester Royal Infirmary, LE1 5WW, United Kingdom

[b]School of Health and Related Research (ScHARR), University of Sheffield, S1 4DA, United Kingdom

Summary

Background & aims—As improved outcomes after esophagectomy have been observed over the last two decades, the focus on care has shifted to survivorship and quality of life. The aim of this review was to determine changes in nutrition after esophagectomy and to assess the evidence for extended nutrition support.

Methods—A search strategy was developed to identify primary research reporting change in nutritional status a minimum of one month after esophagectomy.

Results—Changes in nutritional parameters reported by 18 studies indicated a weight loss of 5–12% at six months postoperatively. More than half of patients lost >10% of body weight at 12 months. One study reported a persistent weight loss of 14% from baseline three years after surgery. Three studies reporting on longer term follow up noted that 27%–95% of patients failed to regain their baseline weight. Changes in dietary intake (three studies) indicated inadequate energy and protein intake up to three years after surgery. Global quality of life scores reported in one study correlated with better weight preservation. There were a high frequency of gastrointestinal symptoms reported in six studies, most notably in the first year after surgery, but persisting up to 19 years. Extended enteral nutrition on a selective basis has been reported in several studies.

Conclusions—Nutritional status is compromised in the months/years following oesophagectomy and may never return to baseline levels. The causes/consequences of weight loss/ impaired nutritional intake require further investigation. The role of extended nutritional support in this population remains unclear.

Keywords

Esophagectomy; Enteral nutrition; Nutrition; Nutritional status; Weight

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*Corresponding author. Dept of Surgery, Level 6 Balmoral Building, Leicester Royal Infirmary, LE1 5WW, UK. Tel.: +44 0116 258 5247; fax: +44 0116 258 6083. djb57@le.ac.uk (D.J. Bowrey).

Statement of authorship

All authors contributed to the study design, planning and data extraction. DJ Bowrey and M Baker drafted the initial manuscript. RN Williams and V Halliday revised the initial manuscript. All authors have seen and approved the final draft.

Conflict of interest

DJ Bowrey and M Baker receive departmental grant support from Nutricia for research unrelated to this submission. DJ Bowrey receives departmental grant funding from Fresenius Kabi for research work unrelated to this submission.

1 Introduction

The incidence of esophageal carcinoma in the Western World is in the range 5–10 per 100,000, with the UK and Ireland having the highest incidence in Europe [1]. In the US, there were an estimated 18,000 new diagnoses of esophageal cancer in 2014 [2] with approximately one third of these patients undergoing esophagectomy [3].

As advances in perioperative care have resulted in improved outcomes in the immediate postoperative period [4,5], the focus on care has shifted to survivorship and quality of life [6]. Nutritional considerations in these patients represent one of the greatest contributors to quality of life [7]. There are manifold reasons for aberrant nutrition after esophagectomy, including altered anatomy, early satiety, loss of appetite, taste and smell, and the post-surgery dumping syndrome [8].

The majority of clinical trials studying nutrition after esophagectomy have focused on the perioperative period, with feeding adjuncts targeted to either the preoperative phase or the immediate (in hospital) postoperative phase [9–12]. These studies have identified minimal or no improvement in clinical outcomes for patients receiving enteral feeding in hospital [9–12]. There has been little written about the potential value of extended nutritional support following discharge from hospital.

There exists a worldwide variation in practice regarding nutritional supplementation after esophagectomy, both in terms of provision and route [10]. Even, within countries there are large geographical disparities. In a review of over 2000 patients undergoing esophagectomy, the 2010 United Kingdom National Oesophagogastric Cancer Audit reported that overall 68% of patients had a feeding jejunostomy placed at the time of surgery [4]. However, the proportion of patients having feeding jejunostomy placed routinely varied between centers from under 25% to in excess of 75% [4].

The aim of this systematic review was two-fold; (1) to determine post hospital discharge changes in nutritional status/intake after esophagectomy, (2) to determine the evidence for the use of extended nutritional support in this population. To be eligible for inclusion, outcome measures had to be reported a minimum of one month after discharge from hospital.

2 Materials and methods

This systematic review followed the PRISMA guidelines [13] and was registered with the Prospero database. It was conducted between October 2014 and April 2015.

2.1 Article selection

To be eligible studies needed to report an objective measure of nutritional status (weight, body mass index, upper arm anthropometry) and, or nutritional intake (energy and protein intakes) after the index hospital admission following esophagectomy. Additional outcome measures, reported in the identified studies that related to nutrition (such as symptoms/ quality of life) were also considered. To be eligible for inclusion, outcome measures had to be reported at least one month after hospital discharge. Publications reporting on pooled surgical populations were excluded, where it was not possible to extract information specifically about participants undergoing esophagectomy. The value of preoperative and immediate perioperative enteral nutrition, including immunonutrition has been considered in recent review articles and is not considered in this review [11,12].

2.2 Search strategy

A database search strategy was formulated using subject headings and keyword search terms combined for "esophagectomy" and "nutrition" (encompassing "nutritional status", "dietary intake" and "nutritional support" terms). Medline, Embase, BNI, CINAHL, and Cochrane databases were systematically searched. Publications were limited to English Language but not year of publication. The reference lists of identified articles and other key review publications were additionally hand searched. The process and inclusion of eligible papers were independently reviewed by MB and DB.

2.3 Assessment of quality: risk of bias

Risk of bias was assessed following guidance from the Cochrane Library [14] with additional information pertaining to selection and attribution bias of non randomised study designs considered with elements from the Newcastle-Ottawa Scale [15] and STROBE [16] statement for reporting observational studies.

2.4 Data extraction

Data was extracted from the included studies by MB and then independently validated by DB,VH and RW. A consensus was reached in areas of controversy.

3 Results

The database search identified 1875 studies of potential interest (including duplication). A further five articles were identified from the bibliographies of retrieved articles (Fig. 1). After full study review, 18 articles met the inclusion criteria and form the basis of this review. There were no randomized controlled trials, 13 descriptive longitudinal studies, and five cross sectional studies. One of the latter studies employed a combination of study designs. Further details of the studies are given in Table 1.

In general, all studies were considered deficient in one or more aspects of their study design/reporting, which increased the likelihood of bias. In terms of selection, no eligibility criteria were reported in two studies [17,26], one prospective study used consecutive patients attending outpatient clinics [18] and all others used convenient samples from defined time periods [19–25,27–33]. Participation rate was reported in 16 of the 18 studies, and ranged between 66 and 100%. No study justified the sample sized used. In terms of attrition bias, five of the 13 studies reported complete outcome data [20,21,26,32,33].

3.1 Changes in nutritional status

Postoperative nutritional parameters, assessed by either change in weight (as a percentage or absolute amount) or body mass index (BMI) were reported in all studies (Table 2). No study reported nutritional status in terms of change in lean body mass and/or fat stores (using anthropometry, hand grip dynamometry or bioelectric impedance). Due to mixed time periods and variability in reporting weight change, it was not possible to combine study results.

The studies demonstrate that deterioration in nutritional status was common after esophagectomy, with changes most marked in the first six months after surgery. At six months, reported weight loss ranged from 5 to 12% [18,21,24,27]. The rate at which nutritional status deteriorated plateaued between six and 12 months after surgery, although in those studies reporting longer-term changes in nutritional status, 27–95% of subjects failed to return to their pre-operative levels [17,23,30]. This suggests that the early weight loss sustained post-operatively is not reversed.

A number of studies considered the frequency of malnutrition, defined by a greater than 10% or 15% loss of baseline weight [21,28,29,32] These found that at six and 12 months after surgery, more than half of the patients had lost more than 10% of their initial weight.

Two studies considered factors associated with postoperative weight loss [29,32]. Premorbid BMI was identified in both studies as a significant factor, with those with higher BMIs losing more weight preoperatively but comparatively less, postoperatively. Other risk factors identified as being associated with greater weight loss were female sex and use of neoadjuvant chemotherapy and gastrointestinal symptoms (see below) [29].

3.2 Changes in dietary intake

Three studies considered dietary intake at different time points after esophagectomy [7,25,27] (Table 3). All estimated adequacy of intake in comparison to daily requirements, but only Haverkort et al. [25] provided details of how energy and protein requirements were calculated. This identified that a quarter of patients did not meet their energy goal, six and 12 months after surgery. Suboptimal intake of multiple vitamins and trace elements were identified with the following frequencies, folic acid (85%), vitamin D (61%), copper (56%), calcium (49%) and vitamin B1 (48%). In 205 patients, Ryan et al. [7] observed that at discharge from hospital, oral intake of energy and nitrogen (protein) were 70% and 65% of the nutritional requirement respectively. No studies assessed the relationship between inadequacy of nutritional intake and change in nutritional status post-operatively.

3.3 Relationship between nutritional factors and quality of life/symptoms

Table 4 summarises the six studies reporting change in nutritional status that also reported on nutrition related symptoms or quality of life [17,22,23,25,27,33]. Two of the studies employed a validated instrument in the assessment of patient reported outcomes [22,23].

Martin et al. [29] employed the EORTC QLQ-C30 assessment tool and identified that global quality of life scores were inversely associated with the degree of weight loss sustained by patients. Aghajanzadeh et al. [17] compared physical function scores from the medical outcomes study 36 short form health survey [34] with the national average (although further details were lacking) and showed these were significantly decreased.

Although the symptom definitions were inconsistent between the studies, all reported high frequencies of gastrointestinal symptoms that persisted across all time points assessed. Four of the studies reported after 12 months [17,23,27,33].

3.4 Surgical approach and technique

Over 98% of the patients reported in the literature (1973 of 2000 patients) underwent esophagectomy for carcinoma (Table 1). The indications for resection in the remaining patients included high grade dysplasia and achalasia. No study reported separately the outcome of those with and without malignant disease, making direct comparison unfeasible.

Where it was possible to extract the information, in the majority of patients the conduit employed was the stomach (1467 patients, 90%), Table 5. The colon was employed in 99 patients (6%) and the jejunum in 57 patients (4%). Only one study [23] reported exclusively on patients with colonic replacement as the conduit. Compared to studies reporting on patients with esophageal replacement by a gastric conduit, there was a suggestion of a numerically lower rate of dysphagia (12% vs. 22–63%) and reflux symptoms (19% vs. 19–65%) for patients having the colon as the conduit. Aghajanzadeh et al. [17] noted that a more favourable weight profile and a reduced risk of oesophagitis was observed with the use of the colon as the esophageal substitute compared to the stomach, although no data were provided to support this assertion. Other factors that might influence nutritional outcome were reported by McLarty et al. [30], who identified a cervical anastomosis to be associated with a lower risk of reflux symptoms compared to an intrathoracic (mediastinal) anastomosis. The authors also observed that dumping symptoms were more common in younger patients and in females compared to males. The authors did not identify the time interval since surgery as a predictor of late functional outcome, although the study only included patients who were at least five years out from surgery.

The majority of patients reported underwent open surgery (1083 patients, 89%). A minimal access approach was reported for 138 patients (11%) in two studies [18,20], one employing an open abdominal and minimal access thoracic approach [20], the other employing a minimal access approach for both phases [18]. There was no evidence that the minimal access approach was associated with less weight loss than conventional open surgery (see Table 2).

3.5 Nutritional support (post discharge after the index admission for oesophagectomy)

This review identified no published interventional studies considering extended nutritional support that reported change in either nutritional status or intake. The use of nutritional support varied in those studies that reported its use, both in regard to eligibility criteria and the quantities of energy and protein provided. In general terms, extended enteral feeding was employed on a selective basis, either in the management of post-operative complications, such as anastomotic leak where a prolonged period of no oral intake was required, or in the management of those with documented insufficient calorie intake.

In the largest of the studies, Ryan et al. [7] reported on 205 patients and found that 26% of patients spent more than 14 days on enteral feeding. Eight percent of patients were discharged home on enteral feeding and a further 6% recommenced enteral feeding in the

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first month after discharge because of unacceptable weight loss. Couper [20] discharged 19% of 48 patient's home on enteral feeding after esophagectomy, some because of poor oral intake, others because of complications being managed by avoiding oral intake. A further 8% of patients had feeding recommenced because of unacceptable nutritional intake. Haverkort et al. [24] reported that 48% of 80 patients were discharged home on enteral feeding, mainly overnight feeding averaging 1000 kcal daily. Six and 12 months after surgery, only 2% and 1% respectively required ongoing enteral feeding.

4 Discussion

This systematic review is the first to summarise the out of hospital nutritional consequences following esophagectomy, with 18 non randomised studies reporting objective measures of nutritional status (weight change) and nutritional intake. The degree of weight loss was most severe in the first six months after surgery with some evidence that the rate of weight loss then plateaued. Pre-operative weight was frequently not reattained. Nutritional intake was reduced with dietary energy intake decreasing within the first month after surgery and remaining suboptimal in the long term. There was no evidence that the outcome after minimal access surgery differed from open surgery.

While both weight loss and reduction in dietary energy and protein intakes were seen, the exact cause was unclear. One study [29] in this series demonstrated that global quality of life was directly related to the extent of weight loss seen post-operatively. In terms of gastrointestinal symptoms, high frequencies of symptom complexes, such as dysphagia and post-prandial dumping were identified in those studies that assessed these aspects. There is likely to be an association between gastro-intestinal symptoms and nutritional status, confirmed by Honda et al. [35] who noted greater body weight loss and reduction in meal quantity in those patients reporting higher symptom scale scores.

Whether deterioration in nutritional status is simply due to inadequate oral intake, and whether it is reduced or reversed by the provision of additional nutrition requires further investigation. To date there have been no randomised studies investigating the effect of extended nutritional support post esophagectomy, either employing oral nutritional support as tailored dietary advice or oral nutritional supplements, or the use of enteral tube feeding. In a randomised study, Hyltander et al. [36] showed no significant benefit of giving supplementary enteral or parenteral nutrition in a heterogeneous study population of 80 participants following curative upper gastrointestinal surgery (gastrectomy, esophagectomy, pancreatectomy), although the amount of supplementary nutrition was relatively small (approximately 120 kcal daily at three months).

In those studies that have used extended enteral feeding, it has been used selectively, with a reported prevalence ranging from 14% to 48% of patients [7,20,24,27,37–40]. The wide variation in the practice of home jejunostomy likely reflects the preferences of individual centres. It has largely been utilised in patients who are malnourished pre-operatively [37], and those with post-operative complications [38]. A population based study from Sweden which did not disclose the number of patients discharged home with a feeding jejunostomy, identified tube placement to be associated with a reduced amount of weight loss in the first six months after surgery and a greater chance of discharge home compared to other destinations [39].

There are UK centres moving towards enteral feeding for longer periods [38]. Discharging patients home on jejunostomy feeding has been shown to reduce length of stay in a small non randomised study [40] but further details on nutritional status were not reported.

It may not be appropriate to simply target increasing nutritional intake without consideration of the management to alleviate any chronic gastro-intestinal symptoms [41] Post-operative malabsorption syndrome has been shown in this patient group [42] and may be a contributing factor to the malnutrition frequently seen.

Nutritional consequences are frequently observed after esophagectomy and warrant further investigation. It might be time to evaluate the use of extended enteral nutritional support in this patient group [43]. Studies need to appropriately assess not only nutrition status but patient reported outcomes, in terms of symptom alleviation and quality of life.

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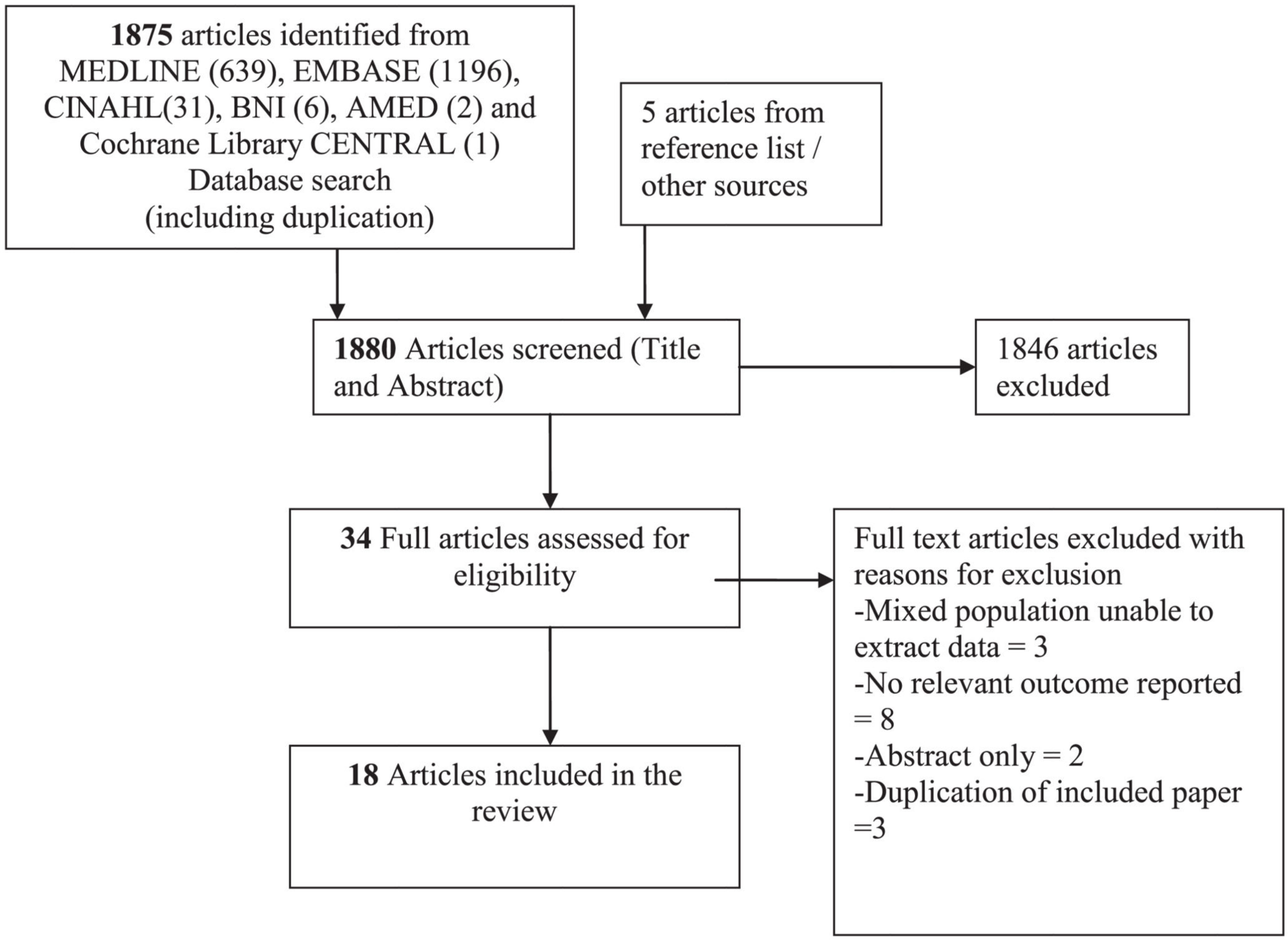

Fig. 1.
Summary of search strategy.

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Table 1

Summary of included studies.

Study	Design	Sample	% with cancer	Setting	Mean or median age in years (range when stated)	% Male	Follow up duration in months	Risk of bias	Reported outcomes		
									Nutritional status	Dietary intake	Symptoms
Aghajanzadeh et al. (2008) [17]	XS	192	100	Iran 3 sites	48 (22–75)	70%	12–48	High	Yes	No	Yes
Brown et al. (2013) [18]	L (p)	117	100	UK Single site	67 (42–84)	85%	12	High	Yes	No	No
Carey et al. (2011) [19]	XS	8/30	87.5	Australia 3 sites	n/r	n/r	32 ± 26	High	Yes	No[a]	No[a]
Couper (2011) [20]	L (r)	48	96	UK Single site	62 (43–82)	n/r	6	High	Yes	No	No
D'Journo et al. (2012) [21]	L (r)	205	100	France Single site	59 (28–81)	81%	>12	High	Yes	No	No
Ginex et al. (2013) [22]	L (p)	218	100	US Single site	63	n/r	12	High	Yes	No	Yes
Greene et al. (2014) [23]	XS	40	71	US Single site	71	n/r	144 (120–228)	High	Yes	No	Yes
Haverkort et al. (2010[b]) [24], (2012[c]) [25]	L (p)	96	97	Holland Single site	62 (SD 10)	76%	12	High	Yes[b]	Yes[c]	Yes[b]
Koizumi et al. (2011) [26]	L (p)	22	100	Japan Single site	65 (41–84)	91%	12	High	Yes	No	No
Ludwig et al. (2001) [27]	L (p)	48	83	US Single site	65 (19–90)	90%	36 ± 25	High	Yes	Yes	Yes
Martin et al. (2007) [28]	XS	233	100	Sweden National	65	77%	6	High	Yes	No	Yes
Martin et al. (2009) [29]	L (p)	203	100	Sweden National	n/r	80%	36	High	Yes	No	No
McLarty et al. (1997) [30]	L (r), XS	107 (64 for Survey)	100	US Single site	n/r	n/r	>60	High	Yes	No	Yes
Ogendo (2007) [31]	L (r)	59	100	Kenya Single site	54 (SD 15)	92%	29	High	Yes	No	No
Ouattara et al. (2012) [32]	L (r)	118	100	France Single site	59 (28–81)	76%	12	High	Yes	No	No
Ryan et al. (2006) [7]	L (p)	205	100	Ireland Single site	62 (29–83)	n/r	1	High	Yes	Yes	No
Suzuki et al. (1994) [33]	XS	81	100	Japan Single site	65 (41–80)	n/r	56 (1–166)	High	Yes	No	Yes

[a] Mixed population, Unable to extract data.

[b/c] Considered jointly as reported different aspects of the same population.

L = longitudinal, n/r = not reported, p = prospective, r = retrospective, SD = standard deviation, XS = cross sectional.

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Table 2

Change in weight and body mass index after esophagectomy.

Author	Change in variable assessed	Change in weight or BMI noted at time points indicated				
		1 m	3 m	6 m	12 m	Other
Brown et al. [18]	% change in BMI	−5%	n/r	−8%	−7%	n/r
Carey et al. [19]	% change in weight	n/r	n/r	n/r	n/r	−14% (32 ± 26 m)
D'Journo et al. [21]	% change in weight	n/r	n/r	−8%	−8%	n/r
Haverkort et al. [24]	% change in weight	−6% (1 wk)	−6%	−5%	−6%	n/r
Ryan et al. [7]	% change in weight	−8%	n/r	n/r	n/r	n/r
Ludwig et al. [27]	% change in weight	n/r	n/r	−12%	−10%	n/r
Aghajanzadeh et al. [17]	% Subjects failing to regain weight back to pre-operative levels	n/r	n/r	n/r	n/r	27% (12–48 m)
Greene et al. [23]		n/r	n/r	n/r	n/r	95% (10–19 yr)
McLarty et al. [30]		n/r	n/r	n/r	n/r	49% (>5 yr)
Ginex et al. [22]	% Subjects reporting weight loss	n/r	n/r	n/r	>60%	n/r
Ogendo [31]		n/r	n/r	52%	n/r	n/r
Ryan et al. [7]	% of patients with ≥5% weight loss	50%	n/r	n/r	n/r	n/r
D'Journo et al. [21]	% of patients with ≥10% weight loss	n/r	n/r	54%	55%	n/r
Martin et al. [28]	% of patients with ≥10% weight loss	n/r	n/r	64%	n/r	n/r
Martin et al. [29]	% of patients with ≥15% weight loss	n/r	n/r	n/r	n/r	33% (36 m)
Ouattara et al. [32]	% of patients with ≥15% weight loss	n/r	n/r	29%	25%	n/r
Koizumi et al. [26]	Absolute change in BMI (kg/m^2).	−1.9 (2.3)	n/r	−2.3 (1.8)	−2.4 (2.7)	n/r
Ludwig et al. [27]	Absolute change in weight (kg)	n/r	n/r	−10 (8) kg	−3 (3) kg	n/r

BMI = body mass index, m = months, n/r = not reported, wk = week, yr = year.

Table 3

Changes in dietary intake after esophagectomy.

Author	Data collection time points	Assessment tool	Daily energy intake (kcal)	% with adequate energy intake	% with adequate protein intake	% with adequate micronutrient intake
Haverkort et al. [25]	6 m, 12 m	3 day diary	n/r	77% (6 m)[a]	91% (6 m)	Vitamins[b]
				76% (12 m)	93% (12 m)	17–86% (6 m)
						15–83% (12 m)
						Trace elements[c]
						40–100% (6 m)
						44–98% (12 m)
Ryan et al. [7]	hospital discharge	Dietitian calculated	n/r	70%[d]	65%	n/s
Ludwig et al. [27]	34 (±22) m	3 day diary	2180	78%[d]	n/r	n/r

[a] Adequate intake defined by ≥90% intake of estimated requirement (Harris Benedict +30%, and 1.5–1.7 g/kg/day Protein in first 6 m, reducing to 1.2–1.3 g/kg/d).

[b] Vitamins included vitamins A, B group, C, D, E and folic acid.

[c] Trace elements included calcium, copper, iron, magnesium, phosphorus, selenium and zinc.

[d] No details provided on how requirements were estimated.

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Table 4

Nutrition related symptoms after esophagectomy

Author	Data collection time points	Assessment tool	Patient reported outcomes or symptoms
Aghajanzadeh et al. [17]	Single point (12–48 m)	Non validated institutional questionnaire	Dysphagia to solids 61% (mild), 25% (severe)
		MOS SF36	Reflux 19%
			Postprandial Dumping (46%)
Ginex et al. [22]	6 m, 12 m	MSAS-SF	Dysphagia 30% (6 m), 22% (12 m)[a]
			Anorexia 33% (6 m), 27% (12 m)[a]
			Feeling bloated 40% (6 m), 42% (12 m)[a]
			Reflux 38% (6 m), 44% (12 m)[a]
Greene et al. [23]	Single point (10–19 yr)	GI QLI index	Dysphagia 12%
		MOS SF-36	Postprandial Dumping 33%
			Early Satiety 50%
			Reflux 19%
Haverkort et al. [25]	1 wk, 1 m, 3 m, 6 m, 12 m	Non validated institutional questionnaire	Dysphagia 53–63% (all time points)
			Postprandial dumping 74–78% (all time points)
			Anorexia 51–76% (all time points)
			Early satiety 87–90% (all time points)
			Reflux 54–65% (all time points)
Ludwig et al. [27]	Single point (34 m)	Non validated institutional questionnaire	Dysphagia (periodic) 38%
			Diarroea 19%
			Nausea (periodic) 19%
			Regurgitation (periodic) 25%
Martin et al. [28]	Single point (6 m)	EORTC QLQ-C30 and QLQ-OES18	Patients experiencing >20% BMI loss postoperatively reported more anorexia, eating difficulties and odynophagia than patients whose BMI remained unchanged. Dysphagia and reflux symptoms did not differ between the groups
McLarty et al. [30]	Single point (5yr)	Non validated institutional questionnaire	Dysphagia 25%
		MOS SF36	Odynophagia 9%
			Postprandial dumping 50%
			Reflux 60%
Suzuki et al. [33]	Single point (1–166 m)	Non validated institutional questionnaire	Dysphagia 22%
			Constipation 19%
			Abdominal fullness 36%

BMI = body mass index, EORTC = European Organisation for Research and Treatment of Cancer, GIQLI = Gastrointestinal Quality of Life Index, GSRS = gastrointestinal symptom rating scale, mo = months, MOS SF 36 = Medical Outcomes Study 36 Item Short Form Health Survey, MSAS-SF = Memorial Symptom Assessment Scale–ShortForm.

[a]Estimated from graph.

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Table 5

Surgical characteristics of included studies.

Study	Conduit			Conduit location	Anastomosis location	Minimal access or open surgery
	Stomach	Colon	Jejunum			
Aghajanzadeh et al. (2008) [17]	154	28	10	Posterior mediastinum 172	Cervical 172 Mediastinum 20	Open 192
Brown et al. (2013) [18]	117	0	0	Posterior mediastinum 117	Cervical 117	Minimal access abdominal & thoracic 117
Carey et al. (2011) [19]	n/r	n/r	n/r	n/r	n/r	n/r
Couper (2011) [20]	48	0	0	n/r	n/r	Open 27 Minimal access thoracic 21
D'Journo et al. (2012) [21]	205	0	0	Posterior mediastinum	Mediastinum 205	Open 205
Ginex et al. (2013) [22]	200	n/r	n/r	Posterior mediastinum 200	Mediastinum 200	n/r
Greene et al. (2014) [23]	0	63	0	Posterior mediastinum 57 Substernal 4	Cervical 63	Open 63
Haverkort et al. (2010b) [24], (2012c) [25]	96	0	0	Posterior mediastinum 96	Mediastinum 50 Cervical 46	Open 96
Koizumi et al. (2011) [26]	22	0	0	Posterior mediastinum 22	Mediastinum or cervical	Open 22
Ludwig et al. (2001) [27]	48	0	0	Posterior mediastinum 48	Cervical 44 Mediastinum 4	Open 48
Martin et al. (2007) [28]	n/r	n/r	n/r	n/r	n/r	n/r
Martin et al. (2009) [29]	156	5	42	Posterior mediastinum 164 Abdomen 39	Mediastinum or cervical	n/r
McLarty et al. (1997) [30]	99	3	4	Posterior mediastinum 99 Abdomen 3	Mediastinum 87 Cervical 20	Open 107
Ogendo (2007) [31]	n/r	n/r	n/r	n/r	n/r	n/r
Ouattara et al. (2012) [32]	118	0	0	Posterior mediastinum 118	Mediastinum 98 Cervical 20	Open 118
Ryan et al. (2006) [7]	204	0	1	Posterior mediastinum	Mediastinum 160 Cervical 45	Open 205
Suzuki et al. (1994) [33]	n/r	n/r	n/r	Posterior mediastinum in 83%	Cervical in 83%	n/r

n/r = not reported, [22] 200 of 208 patients reported underwent Ivor Lewis esophagogastrectomy. The procedure was not stated for eight patients.