Nutritional support and dietary interventions following esophagectomy: challenges and solutions

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REVIEW

Nutritional support and dietary interventions following esophagectomy: challenges and solutions

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Background and aims: Provision of adequate nutrition after esophagectomy remains a major challenge. The aims of this review were to describe the challenges facing this patient population and to determine the evidence base underpinning current nutritional and dietetic interventions after esophagectomy.

Methods: Medline, Embase and CINAHL databases were searched for English language publications of the period 1990–2016 reporting on the outcome of nutritional or dietetic interventions after esophagectomy or patient-related symptoms.

Results: Four studies demonstrated that early reintroduction of oral fluids was safe and was associated with a shorter hospital stay and ileus duration. One of three studies comparing in-hospital enteral nutrition against usual care showed that enteral feeding was well tolerated and was associated with a shorter hospital stay. Eight studies comparing enteral with parenteral nutrition showed similar surgical complication rates. Enteral feeding was associated with a shorter duration of ileus and lower health care costs. In hospital, all types of enteral access (nasoenteral, jejunostomy) were equivalent in their safety profiles. Cohort studies indicate that technical (tube dysfunction) and feed (diarrhea, distention) problems were common with jejunostomies but are easily managed. The mortality risk associated with jejunostomy in hospital is 0.2% (reported range 0%–1%), principally due to small bowel ischemia. There have been no reports of serious jejunostomy complications in patients receiving home feeding. One study demonstrated the advantages of home feeding in weight, muscle and fat preservation. Studies reporting 12 months or more after esophagectomy indicate a high frequency of persistent symptoms, dumping syndrome 15%–75% (median 46%), dysphagia 11%–38% (median 27%), early satiety 40%–90% (median 65%) and reflux 19%–61% (median 29%).

Conclusion: Patients should resume oral intake as soon as possible after surgery. In hospital, all forms of enteral access appear to be safe. Out of hospital, the ability to provide home feeding by feeding jejunostomy is likely where meaningful nutritional improvements can be made. Improving nutrition and related quality of life in the early months might improve the long-term outcome.

Keywords: esophagectomy, enteral nutrition, nutrition, nutritional status, weight

Introduction

Approximately one-third of patients with esophageal cancer will undergo surgical resection (esophagectomy).[1] For many patients, surgery will form part of multimodal therapy that also includes chemotherapy and radiotherapy.[1] As a result, the patient treatment journey is protracted, taking up to 6 months to complete.[1] Nutritional considerations in these patients represent one of the greatest contributors to quality of life.[2–4] Achieving adequate nutritional intake is a cause for concern at all points in the patient pathway.

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Prior to diagnosis, there may be a physical inability to achieve adequate caloric intake because of dysphagia. After surgery, in the immediate postoperative period, most centers restrict oral intake. After discharge from the hospital, nutritional intake remains poor because of the physical effects of the surgery itself, which include early satiety associated with a reduced gastric volume, altered appetite, taste and smell, dumping syndrome and malabsorption.[4]

A recent systematic review of descriptive longitudinal studies indicated that 6 months after surgery, body weight had fallen by 5%–12%, compared to baseline preoperative levels.[2] More than half of the patients experienced an excess of 10% weight loss. In the small number of studies reporting on outcome beyond the first year, many subjects had failed to return to their preoperative weight.[2] In an attempt to ameliorate this weight loss, a small number of centers have moved to a policy of selective or routine home supplementary enteral nutrition.[5]

The aim of this review was to systematically review the evidence and describe the nutritional challenges faced by clinicians and patients after esophagectomy, and the outcome of nutritional or dietetic interventions at any time point after surgery.

Materials and methods

Article selection

To be eligible, studies needed to report a dietetic or nutritional intervention (enteral, oral or parenteral feeding), nutrition-related symptoms or quality of life in patients who had undergone esophagectomy. Studies were considered at any time point after surgery, so as to allow exploration of temporal trends, if present. Furthermore, studies reporting on the morbidity of jejunostomy feed use were included if the sample numbered 50 participants or greater. Series reporting smaller numbers of participants were excluded on the basis that the frequency of complications may be too small to allow meaningful interpretation of the data. Studies that reported purely quality of life, where it was not possible to extract nutrition-related symptom information, were excluded.

Search strategy

A database search strategy was formulated using subject headings and keyword search terms combined for "esophagectomy" and "nutrition therapy" or "enteral nutrition" or "parenteral nutrition" or "quality of life". Medline, Embase and CINAHL were systematically searched (Figure 1). Publications were limited to those reported in the English language during the years 1990–2016. The reference lists of identified articles and other key review publications were additionally hand searched. MP and DJB independently reviewed the process and inclusion of eligible papers.

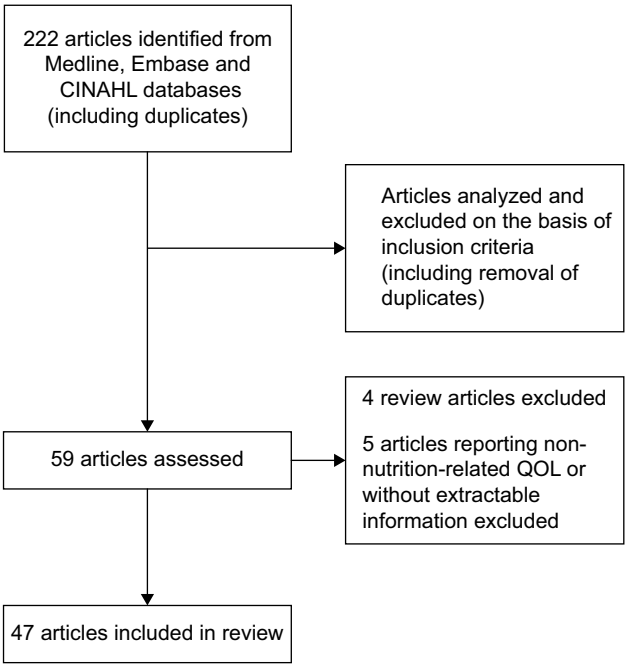

Figure 1 Summary of search strategy for systematic review.
Abbreviation: QOL, quality of life.

Assessment of quality: risk of bias

Risk of bias was assessed using the Cochrane collaborative guidance for randomized controlled trials with additional guidance from the Newcastle–Ottawa Scale for assessing nonrandomized studies.[6,7]

Data extraction

Data were extracted from the included studies by MP and then independently validated by all coauthors. A consensus was reached in areas of controversy.

Results

The database search identified 222 studies of potential interest (including duplication). Three articles were identified from the bibliographies of retrieved articles. Eligibility criteria were generally well reported, but a number of studies included patients who underwent pancreatectomy and gastrectomy as well as esophagectomy.[8–10] The length of postoperative follow-up ranged from the immediate postoperative phase to 38 years.[11] Only two studies were designed on a multicenter basis.[12,13]

After full study review, 47 articles met the inclusion criteria and formed the basis of this review (Table 1). These fell into five categories: two-arm studies comparing the outcome

Table 1 Summary of included studies

Author	Design	Country	Outcome measures of interest	Assessment of quality							
				Cochrane collaboration tool for assessment of risk of bias[6] (randomized control trials)					Newcastle–Ottawa scale[7] (cohort studies)		
				Selection bias	Performance bias	Detection bias	Attrition bias	Reporting bias	Selection (/4)	Comparability (/2)	Outcome (/3)
Sun et al[15]	C	China	Postop complications	n/a	n/a	n/a	n/a	n/a	3	1	2
Wang et al[16]	C	China	Postop complications	n/a	n/a	n/a	n/a	n/a	3	1	1
Kobayashi et al[17]	C	Japan	Postop complications	n/a	n/a	n/a	n/a	n/a	3	1	2
Tomaszek et al[18]	C	USA	Postop complications	n/a	n/a	n/a	n/a	n/a	4	1	2
Bowrey et al[19]	R	UK	Nutrition, nutrition-related QOL, cost	Low	High	High	Low	Low	n/a	n/a	n/a
Barlow et al[12]	R	UK	Postop complications	Low	High	High	Low	Low	n/a	n/a	n/a
Page et al[20]	R	UK	Postop complications	Unclear	High	High	Low	Low	n/a	n/a	n/a
Watters et al[21]	R	Canada	Postop complications	High	High	High	Low	Low	n/a	n/a	n/a
Xiao-Bo et al[22]	R	China	Postop complications	Unclear	High	High	Low	Low	n/a	n/a	n/a
Fujita et al[23]	R	Japan	Postop complications	Unclear	High	No	Low	Low	n/a	n/a	n/a
Seike et al[13]	R	Japan	Postop complications	Low	High	High	Low	Low	n/a	n/a	n/a
Cooper et al[24]	R	UK	Postop complications	Low	High	High	Low	Low	n/a	n/a	n/a
Gabor et al[25]	C	Austria	Postop complications	n/a	n/a	n/a	n/a	n/a	4	1	2
Shiraishi et al[26]	C	Japan	Postop complications	n/a	n/a	n/a	n/a	n/a	3	1	3
Aiko et al[27]	R	Japan	Postop complications	Unclear	High	High	Low	Low	n/a	n/a	n/a
Baigrie et al[28]	R	Australia	Postop complications	Unclear	High	High	Low	Low	n/a	n/a	n/a
Oya et al[29]	C	Japan	Postop complications	n/a	n/a	n/a	n/a	n/a	3	1	2
Huang et al[30]	C	China	Postop complications	n/a	n/a	n/a	n/a	n/a	4	1	2
Han-Geurts et al[31]	R	The Netherlands	Postop complications	High	High	High	Low	Low	n/a	n/a	n/a
Srinathan et al[32]	C	Canada	Postop complications	n/a	n/a	n/a	n/a	n/a	4	0	2
Llaguna et al[8]	C	USA	Postop complications	n/a	n/a	n/a	n/a	n/a	3	0	2
Fenton et al[33]	C	USA	Postop complications	n/a	n/a	n/a	n/a	n/a	3	0	2
Wani et al[34]	C	India	Postop complications	n/a	n/a	n/a	n/a	n/a	4	0	2
Gupta[35]	C	India	Postop complications	n/a	n/a	n/a	n/a	n/a	4	0	2
Ryan et al[36]	C	Ireland	Postop complications, nutrition	n/a	n/a	n/a	n/a	n/a	4	0	2
Sica et al[37]	C	UK	Postop complications	n/a	n/a	n/a	n/a	n/a	4	0	2
Yagi et al[38]	C	Japan	Postop complications	n/a	n/a	n/a	n/a	n/a	4	0	2
McCarter et al[39]	C	USA	Postop complications	n/a	n/a	n/a	n/a	n/a	4	0	2
Wakefield et al[40]	C	UK	Postop complications	n/a	n/a	n/a	n/a	n/a	3	0	2
Gerndt and Orringer[41]	C	USA	Postop complications	n/a	n/a	n/a	n/a	n/a	3	0	2
Huddy et al[14]	C	UK	Gastrointestinal symptoms	n/a	n/a	n/a	n/a	n/a	3	0	2
Deldycke et al[42]	C	Belgium	Symptoms	n/a	n/a	n/a	n/a	n/a	3	0	2
Heneghan et al[9]	C	Ireland	Symptoms	n/a	n/a	n/a	n/a	n/a	2	0	2
Greene et al[11]	C	USA	Symptoms, nutrition-related QOL	n/a	n/a	n/a	n/a	n/a	4	0	2
Carey et al[43]	R	Australia	Nutrition, symptoms, nutrition-related QOL	High	Low	High	Low	Low	n/a	n/a	n/a
Carey et al[10]	C	Australia	Nutrition-related QOL	n/a	n/a	n/a	n/a	n/a	2	0	2

(*Continued*)

Table 1 (*Continued*)

Author	Design	Country	Outcome measures of interest	Assessment of quality								
				Cochrane collaboration tool for assessment of risk of bias[6] (randomized control trials)						Newcastle–Ottawa scale[7] (cohort studies)		
				Selection bias	Performance bias	Detection bias	Attrition bias	Reporting bias	Selection (/4)	Comparability (/2)	Outcome (/3)
Wang et al[44]	C	China	Nutrition-related QOL	n/a	n/a	n/a	n/a	n/a	3	1	2
Djarv et al[45]	C	Sweden	Nutrition-related QOL	n/a	n/a	n/a	n/a	n/a	3	0	2
Haverkort et al[4]	C	The Netherlands	Symptoms	n/a	n/a	n/a	n/a	n/a	2	0	2
Parameswaran et al[46]	C	UK	Symptoms, nutrition-related QOL	n/a	n/a	n/a	n/a	n/a	3	0	2
Aghajanzadeh et al[47]	C	Iran	Symptoms, nutrition-related QOL	n/a	n/a	n/a	n/a	n/a	3	0	2
Martin et al[48]	C	Sweden	Symptoms	n/a	n/a	n/a	n/a	n/a	4	0	2
Viklund et al[49]	C	Sweden	Symptoms, nutrition-related QOL	n/a	n/a	n/a	n/a	n/a	4	2	2
Ludwig et al[50]	C	USA	Symptoms	n/a	n/a	n/a	n/a	n/a	3	0	2
McLarty et al[51]	C	USA	Symptoms, nutrition-related QOL	n/a	n/a	n/a	n/a	n/a	3	0	1
Finley et al[52]	C	Canada	Symptoms	n/a	n/a	n/a	n/a	n/a	2	0	2
Ginex et al[53]	C	USA	Symptoms	n/a	n/a	n/a	n/a	n/a	3	0	2

Notes: The Newcastle–Ottawa scores three domains, selection criteria (scored out of 4), comparability (scored out of 2) and outcomes reporting (scored out of 3). Higher scores indicate lower risk of bias from that variable. The Cochrane Collaborative tool triages bias in randomized controlled trials into low risk, high risk or uncertain risk.

Abbreviations: C, cohort study; n/a, not applicable; QOL, quality of life; R, randomized controlled trial; Postop, postoperative.

of interventions (12 studies), two-arm studies comparing timing of reintroduction of oral fluids after surgery (4 studies), two-arm studies comparing feeding access routes (3 studies), single-arm studies reporting the outcome (usually safety) of feeding access or regimen (13 studies) and single-arm studies reporting patient symptom prevalence (14 studies). One study reported the outcome of enzyme supplementation.[14] Four review articles were excluded from the analysis.

Quality of studies

Table 1 gives an overview of the quality of the studies. No study was considered to be completely free of bias. The limitations to the randomized studies largely related to performance and detection bias due to failure of blinding of patient and/or researcher to the arm of allocation. These reports were considered good in their reporting of patient follow-up and presenting all measured outcome information. The cohort studies were considered good in their reporting of representative cohorts with the condition of interest. The major sources of bias in these studies arise from their limited reporting of comparator populations.

Early challenges

Interruption of oral diet

Because of concerns about anastomotic healing, oral feeding is delayed in the first days after esophagectomy, typically, the first 5–7 days. Strategies to deal with this first week have included 1) administration of intravenous fluids only with no nutrition, 2) administration of parenteral nutrition or 3) provision of jejunal feeding by nasojejunal or jejunostomy tube coupled with intravenous fluids. The approach taken to provision of nutrition in these early days varies between centers. This was highlighted in the UK National Oesophagogastric Cancer Audit.[1] Some centers used feeding adjuncts (generally feeding jejunostomy) for all patients, some used feeding adjuncts on a selective basis in patients considered to be at high risk of nutritional failure, while other centers used no feeding adjunct at all.

Timing of reintroduction of oral diet

Table 2 summarizes the four cohort studies that evaluated optimal timing of reestablishing oral or enteral fluid intake.[15–18] The earlier reintroduction of oral or enteral fluid had no deleterious effects on clinical outcome, specifically anastomotic leak. Rather, the earlier reintroduction of oral or enteral fluids was associated with a reduced length of hospital stay, with a combined mean length of hospital stay of 19±5 vs 25±18 days (mean ± standard deviation [SD]).[15–17] The overall

Table 2 Summary of studies comparing the timing of reintroduction of oral/enteral intake

Study	Design	Sample	Early feeding regimen	Late feeding regimen	Principal study findings
Sun et al[15]	C	135	Oral fluid diet at will from postoperative day 1 (after negative gastric emptying test on the same day); n=68	Enteral feeding by jejunostomy or nasoenteral tube; commencement of oral liquid diet on postoperative day 7; n=65	Reduced length of ileus and length of hospital stay in early feeding group No difference in overall complications between two groups
Wang et al[16]	C	208	Two early enteral nutrition groups; Group 1- feed started within 48 h (n=101), Group 2 feed started 48–72 h (n=87); by nasojejunal tube	Group 3: start of enteral nutrition >72 h; by nasojejunal tube (n=20)	Reduced length of ileus and length of hospital stay in Group 1 Higher rate of pneumonia in delayed feeding group (Group 3) compared to Group 1 No difference in anastomotic leak rate between groups
Kobayash[17]	C	103	Enteral nutrition started within 3 days of surgery by jejunostomy; n=43	Enteral nutrition started after postoperative day 3 by jejunostomy; n=61	Reduced length of ileus and length of hospital stay in early feeding group No difference in postoperative complications between groups
Tomaszek et al[18]	C	386	Oral diet commenced at postoperative day 5–7 following negative contrast swallow study (conventional pathway); n=110	Feeding by jejunostomy only until postoperative week 4 (alternative pathway); n=276	Reduced length of hospital stay in early feeding group Radiologic anastomotic leak rate lower in late feeding group

Abbreviation: C, cohort study.

complication rates were similar between the two groups (40% vs 45%). The three studies that measured duration of postoperative ileus time found that earlier reintroduction of oral or enteral intake reduced duration of ileus from a mean of 7 days (SD 2) to a mean of 5 days (SD 1).[15–17] It should be highlighted that in common with most studies, resumption of eating did not occur until the seventh day, irrespective of when fluids were permitted.

Provision and value of postoperative nutritional support

There have been three studies (Table 3) comparing in hospital enteral nutrition against a control arm of intravenous fluid only.[12,20,21] These showed that enteral feeding was generally well tolerated and safe. A study by Barlow et al[12] was the only one that demonstrated a significant difference in the length of hospital stay; median length of hospital stay was 16 days (interquartile range 9) vs 19 days (interquartile range 11) in favor of enteral feeding compared to usual care (p=0.023). The other two studies showed no advantage for enteral feeding over intravenous fluids alone. It may simply be that the overall contribution from enteral feeding in hospital is too small to confer identifiable benefit. Typically, enteral feeding regimens are stepped up, with infusion rates starting off slowly, typically 20 mL/h, building up to a full feed rate of 75–100 mL/h during the course of the first week. We have previously demonstrated that even with such a planned regimen of jejunostomy feeding in hospital, the contribution from this was only 50% of estimated daily needs. Patients took on average 8 days to achieve full jejunal feeding rate.[54]

It should be borne in mind that up to 40% of patients undergoing esophagectomy will experience a postoperative complication.[1] Provision of nutrition in this group of patients is a challenge and, without enteral access, relies upon provision of parenteral nutrition for a potentially prolonged period of time.

Route of feeding access

Enteral vs parenteral nutrition

The principal routes of nutritional support employed include enteral (nasojejunal, jejunostomy) and parenteral. There have been eight studies comparing the outcome of enteral vs parenteral nutrition (Table 4).[13,22–28] Seven of these looked at the rate of individual complications between the two groups as either a primary or secondary end point.[13,22,23,25–28] The rates of surgical complications were similar in both groups; specifically, the rates of anastomotic leak (enteral: median 10%, range 0%–48%; parenteral: median 19%, range 0%–52%), wound infections (enteral: median 6%, range 2%–16%; parenteral: median 7%, range 0%–15%) and pneumonia/chest infections (enteral: median 13%, range 0%–53%; parenteral: median 11%, range 0%–62%) were comparable in both groups. Overall, these studies concluded that enteral feeding was a safe, acceptable alternative to parenteral nutrition, and that

Table 3 Summary of studies comparing enteral feeding with usual care

Study	Design	Sample	Enteral feeding regimen	Length of hospital stay in days (mean±SD)	Usual care regimen	Length of hospital stay in days (mean±SD)	Duration of follow-up	Principal study findings
Bowrey et al[5,a]	R	54	Jejunostomy: 6 weeks of overnight feeding at home to provide at least 50% of calorific requirements; n=20	19±7	No home feeding unless clinically indicated; n=21	16±7	26 weeks	High levels of compliance with patient/carer jejunostomy tube care and feeding No difference in mean cost between two arms Control group lost on average 4 kg more than intervention group at 6 weeks, with differences maintained at 3 and 6 months
Barlow et al[12,b]	R	121	Jejunostomy: 20–80 mL/h of feed commenced within 12 h of surgery until hospital discharge; n=64	16* (IQR 9)	Intravenous fluids only until oral diet recommenced (day 7–10); n=57	19* (IQR 11)	12 weeks	Reduced rate of wound/chest infections and reduced length of hospital stay in enterally fed group
Page et al[20]	R	40	Nasojejunal: 25–100 mL/h of feed until oral fluid intake re-established; n=20	14±5	Intravenous fluids until oral diet recommenced (day 7–10); n=20	13±5	1 week	Feed safe and well tolerated No difference in postoperative complications between groups
Watters et al[21]	R	28	Jejunostomy: 20–80 mL/h of feed until hospital discharge; n=13	17±9	Intravenous fluids until oral diet recommenced (day 6); n=15	16±7	1 week	No difference in hand grip strength, fatigue or vigor between groups Reduced FEV_1 and FVC in enterally fed group

Notes: [a]Included some patients having total gastrectomy, [b]included some patients having gastrectomy and pancreatectomy, *median values are quoted in study.
Abbreviations: FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; IQR, interquartile range; R, randomized controlled trial; SD, standard deviation.

enteral feeding was linked to a shorter duration of ileus and lower feed-associated costs. Parenteral feeding is no longer used in patients with an intact gastrointestinal system. Its place is solely in patients with loss of gastrointestinal continuity (prolonged ileus, postoperative complications). This is largely due to the risks of venous access complications and the much higher costs associated with parenteral over enteral nutrition.[26]

The majority of centers that administer adjunctive feeding use either nasojejunal or jejunal approaches. The limited evidence available indicates that for in-hospital use, the two are equivalent (Table 5). Although the risk of serious complications is lower with nasojejunal feeding, a robust approach is required because of frequent tube displacements or occlusions.[29–31] Furthermore, it is not a common practice to discharge patients from the hospital with nasojejunal catheters in situ, limiting their longer term use in the community.

Access problems

Table 6 summarizes the clinical outcomes for patients with feeding jejunostomies in studies reporting on 50 patients or greater.[8,30–41] Both technical and feed-related problems are quite common. The former can usually be managed by repositioning or replacing the tube, and the latter by adjusting the rate or type of feed. Tube dysfunction (occlusion or dislocation of the tube) has been reported in 0.5%–17% of patients (median 7%) and tube site infection in 0.5%–16% (median 4.5%). Gastrointestinal side effects were observed frequently, notably diarrhea and distension that were reported in 6%–24% (median 9%) and 3%–18% (median 4%) of patients, respectively.[8,30–41] The frequencies of gastrointestinal side effects shown in Table 6 are those necessitating a change in the feeding regimen (reduced infusion rate, change in type of feed, cessation of feed).

There have been four recorded deaths that were acknowledged to be directly attributable to a jejunostomy tube

Table 4 Summary of studies comparing enteral with parenteral feeding

Study	Design	Sample	Enteral feeding regimen	Parenteral feeding regimen	Principal study findings
Xiao-Bo et al[22]	R	120	Nasojejunal: 40–100 mL/h started on day 1, n=64	7 days, n=56	Earlier restoration of inflammatory markers, lower rates of postoperative infections, reduced duration of ileus and lower nutritional costs in enterally fed group No difference in serious complications or length of hospital stay between groups
Fujita et al[23]	R	154	Jejunostomy: 10–80 mL/h during days 1–6, n=76	6 days by peripheral line (calories), n=88	Reduced rate of life-threatening complications, shorter length of hospital stay, higher completion rate of planned clinical management pathway in enterally fed group No difference in overall complications between groups
Seike et al[13]	R	30	Jejunostomy: 10–60 mL/h during days 1–8, n=15	8 days at 2000 kcal daily, n=15	No difference in postoperative complications or serum immunologic markers between groups
Cooper et al[24]	R	27	Oral diet commenced at postoperative day 4, n=11	7 days at 1500 kcal daily, n=16	Reduced 90-day mortality in parenterally fed group No difference in 1-year mortality between groups
Gabor et al[25]	C	88	Nasojejunal: 10–80 mL/h days 0–6, n=44	7 days by central line, n=44	Reduced duration of ileus and length of hospital stay in enterally fed group No difference in wound infection or anastomotic leak rate between groups
Shiraishi et al[26]	C	15	250–2000 kcal daily days 1–5, N=8	8 days, n=7	No difference in biochemical markers or complication rate between groups Lower costs in enterally fed group
Aiko et al[27]	C	24	Jejunostomy: 500–1500 mL daily days 1–5, n=13	5 days by central line, n=11	No difference in complications or length of hospital stay between groups Reduced levels of immunologic markers in enterally fed group
Baigrie et al[28]	R	97	Jejunostomy: 100 kcal daily days 4–7, n=50	7 days by central line, n=47	No difference in mortality between groups Higher rate of catheter-related sepsis in parenterally fed group

Abbreviations: C, cohort; R, randomized controlled trial.

catheter (N=2510), indicating an average mortality rate of 0.2% overall (range 0%–1%).[13,32,36] Twenty-three patients were reported to require operative intervention for complications attributable to the jejunostomy tube (mean 6%, range 0%–20%).[8,31–34,36,37,40] The complications mandating re-laparotomy comprised small bowel ischemia or perforation (5 patients), small bowel obstruction (5 patients) and tube dislocation/blockage (12 patients). All of these complications occurred during the index admission for esophagectomy. There have been no reports of serious jejunostomy complications in patients receiving home feeding.

The type of feeding regimens reported were broadly similar, starting with water at a rate of 25 mL/h followed by a stepped increase in the rate of enteral feed up to peak infusion rates in the range of 84–110 mL/h.[37,39,40] Where studies reported the type of feed administered, all had used isotonic solutions. It is unclear whether all employed "rest" periods interspersed with the feeding or whether feeding was run continuously for 24 h daily.

Later challenges

Nutrition and weight

The principal challenge after hospital discharge from surgery is the weight loss that ensues. We have previously reviewed this and concluded that at 6 months after surgery, weight loss of 5%–12% was usual, with more than half the patients losing in excess of 10% of their body weight at 12 months. These observations persisted up to 3 years after surgery.[2] There is relatively little published on addressing this weight loss after surgery. In a study of 203 patients, Martin and Lagergren[55] found that 15% of patients had a preoperative weight loss of ≥10%, with 33% of patients losing ≥15% weight 3 years postesophagectomy. Two randomized controlled trials have reported the use of intensive dietetic monitoring and the use of extended enteral feeding at home.[5,43] In the first study, Carey et al randomized patients to intensive dietetic follow-up, which comprised telephone or face-to-face follow-up every 2 weeks or usual care.[43] Intensive monitoring was associated with a nonsignificant improvement in weight, but had no effect on other measures, including global quality of life scores using the European Organization for Research and Treatment of Cancer quality of life questionnaire (EORTC QLQ-C30) tool.

In the second study, we reported on the use of a planned program of home jejunostomy feeding compared to usual nutritional care, after esophagectomy.[5] In this study, supplementary overnight jejunostomy feeds provided at least 50% of energy and protein requirements for a minimum of 6 weeks after hospital discharge. Patients were encouraged to eat and drink without restriction, that is, the jejunal feed was not

Table 5 Studies comparing different routes of enteral access

Study	Design	Sample	Intervention route	Comparator route	Principal study findings
Oya et al[29]	C	378	Duodenostomy, n=111	Jejunostomy, n=267	Fewer catheter site infections with duodenostomy (1% vs 5%, p=0.08) Reduced length of hospital stay with duodenostomy (mean 15 vs 37 days, p<0.001)
Huang et al[30]	C	274	Retrosternal route gastrostomy, n=121	Jejunostomy, n=153	Use of gastrostomy associated with lower risk of intestinal obstruction (0% vs 7%, p=0.003), catheter-related infection (2% vs 6%, p=0.05) and reduced length of hospital stay (11 vs 15 days, p<0.001)
Han-Guerts et al[31]	R	150	Nasoduodenal tube, n=71	Jejunostomy, n=79	No differences in tolerance of enteral feeding (93% vs 89%) or rates of catheter-related complications (29% vs 38%) between groups

Abbreviations: C, cohort; R, randomized controlled trial.

intended to replace oral intake, but was used in addition. Home feeding was shown to have advantages in terms of weight preservation, preservation of muscle and fat stores. The impact of the intervention was further explored in a qualitative study, which interviewed 15 trial participants and 8 family members in an informal carer role.[56] All participants talked about the challenges of living with a feeding tube, but these existed even if the tube was not used for feeding. Those who used the jejunostomy tube for supplementary feeding described an overwhelming sense that the feed had "done them good". High compliance rates with the feeding regimen were seen.

Postsurgical gastrointestinal symptoms

Table 7 summarizes the studies reporting on the most common patient symptoms after surgery.[4,11,42,44–53] These indicate a high prevalence of gastrointestinal symptoms. In studies reporting at 12 months or more, symptoms were seen with the following frequency: dumping syndrome 15%–75% (median 46%), dysphagia 11%–38% (median 27%), early satiety 40%–90% (median 65%) and reflux symptoms 19%–61% (median 29%). Other symptoms reported included odynophagia with a range of 6%–37% (2 studies), delayed gastric emptying 37% (1 study) and malabsorption 73% (1 study).[42,45,47]

In patients with dysphagia, it is important to exclude anastomotic strictures, which affect up to a third of patients after surgery. In general terms, the more proximal the anastomosis, the greater is the risk of anastomotic stricture; therefore, patients with neck anastomoses after transhiatal or three-stage esophagectomy carry the greatest risk. Other risk factors include the anastomosis diameter, with a smaller diameter conferring a greater risk of stricture.[42] Anastomotic strictures can be successfully managed by endoscopic dilatation.[57] Reflux symptoms are the result of surgical removal of lower esophageal sphincter and the formation of an iatrogenic hiatal hernia as part of the esophagectomy procedure. In the author's experience, at least 50% of patients will require long-term antisecretory medications after esophagectomy. Djarv et al[45] investigated whether reduced long-term survival correlated with the markers of health-related quality of life assessed 6 months after esophagectomy. The authors found an association between nutrition-related symptoms and subsequent mortality as follows: loss of appetite (hazard ratio [HR]=1.69; 95% confidence interval [CI]: 1.32–2.14), dysphagia (HR=1.69; 95% CI: 1.13–2.51) and esophageal pain (HR=1.29; 95% CI: 1.02–1.65).

Heneghan et al[9] defined malabsorption by two or more of the following criteria: 1) steatorrhea-specific symptoms by questionnaire; 2) >10% weight loss compared to preoperative weight; 3) fecal elastase-1 level <200 µg/day; 4) fat-soluble vitamin deficiencies; 5) taking pancreatic enzyme replacement therapy and 6) positive hydrogen breath test indicating small intestinal bacterial overgrowth. They found that 73% of patients had evidence of malabsorption, an average of 2 years after surgery.[9] Huddy et al showed that 16% of patients after esophagectomy had fecal elastase-1 levels <200 µg/day, indicating mild–moderate pancreatic enzyme insufficiency.[14] Ninety percent of the treated patients reported symptomatic improvement with the use of pancreatic enzyme replacement therapy.[14]

It is also evident from Table 7 that the gastrointestinal symptoms experienced after esophagectomy persist in the longer term. In a prospective study of 218 patients after esophagectomy, Ginex et al[53] grouped symptoms (gastrointestinal and nongastrointestinal) as follows:

1. Those that had worsened after surgery, but recovered to baseline by 12 months (appetite change, taste change, cough, difficulty sleeping, dry mouth, lack of energy, not looking like self, pain, shortness of breath, weight loss);

Table 6 Jejunostomy-related complications (studies reporting on ≥50 patients)

Author	No. of subjects	Feeding regimen (feed type)	Tube-related mortality (%)	Need for operative intervention (%)	Complications		
					Tube dysfunction	Tube exit site problems	Gastrointestinal side effects
Huang et al[30]	153	N/S	N/S	N/S	2% Dislodged 6% Occlusion 7% Peritonitis	7% Infection	N/S
Srinathan et al[32]	103	N/S for 8* days (standard polymeric formula)	1	3	7% Occlusion 2% Dislodged	3% Infection	39% All side effects
Llaguna et al[8]	73	N/S	0	20	10% Dislodged 1% Occlusion	8% Infection 7% Leakage	N/S
Fenton et al[33]	143	N/S	0	1	4% Occlusion	13% Infection	N/S
Wani et al[34]	463	35–40 kcal/kg daily for 19* days (N/S)	N/S	2	7% Occlusion	N/S	9% Diarrhea 3% Distension
Gupta[35]	203	35–40 kcal/kg daily for 17* days (N/S)	N/S	N/S	6% Occlusion	N/S	8% Diarrhea 7% Distension
Han-Geurts et al[31]	79	30–84 mL/h for 10 days (isotonic Nutrison standard)	0	1	6% Occlusion 11% Dislodged	16% Infection 4% Leakage	N/S
Ryan et al[36]	205	30–100 mL/h for 20 h daily (isotonic Fresubin original)	0.5	1	3% Occlusion 2% Dislodged	1% Infection	11% Diarrhea 4% Distension 18% Constipation
Sica et al[37]	262	30–110 mL/h for 14* days (isotonic Osmolite standard)	1	2	0% Occlusion 1% Dislodged	1% Infection	N/S
Yagi et al[38]	78	1290* kcal daily for up to 69* days (N/S)	0	0	0%	4% Infection	6% Diarrhea 4% Distension
McCarter et al[39]	167	25–100 mL/h daily for 8 days (isotonic Osmolite HN)	0	N/S	6% Malfunction, dislodged or occlusion	N/S	9% Cramps 18% Distension 4% Nausea 24% Diarrhea
Wakefield et al[40]	58	25–100 mL/h daily for 7 days (Nutrison standard)	0	2	5% Dislodged 2% Occlusion	5% Infection	N/S
Gerndt and Orringer[41]	523	N/S	0	N/S	0.5% Dislodged	0.5% Leakage 0.5% Stitch abscess	N/S

Notes: *Mean values. The table shows the frequency of gastrointestinal side effects mandating a change in the feeding protocol, either feed cessation, change to a different formula or change in the infusion rate.
Abbreviation: N/S, not stated.

Table 7 Summary of studies reporting on postesophagectomy gastrointestinal symptoms

Author	Symptom/nutrition-related QOL assessment tool	No. of subjects	Duration of follow-up	Symptom prevalence				
				Dumping syndrome (%)	Dysphagia (%)	Early satiety (%)	Odynophagia (%)	Reflux symptoms (%)
Deldycke et al[42]	Institutional questionnaire (available online)	322	9 months to 12 years	21	36	N/S	N/S	39
Greene et al[11]	GI Quality of Life Index, SF-36	63	10–38 years	43	11	40	N/S	19
Ginex et al[53,a]	Memorial	185	Baseline	N/S	31	N/S	N/S	27
	Symptom	140	Postoperative	N/S	29	N/S	N/S	23
	Assessment Scale	111	6 months	N/S	30	N/S	N/S	38
		98	12 months	N/S	21	N/S	N/S	45
Djarv et al[45]	EORTC QLQ-C30 and OES-18	401	6 months	N/S	9	N/S	37	N/S
Haverkort et al[4]	Institutional questionnaire	80	1 week	74	N/S	89	N/S	60
		76	3 months	78	N/S	87	N/S	54
		69	6 months	78	N/S	87	N/S	65
		59	12 months	75	N/S	90	N/S	61
Aghajanzadeh et al[47]	Institutional questionnaire, SF36	194	12–48 months	61	34	N/S	6	19
Ludwig et al[50]	Institutional questionnaire	48	36 months	15	38	N/S	N/S	25
McLarty et al[51]	Institutional questionnaire, SF-36	107	5–23 years	50	21	N/S	N/S	29
Finley et al[52]	Institutional questionnaire	283	3 months	5	36	N/S	N/S	5
				Symptom score				
Wang et al[44,b]	EORTC QLQ-C30 and OES-18	97	2 weeks	N/S	39	N/S	N/S	29
			4 weeks	N/S	31	N/S	N/S	31
			12 weeks	N/S	24	N/S	N/S	35
			24 weeks	N/S	24	N/S	N/S	35
Djarv et al[45,b,c]	EORTC QLQ-C30 and OES-18	401	6 months (mean)	N/S	24	N/S	27	N/S
			6 months (median)	N/S	22	N/S	22	N/S
Haverkort et al[4,d]	Institutional questionnaire	80	1 week	3.7	3.3	N/S	N/S	N/S
		76	3 months	3.9	3.4	N/S	N/S	N/S
		69	6 months	3.8	3.5	N/S	N/S	N/S
		59	12 months	3.9	3.5	N/S	N/S	N/S
Parameswaran et al[46]	EORTC QLQ-C30 and OES-18	55	Baseline	3	25	N/S	14	21
		46	6 months	13	18	N/S	15	5
		40	12 months	13	16	N/S	18	26
Martin et al[48,d]	EORTC QLQ-C30 and OES-18	226	6 months	N/S	23	N/S	26	25
Viklund et al[49,b]	EORTC QLQ-C30 and OES-18	282	6 months	N/S	25	N/S	26	26

Notes: Haverkort et al[4] employed a scoring tool ranging from 0 to 7 for each symptom. The EORTC tools[58,59] use scores in the range 0–100, with higher symptom scores indicating more severe symptoms. [a]Extrapolated from Ginex et al.[53] [b]mean value reported, [c]median value reported, [d]weighted mean reported.

Abbreviations: N/S, not stated; QOL, quality of life; EORTC QLQ and OES-18, European Organization for Research and Treatment of Cancer and Oesophago-gastric disease specific 18; SF36, Short form (36 item).

2. Those that had worsened after surgery, but did not recover by 12 months (bloating, diarrhea, drowsiness, early satiety, nausea);
3. Those that had worsened after surgery and further deteriorated at 12 months (reflux) and
4. Those that were unchanged at 12 months after esophagectomy (difficulty concentrating, difficulty swallowing, sexual issues).[53]

Carey et al[10] in an interview study reported a period of adjustment to new eating patterns after esophagectomy and how patients developed a "love–hate" relationship with food and how this impacted on their socialization experiences. Patients reported specifically avoiding social situations that involved food to prevent the embarrassment of not being able to eat as much as their peers and, without warning, vomiting if they had overeaten.[43]

Conclusion

One-third of patients with esophageal cancer will undergo esophagectomy.[1] Therefore, there is a significant need to appreciate the dietetic and nutritional demands required by this cohort from the time of diagnosis through the treatment journey and beyond. Optimization of nutritional intake in order to minimize weight loss is vital to maintain the physiologic reserve required for surgery.

On the basis of the evidence presented, it is no longer feasible to routinely keep patients without oral intake for at least 7 days postoperatively due to concerns regarding anastomotic leak/damage. Early oral intake within 72 h of surgery has been shown to be safe. We have recently moved to starting oral fluids the day after surgery. There is little role for parenteral nutrition in the postoperative phase unless there is loss of gastrointestinal continuity or function. In hospital, all forms of enteral access have been shown to be safe. It is the authors' preference to place a feeding jejunostomy and to discharge patients from the hospital with this access in situ for a minimum of 6 weeks. The main benefit of enteral feeding lies in the out-of-hospital setting, where meaningful contributions to calorie and protein requirements can be made. Serious complications of jejunostomy feeding and access are limited to the immediate postresection hospitalization. It is the authors' preference to limit the jejunal feeding rate to 40 mL/h for the first 72 h after surgery or if patients are ventilated or requiring inotropic support. Complications of enteral feeding after discharge are limited to minor tube site problems and gastrointestinal symptoms. The latter can be managed by adjusting the rate or type of feed.

In the longer term, it is evident that many patients suffer from postsurgical symptoms, principally gastrointestinal. These have a deleterious effect on the quality of life and persist years after esophagectomy. The focus of future work should be on the strategies to ameliorate these symptoms.

Author contributions

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

Disclosure

The authors report no conflicts of interest in this work.

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