

2017

Impact of supplemental home enteral feeding postesophagectomy on nutrition, body composition, quality of life, and patient satisfaction

C.L. Donohoe

L.A. Healy

M. Fanning

See next page for additional authors

Follow this and additional works at: <https://arrow.tudublin.ie/scschbioart>



Part of the [Surgery Commons](#)

This Article is brought to you for free and open access by the School of Biological Sciences at ARROW@TU Dublin. It has been accepted for inclusion in Articles by an authorized administrator of ARROW@TU Dublin. For more information, please contact arrow.admin@tudublin.ie, aisling.coyne@tudublin.ie, gerard.connolly@tudublin.ie.



This work is licensed under a [Creative Commons Attribution-NonCommercial-Share Alike 4.0 License](#)

Authors

C.L. Donohoe, L.A. Healy, M. Fanning, Suzanne Doyle, A. McHugh, J. Moore, N. Ravi, and J.V. Reynolds

Impact of supplemental home enteral feeding postesophagectomy on nutrition, body composition, quality of life, and patient satisfaction

C. L. Donohoe,¹ L. A. Healy,² M. Fanning,² S. L. Doyle,^{1,3} A. Mc Hugh,² J. Moore,¹ N. Ravi,¹ J. V. Reynolds¹

¹ Department of Surgery, ² Clinical Nutrition, St. James's Hospital and Trinity College Dublin, and ³ School of Biological Sciences, Dublin Institute of Technology, Dublin, Ireland

SUMMARY. The aim of this prospective cohort study is to analyze the impact of supplemental home enteral nutrition (HEN) post-esophageal cancer surgery on nutritional parameters, quality of life (QL), and patient satisfaction. A systematic review reported that over 60% of patients lose >10% of both body weight and BMI by 6 months after esophagectomy. Enteral feeding (EF) is increasingly a modern standard postoperatively; however, the impact of extended HEN postdischarge has not been systematically studied. One hundred forty-nine consecutive patients [mean age 62 ± 9, 80% male, 76% adenocarcinoma, 66% on multimodal protocols, and 69% with BMI ≥ 25 kg/m²] were studied. Jejunal EF commenced day 1 postoperatively, and supplemental overnight HEN (764 kcal; 32g protein) continued on discharge for a planned further 4 weeks. Weight, BMI, and body composition analysis (bioimpedance analysis) were measured at baseline, preoperatively and at 1, 3, and 6 months, along with the EORTC QLQ-C30/OES18 QL measures. A patient satisfaction questionnaire addressed eight key items in relation to HEN (max score 100/item). Median (range) total duration of EF was 49 days (28–96). Overall compliance was 96%. At 6 months, compared with preoperatively, 58 (39%) patients lost >10% weight, with median (IQR) loss of 6.8 (4–9) kg, and 62 (41%) patients lost >10% BMI. Lean body mass and body fat were significantly ($p < 0.001$) decreased. Mean global QL decreased ($p < 0.01$) from 82 to 72. A high mean satisfaction score ($> 70 \pm 11/100$) was reported, >80 for practical training, activities of daily living, pain, anxiety, recovery and impact on caregivers, with lower scores for appetite (33 ± 24) and sleep (63 ± 30). Supplemental HEN for a minimum of one month postdischarge is associated with high compliance and patient satisfaction. Weight and BMI loss may still be substantial, however this may be less than published literature, in addition the impact on HR-QL may be attenuated. HEN has both subjective and objective rationale and merits further validation toward optimizing nutritional recovery and overall wellbeing.

KEY WORDS: cancer esophagus, nutrition, surgery.

INTRODUCTION

Multiple methods exist to supplement nutritional intake following esophagectomy including parenteral

and enteral routes.^{1,2} While there have been small randomized trials of the role of early enteral nutrition after esophagectomy with inconclusive outcomes, the routine placement of a feeding jejunostomy tube is increasingly the standard of care, with 68% of patients having one placed in a national audit in 2010 of centers in the UK.³ Notwithstanding an emerging acceptance of jejunostomy feeding as part of standard ERAS protocols, complications can occur, with a revision laparotomy rate of 0.9% (0%–3%) and some directly related mortalities (0%–0.5%) reported.^{8,9}

There are few cancers that are as attritional as esophageal cancer on nutritional status and nutrition-related outcomes. Weight loss, in particular muscle loss or sarcopenia, is common prior to diagnosis due to an inability to eat sufficiently, it may be affected by

Address correspondence to: Prof John V. Reynolds, Trinity College Dublin, Dublin, Ireland. Email: reynoljv@tcd.ie

Dr. L. A. Healy and Ms C. L. Donohoe are co-first authors.

Conflicts of interest: The authors declare that they have no conflicts of interest.

Specific author contributions: Claire L. Donohoe, Laura A. Healy, Suzanne L. Doyle, John V Reynolds drafted the manuscript. Michelle Fanning, Aisling Mc Hugh, Jennifer Moore, Narayanasamy Ravi co-authored the writing of the manuscript. Claire L. Donohoe, Laura A. Healy, Suzanne L. Doyle, John V. Reynolds participated in the design of the study and Laura A. Healy, Michelle Fanning, Aisling Mc Hugh, Jennifer Moore, Narayanasamy Ravi were involved in data collection. All authors read and approved the final manuscript.

neoadjuvant chemoradiation or chemotherapy, and esophagectomy itself results in significant challenges to nutritional intake as well as significant catabolism and alteration in gastrointestinal function.⁴ The most marked weight loss occurs in the first 6 months following surgery.⁵ A population-based study in Sweden reported two-thirds of patients losing more than 10% body weight in the first six months after surgery and one in five losing more than 20%.⁶ This time period is also associated with significant impairment in quality of life, and persistent weight loss is hypothesized to be a contributing factor although not previously studied.^{7–9}

Accordingly, attention to nutritional support throughout the management of patients with esophageal cancer has a compelling rationale. In the published prior experience from this Center, patients were treated with supplementary inpatient enteral nutrition for a median of 15 days, however a large proportion (26%) were not satisfactorily meeting their nutritional requirements and required additional supplementary home feeding at the time of discharge (8%) or re-commencement following discharge (12%).¹⁰ This led to a change in practice where all patients were discharged with a jejunostomy with planned supplementary nutrition for a total of four weeks. We report herein our experience with this policy, with a particular focus on compliance, nutritional outcomes, and patient satisfaction.

METHODS

Data were prospectively collected on a consecutive series of patients with esophageal cancer undergoing treatment with curative intent as determined by staging with PET-CT, EUS and multidisciplinary consensus over the period 2011–2014.¹¹ Preoperatively patients received 220 mL oral nutritional supplementation twice daily for 5 days as per departmental protocol. Patients provided written informed consent for this study and ethical approval was obtained from the institutional review board.

Patient's anthropomorphic data were measured preoperatively by a single observer (registered dietitian). Weight was measured to the nearest 0.1 kg with the patient dressed but without shoes or heavy outerwear. Height was measured to the nearest 0.5 cm with the patient barefoot. Body mass index (BMI) was calculated as weight (kg)/height (m²). All patients were asked about their baseline bodyweight at 12 months prior to diagnosis to allow an estimation of weight loss at diagnosis. Self-reported weight in patients with esophageal cancer has been reported to correlate well with measured weight.⁶ Ideal body weight was calculated using the formula developed by Robinson *et al.*¹²

Segmental body composition was analyzed using the Tanita BC 418 MA bioelectrical impedance analyzer (Tanita UK Ltd., Middlesex, UK), which gives relative information on the amount of lean and fat tissue mass. Body composition measures were recorded at diagnosis, preoperatively, and at one, three and six months postoperatively.

Health-related quality of life

Data on esophageal function and quality of life were collected through written validated European Organisation for Research and Treatment of Cancer (EORTC) quality of life questionnaires.¹³ QLQ-C30 version 3.0 incorporates five functional scales (physical, role, cognitive, emotional and social), three symptom scales (fatigue, pain, nausea, and vomiting), a global health status/HRQL scale and a number of single items assessing additional symptoms commonly reported by cancer patients (dyspnoea, loss of appetite, insomnia, constipation and diarrhea) and perceived financial impact of the disease. This is a standardized questionnaire, which is self-administered and permits group comparisons in conceptual areas covering general health. EORTC QLQ-OES18 is an esophageal cancer-specific questionnaire designed to collect information on disease- and treatment-specific symptoms and side effects.^{13–17}

Questionnaire items had four categories on a Likert scale: 1. 'not at all,' 2. 'a little,' 3. 'quite a bit,' and 4. 'very much.' In addition, the global quality of life scale had a seven step scale from 'very poor' to 'excellent.' A numeric score is computed for the answers in each of the conceptual areas as recommended by EORTC.¹⁸ Linear transformation leads to a score from 0 to 100. A higher global quality of life score equates to better overall quality of life. For functional scores, a higher score corresponds with better function, while on symptom scales, a higher score indicates worse symptoms (other than the 'dysphagia' score).

Patient satisfaction

A 24-item questionnaire was developed that addressed the practical training and management of home enteral feeding, its effect on activities of daily living (ADLs), role in recovery, psychological tolerance, specific symptoms, and its effect on family or caregivers. Questionnaires were posted to eligible patients retrospectively and a stamped address envelope was also included ($n = 113$). Questions were formatted as statements, and assessed on a five-point Likert scale graded from 'not at all' to 'yes very much.' Each individual question is scored (0–4) and data were transformed to a linear score 0–100 for analysis. Questions that addressed similar issues were grouped together for analysis into eight themes, the higher the score the better HEN is tolerated. Additional open questions

asked what HEN meant to the patient, as well as any suggestions for improving the HEN process. The responses of which were subjected to thematic analysis. The reliability of the questionnaire was testing using the Cronbach alpha, which is 0.863 and indicates good internal consistency so all items were retained.

Enteral nutrition protocol

Patients undergoing esophagectomy had a 10Ch feeding jejunostomy (Cook, UK) placed as per manufacturer's instructions approximately 40 cm beyond the duodenojejunal flexure.¹⁰ Jejunal enteral feeding was commenced at 8 am on postoperative day 1 at 30 mL/hour. Following 8 hours this was increased to 60 mL/hour and after a further 8 hours feeding at full nutritional requirement was reached. Oral feeding resumed following bedside assessment of swallow for patients who underwent esophagectomy with cervical anastomosis (transhiatal/three stage) or oral water-soluble contrast fluoroscopic swallow for those with an intrathoracic anastomosis (two-stage esophagectomy) on postoperative day 4 or 5. From that time, patients recommenced a graded introduction to diet from sips to free fluids, light diet (soup/jelly/ice-cream) and half portions of normal diet by day 7 or 8. At this point, the feeding jejunostomy feeds were reduced to supplemental night feeds. Supplemental overnight enteral nutrition (500 mL at 50 mL/hour; 755 kcal; 31 g protein) was continued on discharge for a planned duration of 4 weeks (supplemental Table S1). At the 4 week postdischarge review, if oral intake was adequate as assessed by a senior dietician and weight maintained within 5 kg of discharge weight the jejunostomy catheter was removed. In select cases of poor dietary intake or continued weight loss, supplemental feeding was continued for longer than 4 weeks.

Statistical analysis

Statistical analysis was performed using the IBM SPSS® (version 21.0) software (SPSS, Chicago, IL, USA). The Kolmogorov–Smirnov test was used to test for normal distribution. As none of the transformed quality of life scores were normally distributed non-parametric tests were used throughout. Body mass index and weight data were positively skewed so median rather than mean has been used as a measure of central tendency throughout. Continuous data and HRQL questionnaire results are presented as median (standard deviation). Continuous variables were compared using unpaired t tests for reference groups and paired t-tests for matched cases. Association of categorical variables (differences for dichotomous variables between groups) was assessed using the chi-square test. Spearman's rho was used to assess the correlation between continuous data. In this study, the

Cronbach alpha coefficient for EORTC QLQ-30 was 0.824, representing good internal consistency. Logistic regression analysis using a forward likelihood ratio selection method was used to identify predictors of weight loss, variable with $p < 0.1$ on univariate were included in the multivariate analysis. A significance level of 0.05 was used for all analyses and all p values reported are two tailed.

RESULTS

Demographics

One hundred forty-nine consecutive patients were included in the final analyses, 119 males (80%) with a mean age 62 years ± 9 . One hundred twenty patients had adenocarcinoma, the remainder were squamous cell tumors (29, 19.5%). 84 (56%) had a two-stage esophagectomy, 29 (20%) had a three-stage procedure, and 35 (25%) had a transhiatal operation. Ninety-nine patients underwent neoadjuvant chemoradiation (66%) (Table 1). Overall postoperative complications (62%) are reported in supplemental Table S2 with no postoperative mortalities and a major complication rate (Clavien–Dindo 3b/4) of 9%.

Median (range) total duration of EF was 49 days (28–96). Overall compliance was 96%.

Jejunostomy-related complications

Eleven patients (11/160; 6.9%) did not have a feeding jejunostomy *in situ* at the time of discharge and were excluded from this prospective analysis. Of this cohort, four patient's feeding catheters became blocked in the first postoperative week and could not be unblocked; two patients' feeding tubes became dislodged. Two patients pulled out their feeding tube during postoperative delirium. One patient complained of pain at the jejunostomy site and the catheter was removed and another requested that the tube be removed at the time of discharge. These patients resumed oral diet and were discharged on normal diet and oral nutritional supplements (ONS). The median % change in BMI from usual body weight to one month postoperative was 9.6% (5.3–33.8) and from preoperative BMI to one month postoperative was 10.5% (5.9–14.7). There was one serious catheter-related complication. On the sixth postoperative day, the patient developed signs of peritonitis related to peritoneal contamination from feed, at laparotomy the catheter was removed, the small bowel repaired primarily and the peritoneal cavity irrigated, the course was uncomplicated thereafter.

Changes in body weight and BMI over time

At the time of diagnosis, 96 patients (64.4%) had stable weight (<5% change from usual BMI), 26 patients

Table 1 Patient tumor and treatment characteristics according to 10% change in BMI from usual body weight to 6 months postesophagectomy

	<10% ΔBMI (n = 62)	>10% ΔBMI (n = 87)	All (n = 149)	P-value
Mean age ± SD (range)	62.3 ± 10.4	61.2 ± 7.8	62.2 ± 8.4	0.452
Male sex	49 (79.0%)	70 (80.5%)	119 (79.9%)	0.839
ASA grade				0.019
1	44 (71.0%)	43 (49.4%)	87 (58.4%)	
2	14 (22.6%)	39 (44.8%)	53 (35.6%)	
3	4 (6.5%)	5 (5.7%)	9 (6.0%)	
Usual reported BMI				0.006
<20	2 (3.2%)	3 (3.4%)	5 (3.4%)	
20–25	12 (19.4%)	34 (39.1%)	46 (30.9%)	
25–30	20 (32.3%)	10 (11.5%)	30 (20.1%)	
30+	28 (45.2%)	40 (46.0%)	68 (45.6%)	
Mean weight loss preop	0.2 ± 4.1	−4.9 ± 6.2	−2.8 ± 5.9	<0.001
Type of cancer				0.773
HGD	1 (1.6%)	3 (3.4%)	4 (2.7%)	
Adenocarcinoma	47 (75.8%)	69 (79.3%)	116 (77.9%)	
SCC	14 (22.6%)	15 (17.2%)	29 (19.5%)	
Treatment				0.08
MM	33 (%)	63 (75.9%)	99 (66.4%)	
Surgery	24 (%)	26 (31.3%)	50 (33.6%)	
Pathological stage				0.087
Stage 0	10 (16.1%)	11 (12.6%)	21 (14.1%)	
Stage 1	17 (27.4%)	26 (29.9%)	43 (28.9%)	
Stage 2	23 (37.1%)	18 (20.7%)	41 (27.5%)	
Stage 3	11 (17.7%)	30 (34.5%)	41 (27.5%)	
Stage 4	1 (1.6%)	2 (2.3%)	3 (2.0%)	
Operation type				0.338
Two stage	32 (51.6%)	52 (59.8%)	84 (56.4%)	
Three stage	16 (25.8%)	13 (14.9%)	29 (19.5%)	
Transhiatal	14 (22.6%)	21 (24.1%)	35 (23.5%)	
Esophagogastrectomy	0	1 (1.1%)	1 (0.7%)	
Nutritional risk index ³⁹				0.183
None	9 (14.5%)	9 (10.3%)	18 (12.1%)	
Mild	7 (11.3%)	22 (25.3%)	29 (19.5%)	
Moderate	45 (72.6%)	54 (62.1%)	99 (66.4%)	
Severe	1 (1.6%)	2 (2.3%)	3 (2.0%)	

Table 2 Cumulative percentage change in BMI over time

%ΔBMI change (vs. usual BMI)	Cumulative			
	Pre-op (n = 149)	1 month	3 months	6 months
Stable or increased	72	22	18	12
1%–5%	24	28	15	21
5%–9.9%	26	55	39	33
10%–14.9%	16	22	49	45
15%–19.9%	7	15	19	19
>20%	4	7	9	19

(17.5%) lost 5%–9.9%, 16 patients (10.8%) lost 10%–14.9%, 11 patients (7.4%) lost >15% of usual BMI. The mean weight loss from usual body weight to time of diagnosis was 2.8 kg ± 5.9. Excluding patients who had less than one kilogram weight loss, i.e. in those patients who lost more than 1 kg at time of diagnosis, the mean weight loss was 6.1 kg ± 5.1.

At 6 months, compared with preoperatively, 58 (39%) patients lost >10% weight, with median (IQR) loss of 6.8 (4–9) kg, and 62 (41%) patients lost >10% BMI. Compared to usual body weight, 87 patients (58.3%) had more than 10% change in BMI compared to their usual body weight at 6 months (Table 2).

Twenty-five patients (16.4%) had stable weight from time of diagnosis to 6 months postoperatively,

29 patients (19.1%) lost weight prior to surgery but did not lose any weight in the postoperative period. The remaining 94 patients (63.1%) lost weight in the postoperative period. Overall weight loss from usual body weight to time of follow-up did not differ according to whether patients had neoadjuvant treatment or not. The neoadjuvant treatment regimen (type of chemotherapy, chemoradiotherapy) did not affect the overall weight loss.

The mean percentage change in BMI was greatest in the preoperative period and in the first month postoperative: 3.3 ± 7.2% and 4.4 ± 3.9%, respectively. From 1 to 3 months, the average loss in BMI was 3.1 ± 3.5% and from 3 to 6 months 1.2 ± 3.4%. The rate of weight loss slowed in the 3–6 month time period postoperative. Only 12 patients lost more than 5% BMI during this window—i.e. had persistent weight loss by this time (Supplementary Table S5). The median% change in BMI during the in-hospital stay was 1.2% (range: 6.75% gain to 12.1% loss). The change in weight during the hospital stay was moderately correlated with the comprehensive complications index (CCI) (Pearson's rho: 0.347, *p* < 0.01) and length of stay (0.547, *p* < 0.01). CCI did not correlate with usual body mass or overall weight loss but it did weakly correlate with weight loss from usual body weight to

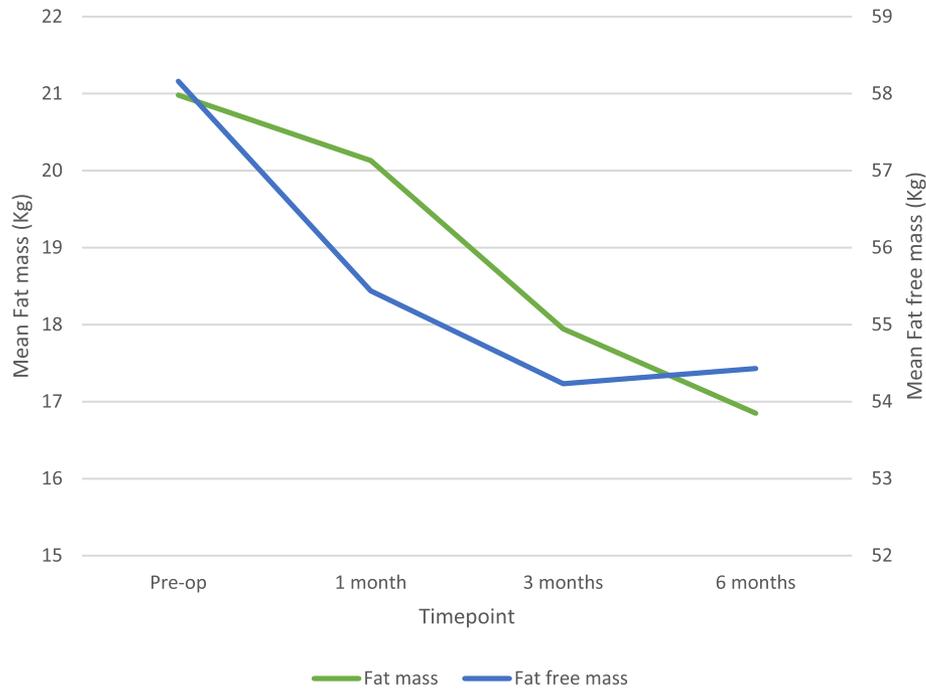


fig. 1 Change in fat mass and fat-free mass over time.

preoperative weight ($0.174, p < 0.01$). Compared to their preoperative BMI, 40 patients (26.8%) had stable or $<5\%$ change in BMI at 6 months following discharge from hospital, 42 patients (28.0%) lost between 5% and 9.9% of BMI, 37(25%) patients lost 10%–14.9% BMI and 25 patients (17%) lost $>15\%$ BMI in the first 6 months following surgery.

Weight change compared to ideal body weight

At the time of long-term followup, 23 patients (15%) were more than 5 kg under their ideal weight. The remainder of patients were at, or above, their ideal body weight in spite of weight loss. Patients who had a usual BMI of 25 kg/m^2 or lower had a mean 1.8% (± 1.63) change in BMI by 6 months, which was significantly less than the mean $\%$ change in BMI ($3.81\% \pm 2.3$) of those who were overweight or obese usually.

Changes in body composition over time

Overall the mean percentage loss of fat mass was $14.76 \pm 30.3\%$ and of lean body mass was $6.1 \pm 7.04\%$. Most weight was lost in the first 3 months postoperatively with a relative preservation of lean body mass between 3 and 6 months but a further decrease in fat mass (Fig. 1). Overweight or obese patients prior to diagnosis had a mean percentage change of fat mass of $18.95\% \pm 18.48\%$ versus those with BMI $< 25 \text{ kg/m}^2$ ($2.5\% \pm 49.5\%$, $P = 0.006$). The percentage change in lean body mass was not significantly different between BMI $>$ vs. $< 25 \text{ kg/m}^2$ ($6.5 \pm 6.5\%$ vs. $4.9 \pm 8.5\%$, $p = 0.252$).

In patients who had a greater than 10% change in BMI to the point of long-term follow-up, the mean change in fat mass was $30.6 \pm 16.24\%$ and was significantly greater than those who had lesser changes ($<10\%$) in BMI (mean change in fat mass $3.2\% \pm 32.9$, $p < 0.001$). The correlation between fat mass at the time of diagnosis and percentage change in BMI was weak ($\rho = 0.251$ ($P = 0.002$)).

In patients who had lost the most weight at time of diagnosis compared to usual body weight, the degree of weight loss following surgery was less compared to those who had lost little weight at the time of diagnosis i.e. $\%$ loss of BMI in postoperative period (mean \pm SD): $<5\%$ loss or stable weight at time of diagnosis: $8.3\% \pm 6.1\%$; 5%–10% loss at diagnosis: $5.9\% \pm 5.2$; 10%–15% loss at diagnosis: $5.8\% \pm 5.8$, $>15\%$ loss at diagnosis: $3.3\% \pm 5.5$, $p = 0.016$.

Predictors of weight loss

There were no significant differences in overall survival between patients who lost $>10\%$ of BMI and those who lost $<10\%$ (42.5 ± 2.2 months vs. 50.3 ± 2.7 , $p = 0.112$). Weight loss of those who died within 1 year of diagnosis did not differ compared to those who survived for longer (13.4 vs. 11.3% , $p = 0.68$). 67.9% ($n = 19$) of patients with squamous tumors had no weight loss or weight gain at the time of long-term follow-up compared to 29.4% ($n = 35$) of patients with adenocarcinoma ($p < 0.001$). 16.7% of patients with squamous tumors lost $>10\%$ BMI compared with 45% of patients with adenocarcinoma ($p = 0.003$).

Table 3 Predictors of weight loss: multivariate analysis greater and less than 10% from usual body weight at time of long-term follow up

Factor	Univariate analysis		Multivariate analysis	
	Hazard ratio (95%CI)	P-value	Hazard ratio (95%CI)	P-value
Sex (male vs. female)	0.91 (0.41–2.04)	0.815	Not entered	
Age at diagnosis (years)	0.99 (0.95–1.02)	0.503	Not entered	
Adenocarcinoma	1.31 (0.587–2.935)	0.508	Not entered	
Pathological N stage (negative versus positive)	1.88 (0.911–3.878)	0.087		0.272
R0 resection RCP	1.199 (0.547–2.627)	0.65	Not entered	
CAP	3.038 (0.622–14.829)	0.17		
Pathological T stage (pT3/4)	1.515 (0.777–2.956)	0.223	Not entered	
Major post op complication (Clavien 3/4)	1.21 (0.55–2.68)	0.638	Not entered	
Neoadjuvant therapy	1.799 (0.909–3.558)	0.092		0.938
Usual BMI (>30)	2.63 (1.23–5.62)	0.013		0.197
Usual BMI (>25)	3.36 (1.54–7.34)	0.002	3.123 (1.406–6.939)	0.005
ASA grade (3 vs. others)	2.29 (0.54–9.73)	0.263	Not entered	
(2 vs. others)	0.78 (0.197–3.11)	0.727		
Clinical T stage (cT3./4)	2.196 (1.106–4.36)	0.025	2.156 (1.064–4.366)	0.032
Clinical N stage (cNpositive)	1.059 (0.552–2.034)	0.863	Not entered	

On multivariate logistic regression analysis (supplemental Table S4), significant independent predictors of >10% loss of BMI from usual body weight were: Usual BMI ≥ 25 kg/m² (OR: 3.123 (1.406–6.939), $p = 0.005$) and Clinical (predicted preoperative) T stage 3/4 (OR: 2.156 (1.064–4.366), $p = 0.032$) (Table 3). Only R0 resection was a significant independent negative predictor of >10% loss of BMI in the postoperative period (OR 0.176 (0.05–0.611), $p < 0.006$) (Supplemental Table S2).

Quality of life

Mean global QL decreased ($p < 0.01$) from 82 to 72. There was no correlation with weight loss at time of diagnosis and any of the HRQL scales measured at baseline (supplemental Table S5). Global HRQL at long-term follow-up was not significantly different in those with <10% weight loss versus those with >10% (68.7 \pm 20.6 vs. 70.95 \pm 17.5, $p = 0.519$) (supplemental Table S3). In those that had persistent weight loss (>5% BMI) in the 3 to 6 months postoperative period ($n = 12$), there was a clinically relevant >10 point decrease in HRQL in physical (76.7 vs. 87.5, $p = 0.066$) and social function (76.4 vs. 87.8, $p = 0.034$).

Patient satisfaction

The response rate to the study specific patient questionnaire was 81% ($n = 92$), although 14 patients were excluded due to incomplete data ($n = 78$). The median time from operation date to completing questionnaire was 14 months (6–28 months). Overall supplementary HEN was viewed very positively by patients with a high overall total score awarded. The main themes that emerged from responses to open questions were HEN enhanced recovery, allowed earlier discharge, as well as increasing confidence and providing reassurance about the adequacy of nutritional intake. HEN

also reduced worry about further weight loss with sub optimal dietary intakes post discharge. All patients were advised to use HEN at night to encourage a return to eating; as such sleep disturbance was an issue for some. Increased community support, more secure attachment of JEJ tube and more information on unblocking JEJ tube, were some suggestions made by patients.

A high mean satisfaction score (>70/100 \pm 11) was reported, >80 for practical training, activities of daily living, pain, anxiety, recovery and impact on caregivers, with lower scores for appetite (33 \pm 24) and sleep (63 \pm 30).

DISCUSSION

Alterations in weight following esophagectomy are substantial and attributable to changes in anatomy, gastrointestinal hormonal physiology, appetite, nutritional intake, malabsorption, and cachexia. Oral intake at the time of discharge from hospital is often suboptimal¹⁰ and remains less than required for at least 6 months after surgery in a large proportion of patients, 25% in one study.¹⁹ A number of nutrition-related symptoms are described after esophagectomy¹ including early satiety (affecting 90% of patients), postprandial dumping (75%), difficulty swallowing high viscosity foods (72%), reflux and absence of hunger (50%).²⁰ In a study from the Netherlands, 75% of patients required some form of enteral nutrition support after discharge from hospital in order to meet their nutritional requirements, consistent with previous reports from this Center.^{20,10} These issues, allied with the substantial weight loss noted after esophagectomy,^{1,4} make interventions aimed at improving intake and halting weight loss compelling.

Although early oral feeding is the standard of care increasingly for gastrointestinal surgery as part

of enhanced recovery protocols, concerns exist in esophageal cancer surgery and only one study has reported on the safety of early oral intake.²¹ Consequently, at this time, feeding jejunostomies are increasingly standard. In a systematic review published in 2015, of 12 studies reporting outcomes for jejunostomy placement in 3293 patients, it was concluded that this was an effective means of meeting nutritional requirements in the early postoperative period but with a small potential for serious complications.²² However, data on patient satisfaction and long-term nutritional outcomes were lacking in this review and in individual series. It is surprising, given the opportunity for continued enteral support provided via this access, that few studies report on purposeful continued home enteral nutrition, and none on a systematic analysis of nutritional and clinical outcomes reported in this study, as well as patient's satisfaction and perspectives. Some cohort studies report the feasibility of routine home enteral supplementation as part of a standardized perioperative clinical pathway but no prospective studies to date have not analyzed the impact of home enteral nutrition on intermediate term changes in body composition or quality of life,^{23–26} important endpoints for patients. The most comparable study is a randomized trial of 54 patients comparing home enteral nutrition for 6 weeks with usual standard, and reporting a mean difference in weight loss at 6 months of 2.5 kg favoring the supplemented cohort, nutritionally supported for between 54 and 172 days, and improvements in muscle strength and anthropometric measurements.²⁷

This prospective study of prolonged home enteral nutritional supplementation highlights several findings. First, weight loss after esophagectomy is almost universal and loss of >10% BMI occurs frequently, despite dedicated dietetic support and prolonged home enteral supplementation. Previous studies have reported weight loss of greater than 10% in the first 6 months postoperatively in two thirds of patients and of more than 20% in one fifth.⁶ In this study, the relevant figures were 39% of patients experiencing >10% weight loss compared to preoperative weight and only 4% had >20% weight loss during this time period, these data suggesting that dedicated dietetic support and supplemental nutrition may limit more severe degrees of weight loss in the postoperative period. This study also provides a comparison from usual body weight and permits assessment of the change in weight during the time course of the illness.

Second, weight and BMI loss postoperatively strongly relates to preoperative weight loss, and usual weight and BMI. In a population-based survey of 340 Swedish patients, postoperative weight loss was greatest in those who lost least weight preoperatively: for those who lost <15% BMI preoperatively the adjusted OR for postoperative weight loss was 0.13 (0.03–0.65) versus those who had lost <10% BMI

preop.⁵ These findings were also broadly similar in this cohort, with patients either losing most weight either before surgery or after but culminating in weight loss for the majority (92%) and substantial (>10%BMI) in 56% of cases. Consistent with the Swedish study, we did not find tumor factors or survival to be associated with weight loss up to 6 months, but patients who were overweight or obese were most likely to lose >10% BMI over the course of treatment and follow-up.⁴ Most patients regressed to their ideal body weight, with only 15% significantly below ideal body weight. Weight loss was accelerated in those who had most excess body weight at baseline. Previous studies in Asian populations post-total gastrectomy have shown that weight loss in the first 3–6 months postoperatively was mainly body protein.²⁸ This study shows that while there is loss of both lean and fat mass, a greater proportion of the overall weight loss is from the body stores of adipose tissue in this Western population and the greater weight loss noted in obese patients was attributable to loss of excess fat mass rather than lean body mass.

Although dietary intake and weight loss are important determinants of functional quality of life in qualitative studies,²⁹ in this study there were no observed differences in HRQL according to differences in weight loss. It should be noted that the health-related quality of life scores at 6 months of the present cohort are significantly greater than the means reported in most other large studies of HRQL postesophagectomy^{8,30,31} and this could be hypothesized to be attributable to home enteral nutrition but is unlikely to be due to a single factor. Specifically the mean emotional and social role scores show both a clinically relevant and statistically significant >10 point difference compared to the largest single series of 132 patients at 6 months post-esophagectomy.⁷ Since we did not note any substantial differences in HRQL among those who lost significant amounts of weight nor those who fell below their ideal weight, it may suggest that weight loss does not correlate with quality of life, perhaps because the majority of patients with esophageal adenocarcinoma are overweight or obese, and many happily accept a loss of 10%–15% of BMI. Few patients were below their estimated ideal body weight at 6 months of follow-up and perhaps this is a more valid goal than usual body weight.

Since weight loss to some degree is almost universal following esophagectomy the question arises whether this weight loss is inevitable and if nutritional support can succeed in reversing it. Since anatomical and physiological changes after esophagectomy may be analogous to bariatric surgery,³² it should not be surprising that some of the effects mirror those of these surgeries^{33,34} and may not be undesirable. The alternative is that these changes are in part attributable to the multifactorial syndrome of cachexia, which

by definition is not reversible by nutritional supplementation alone.³⁵ Since cachexia encompasses numerous metabolic alterations in adipose tissue, skeletal muscle, central nervous and immune systems, and heightened systemic inflammation and cytokine release, a single approach to its treatment, such as nutritional supplementation alone, may not be effective.^{36–38}

Limitations of the study are acknowledged, including the fact that supplementation was modest, and continued just for a median of 49 days. A detailed dietary history of individual patients on supplemental home enteral nutrition, and beyond that, would also be of interest, but was beyond the scope of this study. Assessment of functional outcomes relating weight loss to exercise and physical function would allow enhanced understanding of the impact of weight loss on patient-related outcomes.

In conclusion, home enteral nutrition was delivered with high compliance and patient satisfaction, and complications were rare. Weight loss and negative consequences on quality of life occurs despite supplemental nutrition in the majority of patients, but the severity of weight loss and impact on quality of life may be less than published benchmarks. More fat mass is lost than previously thought, especially in patients who are overweight or obese at baseline. This study raises important questions regarding the goals of care following esophagectomy, such as how much weight loss is acceptable to patients and to what degree weight loss impacts on quality of life. We suggest that these data provide useful baseline parameters as well as a solid hypothesis for the design of a randomized trial of the impact of prolonged home enteral nutrition on weight and body composition changes as well as HRQL.²⁷

References

- Baker M, Halliday V, Williams RN *et al*. A systematic review of the nutritional consequences of esophagectomy. *Clin Nutr* 2015; 35 (5): 987–94.
- Markides G, Al-Khaffaf B, Vickers J. Nutritional access routes following esophagectomy—a systematic review. *Eur J Clin Nutr* 2011; 65: 565–73.
- Audit NO-GC. Third annual report. Leeds: NHS Information Centre 2010.
- Martin L, Lagergren P. Long-term weight change after esophageal cancer surgery. *Br J Surg* 2009; 96: 1308–14.
- Martin L, Jia C, Rouvelas I *et al*. Risk factors for malnutrition after esophageal and cardia cancer surgery. *Br J Surg* 2008; 95: 1362–8.
- Martin L, Lagergren J, Lindblad M *et al*. Malnutrition after esophageal cancer surgery in Sweden. *Br J Surg* 2007; 94: 1496–500.
- Djävrv T, Metcalfe C, Avery K N L *et al*. Prognostic value of changes in health-related quality of life scores during curative treatment for esophagogastric cancer. *J Clin Oncol* 2010; 28: 1666–70.
- Donohoe C L, McGillicuddy E, Reynolds J V. Long-term health-related quality of life for disease-free esophageal cancer patients. *World J Surg* 2011; 35: 1853–60.
- Jacobs M, Macefield R, Elbers R *et al*. Meta-analysis shows clinically relevant and long-lasting deterioration in health-related quality of life after esophageal cancer surgery. *Qual Life Res* 2014; 23: 1155–76.
- Ryan A M, Rowley S P, Healy L A *et al*. Postesophagectomy early enteral nutrition via a needle catheter jejunostomy: 8-year experience at a specialist unit. *Clin Nutr* 2006; 25: 386–93.
- Reynolds J V, Donohoe C L, McGillicuddy E *et al*. Evolving progress in oncologic and operative outcomes for esophageal and junctional cancer: lessons from the experience of a high-volume center. *J Thorac Cardiovasc Surg* 2012; 143 (5): 1130–7.
- Robinson J, Lupkiewicz S, Palenik L *et al*. Determination of ideal body weight for drug dosage calculations. *Am J Health Syst Pharm* 1983; 40: 1016–9.
- Aaronson N K, Ahmedzai S, Bergman B *et al*. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 1993; 85: 365–76.
- Blazeby J M, Alderson D, Winstone K *et al*. Development of an EORTC questionnaire module to be used in quality of life assessment for patients with esophageal cancer. *Eur J Cancer* 1996; 32: 1912–7.
- Blazeby J M, Kavadas V, Vickery C W *et al*. A prospective comparison of quality of life measures for patients with esophageal cancer. *Qual Life Res* 2005; 14: 387–93.
- Clifton J C, Finley R J, Gelfand G *et al*. Development and validation of a disease-specific quality of life questionnaire (EQOL) for potentially curable patients with carcinoma of the esophagus. *Dis Esophagus* 2007; 20: 191–201.
- Blazeby J M, Conroy T, Hammerlid E *et al*. Clinical and psychometric validation of an EORTC questionnaire module, the EORTC QLQ-OES18, to assess quality of life in patients with esophageal cancer. *Eur J Cancer* 2003; 39: 1384–94.
- on GroupFayers PM AN, Bjordal K, Groenvold M, Curran D, Bottomley A, . botEQoL. The EORTC QLQ-C30 Scoring Manual, 3rd edn. Brussels, European Organisation for Research and Treatment of Cancer, 2001.
- Haverkort E B, Binnekade J M, de Haan R J *et al*. Suboptimal intake of nutrients after esophagectomy with gastric tube reconstruction. *J Acad Nutr Diet* 2012; 112: 1080–7.
- Haverkort E, Binnekade J, Busch O *et al*. Presence and persistence of nutrition-related symptoms during the first year following esophagectomy with gastric tube reconstruction in clinically disease-free patients. *World J Surg* 2010; 34: 2844–52.
- Lewis S J, Andersen H K, Thomas S. Early enteral nutrition within 24 h of intestinal surgery versus later commencement of feeding: a systematic review and meta-analysis. *J Gastrointest Surg* 2009; 13: 569–75.
- Weijs T J, Berkelmans G H, Nieuwenhuijzen G A *et al*. Routes for early enteral nutrition after esophagectomy. A systematic review. *Clin Nutr* 2015; 34: 1–6.
- Preston S, Markar S, Baker C *et al*. Impact of a multidisciplinary standardized clinical pathway on perioperative outcomes in patients with esophageal cancer. *Br J Surg* 2013; 100: 105–12.
- Tomaszek S C, Cassivi S D, Allen M S *et al*. An alternative postoperative pathway reduces length of hospitalisation following esophagectomy. *Eur J Cardio Thorac Surg* 2010; 37: 807–13.
- Porteous G H, Neal J M, Slee A *et al*. A standardized anesthetic and surgical clinical pathway for esophageal resection: impact on length of stay and major outcomes. *Reg Anesth Pain Med* 2015; 40: 139–49.
- Bolton J S, Conway W C, Abbas A E. Planned delay of oral intake after esophagectomy reduces the cervical anastomotic leak rate and hospital length of stay. *J Gastrointest Surg* 2014; 18: 304–9.
- Bowrey D J, Baker M, Halliday V *et al*. A randomised controlled trial of six weeks of home enteral nutrition versus standard care after esophagectomy or total gastrectomy for cancer: report on a pilot and feasibility study. *Trials* 2015; 16:531.
- Kiyama T, Mizutani T, Okuda T *et al*. Postoperative changes in body composition after gastrectomy. *J Gastrointest Surg* 2005; 9: 313–9.

- 29 Wainwright D, Donovan J L, Kavadas V *et al*. Remapping the body: learning to eat again after surgery for esophageal cancer. *Qual Health Res* 2007; 17: 759–71.
- 30 Djärv T, Blazeby J M, Lagergren P. Predictors of postoperative quality of life after esophagectomy for cancer. *J Clin Oncol* 2009; 27: 1963–8.
- 31 Viklund P, Wengström Y, Rouvelas I *et al*. Quality of life and persisting symptoms after esophageal cancer surgery. *Eur J Cancer* 2006; 42: 1407–14.
- 32 Elliott J A, Jackson S, King S *et al*. Gut Hormone Suppression Increases Food Intake After Esophagectomy With Gastric Conduit Reconstruction. *Ann Surg* 2015; 262: 824–30.
- 33 Buchwald H, Avidor Y, Braunwald E *et al*. Bariatric surgery: a systematic review and meta-analysis. *JAMA* 2004; 292: 1724–37.
- 34 O'Brien PE, McPhail T, Chaston TB *et al*. Systematic review of medium-term weight loss after bariatric operations. *Obes Surg* 2006; 16: 1032–40.
- 35 Fearon K, Strasser F, Anker S D *et al*. Definition and classification of cancer cachexia: an international consensus. *Lancet Oncol* 2011; 12: 489–95.
- 36 Donohoe C L, Ryan A M, Reynolds J V. Cancer cachexia: mechanisms and clinical implications. *Gastroenterol Res Pract* 2011; doi:10.1155/2011/601434.
- 37 Fearon K C, Glass D J, Guttridge D C. Cancer cachexia: mediators, signaling, and metabolic pathways. *Cell Metab* 2012; 16: 153–66.
- 38 Argiles J M, Busquets S, Stemmler B *et al*. Cancer cachexia: understanding the molecular basis. *Nat Rev Cancer* 2014; 14: 754–62.
- 39 Wolinsky F D, Coe R M, McIntosh W A *et al*. Progress in the development of a nutritional risk index. *J Nutr* 1990; 120: 1549–53.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article.

Supplementary Table S1. Composition of Feeds.

Supplementary Table S2. Post-operative Complications.

Supplementary Table S3. % change in BMI within each time period.

Supplementary Table S4. Predictors of weight loss: multivariate analysis Greater and less than 10% loss of BMI from time of surgery to long-term follow-up.

Supplementary Table S5. HRQL at 6 months post esophagectomy according to weight loss post-operatively.