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Original article

Oesophageal cancer: The effect of early nutrition support on clinical outcomes

S.J. Davies [a, *], M.A. West [b], S.A. Rahman [b], T.J. Underwood [b], L.V. Marino [a, c, d]

[a] Department of Dietetics/ Speech and Language Therapy, University Hospital NHS Foundation Trust Southampton, Tremona Road, Southampton, SO16 6YD, UK
[b] School of Cancer Sciences, Faculty of Medicine, University of Southampton, UK
[c] NIHR Biomedical Research Centre Southampton, University Hospital NHS Foundation Trust Southampton, UK
[d] Nutrition and Dietetics, Faculty of Health and Well Being, University of Winchester, UK

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SUMMARY

Background and aims: Malnutrition is prevalent in oesophageal cancer. Evidence for the use of nutrition support and prehabilitation in this cohort is variable. The aim of this study was to examine the effect of early nutrition support and functional measures of nutritional status on post-operative outcomes in adult patients with oesophageal cancer.
Methods: Retrospective review of adults with oesophageal cancer undergoing oesophagectomy (n = 151). Early nutrition support was defined as: oral or enteral nutrition supplementation during neoadjuvant treatment. Late nutrition support defined as: oral or enteral nutrition supplementation prescribed post-operatively. Nutrition outcome measures were; percentage weight loss from 3 to 6 months prior to diagnosis, peri- and post-operatively, and pre-operative assessment of handgrip-strength (HGS).
Results: Pre-operative weight loss ≥10% was a significant predictor of mortality at 1 year (OR 2.84, 95%CI 1.03–7.83, p = 0.04) independent of tumour stage, adjuvant treatment, age and gender. Adults prescribed early nutrition support during neoadjuvant treatment experienced less weight loss at 12-months post-oesophagectomy compared to adults prescribed late oral nutrition support (p=<0.05). Pre-operative HGS measurements were not a useful predictor of postoperative complications (p = 0.2), length of stay (p = 0.9) or 90-day mortality (p = 0.6).
Conclusions: Pre-operative weight loss ≥10% was associated with mortality. Early nutrition support was associated with less weight loss at 12-months post-operatively. Pre-operative HGS measures did not have prognostic value as a stand-alone measure. Future work should investigate the efficacy of early nutrition support in reducing both pre- and post-operative weight loss to improve nutritional status and surgical outcomes as part of a multimodal prehabilitation programme in adults with oesophageal cancer.

What we know:

- Patients with oesophageal cancer are at high risk of malnutrition
- Improving nutritional status prior to surgery has been identified as an important priority in improving clinical outcomes in adults with cancer

What this study adds:

- Significant pre-operative weight loss ≥10% was associated with increased mortality at 90 days and 1 year post-operatively
- Early nutrition support during neoadjuvant treatment was associated with less weight loss at 12 months post-operatively
- Handgrip strength was not a useful predictor of post-operative clinical outcomes

* Corresponding author. University Hospitals Southampton NHS Foundation Trust, Mailpoint 32, Tremona Road, Southampton, SO16 6YD, UK.
E-mail address: sarah.davies2@uhs.nhs.uk (S.J. Davies).

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1. Introduction

Approximately 9100 people per annum are diagnosed with oesophageal cancer in the United Kingdom (UK) [1]. Around 38% of those diagnosed are managed with curative intent in the form of oesophagectomy, often preceded with neoadjuvant chemotherapy or chemoradiotherapy. Overall post-operative complication rates of 65% have been reported, with major complications (Clavien-Dindo ≥3b) occurring in 16.9% [2]. The incidence of malnutrition in patients with oesophageal cancer is reported to be 22–62% [3]. Individuals are at increased risk of malnutrition arising from disease related symptoms including dysphagia, vomiting, loss of appetite and paraneoplastic effects, further exacerbated by side effects of neoadjuvant treatment [4].

Identifying those individuals at risk of malnutrition is important and although many nutrition screening tools exist, there is no consensus related to the optimal screening tool for use in the pre-operative surgical patient [5]. Simple measures such as body mass index (BMI) do not discriminate between lean or fat mass, or measures of body composition. Nutritional status may be an important risk factor for major complications after oesophagectomy [6] and assessment should be undertaken in all patients with a view to detecting and optimising nutritional status before surgery [7].

Improving nutritional status prior to surgery has been identified as an important priority in improving clinical outcomes for adults with cancer. Identifying those individuals at risk of malnutrition is important as current measures of body mass index (BMI) are inadequate as this does not discriminate between lean or fat mass and measure muscle function.

Techniques including the use of handgrip strength (HGS) have been shown to be a functional measure of muscle mass [8] and may be a simple, cost-effective measurement to complete in an outpatient setting [9]. Low handgrip strength is associated with increased mortality in a mixed cohort of cancer diagnoses [10,11], treatment modification (such as delay in chemo/radiotherapy >1 week, dose reduction, hospital admission or discontinuation of treatment) during chemoradiotherapy in oesophageal cancer [12] and as a predictor of postoperative complications in adults following oesophagectomy [13–15].

Pre-operative nutritional interventions have been shown to specifically improve perioperative outcomes in GI and cancer surgical patients [16]. Prehabilitation is the process of enhancing functional capacity in advance of a known physiologically stressful event, such as cancer therapy or surgery, and aims to 1) empower adults with cancer to take ownership of their treatment, 2) reduce the risk of post-operative morbidity, and 3) improve the rate of post-operative recovery [17]. It has increasingly become focussed on three components; exercise, nutritional optimisation and psychological support, which in a research setting has been found to provide complementary benefit as a multimodal approach [18].

The aims of this study were to examine the effect of early nutrition support on outcomes in adults with oesophageal cancer following an oesophagectomy; and to assess if functional markers of nutritional status were predictive of clinical outcomes in adults with oesophageal cancer following an oesophagectomy.

2. Materials and methods

2.1. Study design and patient population

A retrospective study was completed with inclusion criteria being all adults who underwent an oesophagectomy for adenocarcinoma or squamous cell carcinoma (SCC) in a specialist regional centre in the UK between April 2016 and July 2019. Data were anonymised, collected from electronic medical notes and dietetic record cards. Exclusion criteria included patients who underwent partial or total gastrectomy, colonic interposition graft or oesophagectomy for benign perforation or neuroendocrine pathology. After consulting the local research ethics committee, the need for ethics approval was waived due to the retrospective nature of the study. It was however registered through the University Hospital Southampton NHS Foundation Trust Clinical Governance system (Audit number 6308).

2.2. Nutrition support

Patients were categorised into two groups of early and late nutrition support. Early nutrition support: adults with oesophageal cancer who were referred by a clinician for nutrition assessment and individualised nutrition support by a dietitian before or during neoadjuvant treatment. Duration of early nutrition support was therefore commenced a minimum of 8–10 weeks pre-operatively. Adherence to the prescribed nutrition support was recorded according to the clinical judgement of the dietitian. Late nutrition support: adults with oesophageal cancer in the late group were subjectively not deemed by a clinician to require nutrition support pre-operatively.

All patients were assessed by a dietitian at the pre-operative assessment clinic, reviewed daily during post-operative hospital stay and reviewed post discharge at the multi-disciplinary clinic. Patients followed a published and validated enhanced recovery programme [19] with early oral feeding commenced and built up to a purée consistency diet by Day 5 post-operatively. In the post-operative phase individuals were prescribed 2 × 125ml high protein oral nutritional supplements (ONS) as a first line in addition to oral diet. Surgical jejunostomy tubes were not routinely placed, but at the discretion of the surgeon if concerns of post-operative complications arose which would delay or prevent early oral feeding were suspected, or if the dietitian raised concerns regarding the individuals' nutritional status following nutritional assessment.

2.3. Nutritional status

Before each appointment with a dietitian patients were weighed on a standing scale, with shoes and outerwear removed, with minimal clothing. Patients were also weighed weekly during neoadjuvant chemoradiotherapy or prior to each cycle of chemotherapy. Baseline weight was recorded 3–6 months prior to diagnosis and at 12 months post-operatively. This was obtained from hospital or GP records where available, or through patient-reported weight. Height was measured using a Leicester height measure at their first clinic appointment. BMI was calculated and weight loss was calculated and recorded as a percentage (categorised as <10% or ≥10% from baseline).

Handgrip strength was measured by the dietitian at the surgical pre-operative assessment clinic using a Jamar Hydraulic hand dynamometer. The patient was asked to sit in a chair with the arm held in a right angle position. Measurements were taken from alternative arms, with an average of three measurements from the non-dominant side recorded. Low HGS was defined as <27 kg for men and <16 kg for women as per European guidelines [20].

2.4. Clinical outcomes

The primary outcome measure was post-operative complications, with severity graded according to the Clavien-Dindo Classification [21]. A major complication was regarded as Clavien-Dindo

≥3b. Secondary outcomes were post-operative length of hospital stay and mortality at 30 days, 90 days and 1 year.

2.5. Statistical analysis

SPSS (Version 25; IBM Corporation, USA) was used to perform statistical analysis. Data were assessed for normality of distribution and appropriate statistical tests chosen for parametric or non-parametric data. Univariate analyses were used to investigate associations with statistical significance set at $p = \leq 0.05$. In order to establish if pre-operative weight loss was a predictor of mortality independent of known pre-operative and treatment variables, we then trained a multivariate logistic regression model with age, gender, pre-operative tumour staging (cT and cN), adjuvant treatment and pre-operative weight loss of ≥10% to predict mortality at 90 days and 1 year.

3. Results

3.1. Demographics

151 eligible adults underwent oesophagectomy during the study period. The median age was 66 years (IQR 59–74) and 78.1% were male (Table 1). The median length of hospital stay was 10 days (IQR 8–14). Tables 2 and 3.

Some 92 (60.9%) individuals experienced a post-operative complication, with 15 (9.9%) being anastomotic leak, 56 (37.1%) pulmonary complications and 8 (5.3%) chyle leak. Major complications graded Clavien-Dindo grade 3b or above occurred in 32 individuals (21.2%) with 30 day mortality in 3 (2.0%) individuals and 90 day mortality in 7 (4.6%) individuals. Adjuvant treatment was administered to 11 patients (7.3%).

Table 1
Patient demographics.

Patient characteristics	Oesophagectomy n = 151
Age in years, median (IQR)	66 (59–74)
Gender, n (%)	
Male	118 (78.1)
Female	33 (21.9)
Pre-diagnosis BMI kg/m^2, median (IQR)	28.2 (26.1–31.6)
Histology, n (%)	
Adenocarcinoma	129 (85.4)
Squamous cell carcinoma	22 (14.6)
Pre-operative cT stage, n (%)	
0	2 (1.3)
1	3 (2.0)
2	35 (23.2)
3	95 (62.9)
4	16 (10.6)
Pre-operative cN stage, n (%)	
0	39 (25.8)
1	81 (53.6)
2	30 (19.9)
3	1 (0.7)
Neoadjuvant treatment, n (%)	
Yes	114 (75.5)
No	37 (24.5)
Type of neoadjuvant treatment, n (%)	
Chemotherapy	35 (30.7)
Chemoradiotherapy	79 (69.3)
Surgical approach (chest/abdomen), n (%)	
Open/Open	38 (25.2)
Open/Laparoscopic	64 (42.4)
Totally minimally invasive (laparoscopic)	49 (32.5)
Adjuvant treatment given	
Yes	11 (7.3)
No	140 (92.7)
Pre-operative HGS measurement available, n (%)	87 (57.6)

3.2. Early compared to late nutrition support

Individuals given early nutrition support were prescribed a mean of 14.2 kcal/kg (±8.9) and 0.6 g/kg (±0.4) of protein per day during neoadjuvant treatment. Adherence to the prescribed nutrition support was 77.8%. There was no difference in Clavien-Dindo complication grade ≥3b ($p = 0.3$), length of hospital stay ($p = 0.2$), 30 day mortality ($p = 0.7$), 90 day mortality ($p = 0.5$) or 1 year mortality ($p = 0.3$) between the groups.

The early nutrition support group lost significantly less weight at 12 months post-operatively when compared to the late nutrition support group, both absolutely (13.0 kg vs 17.9 kg, p=<0.01) and as a percentage of pre-treatment weight (20.1% vs. 25.4%, p=<0.05, Fig. 1).

3.3. Relationship between nutritional status and mortality

Although weight loss ≥10% from baseline to pre-operatively was not associated with major post-operative complications ($p = 0.3$) or length of hospital stay ($p = 0.4$), it was significantly associated with both 90 day ($p = 0.001$) and 1 year mortality in univariate analyses (p=<0.01) respectively.

Multivariate logistic regression after adjusting for age, gender, pre-operative tumour staging (tumour (T) and nodal (N)) and adjuvant treatment showed pre-operative weight loss ≥10% remained a significant predictor of mortality at 90 days (OR 19.9, 95%CI 2.04–194.37, $p = 0.010$) and 1 year (OR 2.84, 95% CI 1.03–7.83, $p = 0.044$). This difference in survival to 1 year is also demonstrated using the Kaplan Meier estimator (Log-Rank p=<0.01, Fig. 2).

3.4. Relationship between handgrip strength and post-operative outcomes

Pre-operative HGS measurement was available for 87 individuals. 23 (26.4%) of adults were classified as having low HGS <27 kg in men and <16 kg in women. Pre-operative HGS was not associated with post-operative complications Clavien-Dindo grade 3b or above ($p = 0.2$), LOS ($p = 0.9$), 30 day mortality ($p = 0.5$) or 90 day mortality ($p = 0.6$).

4. Discussion

The results of this retrospective study suggest pre-operative weight loss ≥10% was associated with 90 day and 1 year mortality. This has similarly been reported in other work, where a weight loss >10% was associated with increased risk for all-cause mortality [22] as well as increased 5 year mortality [23]. However, this association is not consistent with other work where pre-operative weight loss >10% was not significantly associated with perioperative mortality or short-term prognosis [24]. Adjuvant treatment had no significant effect on post-operative weight loss, which has similarly been reported in other studies [25–27]; however it should be considered that within our study relatively few patients received adjuvant therapy.

Our other key finding related to the early intervention with nutrition support during neoadjuvant treatment. Disease associated malnutrition is common, and to ameliorate this risk nutrition support in the form of oral nutrition supplements or enteral feeds are often started early. Although, in this study, interestingly we did not observe any benefit of nutrition support on short term post-operative outcomes, the benefit of nutrition support appeared to be evident later in the treatment pathway, suggesting a latent effect of nutrition support. All individuals lost weight post-operatively; however, at 12 months those

Table 2
Early compared to late nutrition support.

	'Early' nutrition support, n = 45	'Late' nutrition support, n = 69	P value
Age	67 (61.5–72.0)	64 (54.5–72.0)	0.1 ¶
Pre-operative cT stage			
2	4 (8.9)	11 (15.9)	0.6 §
3	35 (77.8)	49 (71.0)	
4	6 (13.3)	9 (13.0)	
Pre-operative cN stage			
0	7 (15.6)	7 (10.1)	0.2 §
1	32 (71.1)	41 (59.4)	
2	6 (13.3)	20 (29.0)	
3	0	1 (1.4)	
Neoadjuvant treatment (NAT)			
Chemotherapy	3 (6.7)	32 (46.4)	<0.001* §
Chemoradiotherapy	42 (93.3)	37 (53.6)	
Degree of dysphagia during NAT			
Normal diet	7 (15.6)	13 (72.2)	<0.001* §
Soft diet	19 (42.2)	4 (22.2)	
Puree diet	7 (15.6)	0	
Liquid diet	6 (13.3)	0	
Complete dysphagia	6 (13.3)	1 (5.6)	
Not recorded	0	51	
Post-operative length of hospital stay (days)	10 (8–13.75)	9 (8–12.75)	0.2 ¶
Clavien Dindo complications >3b			
Yes	11 (24.4)	13 (18.8)	0.3 §
No	34 (75.6)	56 (81.2)	
Adjuvant treatment given			
Yes	3 (6.7)	8 (11.6)	0.4§
No	42 (93.3)	61 (88.4)	

Data presented as absolute number (%) and median (IQR), *<0.05, § χ^2 test, ¶ Mann–Whitney U test.

Table 3
Nutritional status.

	<10% weight loss, n = 111	≥10% weight loss, n = 40	P value
Pre-operative cT stage			
0	2 (1.8)	0	0.01* §
1	3 (2.7)	0	
2	32 (28.8)	3 (7.5)	
3	66 (59.5)	29 (72.5)	
4	8 (7.2)	8 (20.0)	
Pre-operative cN stage			
0	32 (28.8)	7 (17.5)	0.2 §
1	58 (52.3)	23 (57.5)	
2	21 (18.9)	9 (22.5)	
3	0	1 (2.5)	
Neoadjuvant treatment (NAT)			
Chemotherapy	23 (20.7)	12 (30.0)	<0.05* §
Chemoradiotherapy	55 (49.5)	24 (60.0)	
Did not receive NAT	33 (29.7)	4 (10.0)	
Clavien Dindo complications >3b			
Yes	22 (19.8)	10 (25.0)	0.3 §
No	89 (80.2)	30 (75.0)	
Post-operative length of hospital stay (days)	10 (8–15)	10 (8–12.5)	0.4 ¶
Adjuvant treatment given			
Yes	8 (7.2)	3 (7.5)	1.0§
No	103 (92.8)	37 (92.5)	
90 day mortality			
Yes	1 (0.9)	6 (15.0)	0.001* §
No	110 (99.1)	34 (85.0)	
1 year mortality			
Yes	13 (12.5)	12 (33.3)	<0.01* §
No	91 (87.5)	24 (66.7)	
Time point not reached	7	4	

Data presented as absolute number (%) and median (IQR), *<0.05, § χ^2 test, ¶ Mann–Whitney U test.

individuals given earlier nutrition support lost significantly less weight than the late nutrition support group. However Ligthart-Melis et al. [28] reported a group of participants given 'intensive nutrition support' during neoadjuvant treatment experienced significantly fewer post-operative complications and reduced length of hospital stay.

Therefore, intervention with early nutrition support may have the potential to influence both the short-term outcomes during neoadjuvant treatment and longer term outcomes following surgery and a prospective study would be warranted to investigate this further. It should also be considered whether early nutrition support may also help to prevent such significant pre-operative

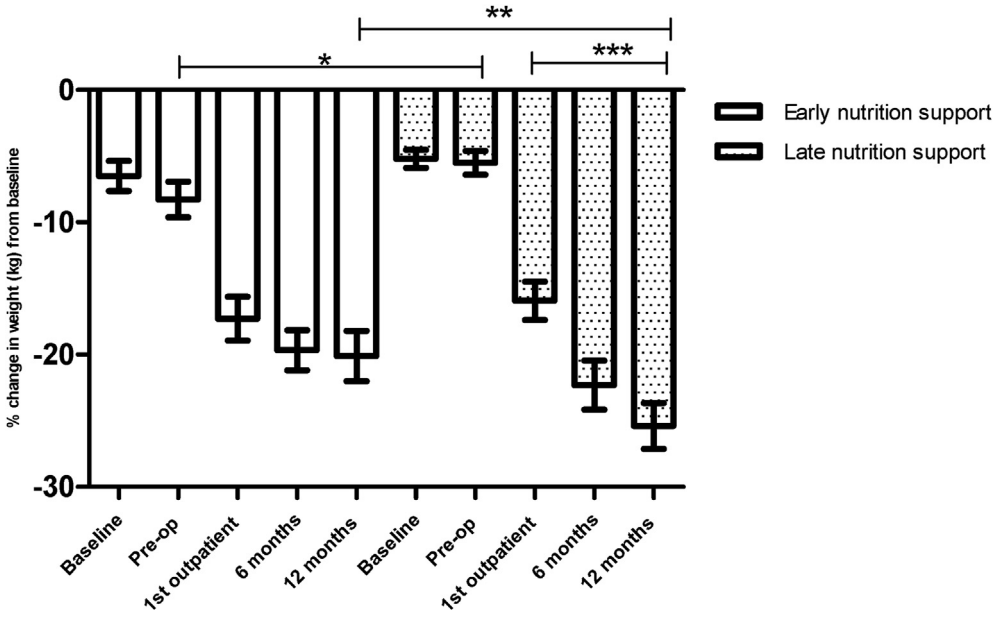

Fig. 1. Effect of early or late nutrition support on post-operative weight (*p=<0.05, **p=<0.05, ***p=<0.001).

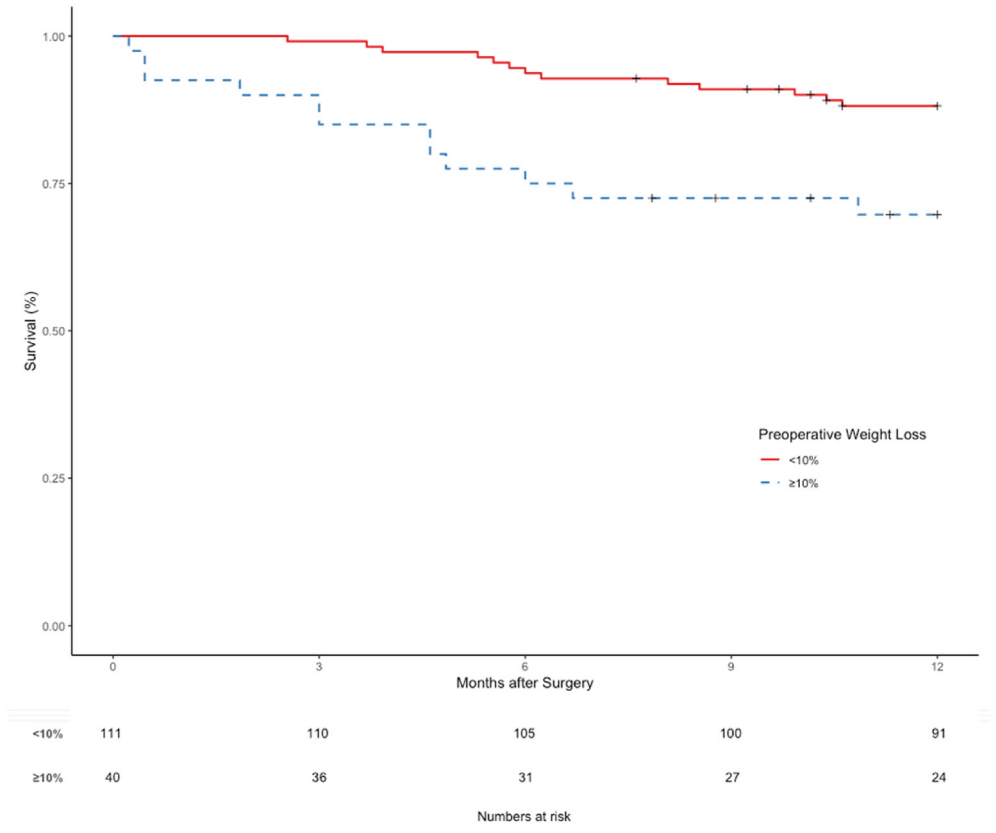

Fig. 2. Kaplan–Meier survival curve (colour to be used for figure in print). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

weight loss and hence help to reduce post-operative mortality rates. Other studies have demonstrated that early and regular nutrition support during chemo and/or radiotherapy is clinically beneficial and has resulted in improved treatment tolerance and reduced weight loss during treatment [29,30]. Future work could also consider patient reported outcome measures in relation to nutrition support in individuals with oesophageal cancer.

HGS did not add value to nutritional assessment as a standalone pre-operative measure within our study. However, it may be that alternative measures of body composition such as CT analysis of

skeletal muscle index, bioelectrical impedance or dual-energy X-ray absorptiometry may provide more reliable prognostic ability and further work should be undertaken in large patient cohorts [31–33].

Early nutrition support in addition to exercise and psychological support in the form of a multimodal prehabilitation programme may be effective at improving post-operative outcomes, which has already been proven in colorectal cancer [34]. Results to date specifically related to oesophageal cancer are heterogeneous mainly due to the majority studies to date being on mixed cohorts of GI cancer and wide variation in the design of prehab programmes, for example unimodal or multimodal [35,36]. Several studies are currently underway examining the effect of prehabilitation in oesophageal cancer specifically and the results of these are eagerly anticipated and may help to add to the current evidence base for the use of early nutrition support within this setting [37,38].

There are a number of limitations to this present study due to the retrospective nature of the cohort. There was wide variation in the amount and type of nutrition support provided due to the complexity of this patient group, for example some patients were able to tolerate oral diet in addition to supplementary oral nutrition supplements, however others required exclusive nutrition support through ONS of enteral tube feeding due to their degree of dysphagia. Participants were split into two pragmatic groups for 'early' and 'late' nutrition support retrospectively according to whether they were referred for dietetic assessment during neo-adjuvant treatment. A randomised controlled trial could be considered in the future to attempt to control for these confounding factors.

5. Conclusion

Significant pre-operative weight loss (≥10%) was associated with post-operative 90 day and 1 year mortality. Early nutrition support during neoadjuvant treatment was beneficial for post-operative weight maintenance and we therefore recommend dietetic assessment and intervention early within the treatment pathway, which may also help prevent such significant weight loss pre-operatively.

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Contributor's statement

All authors have made substantial contributions to the following: SD, LM and MW designed the research; SD carried out the data collection; SD completed the data and statistical analyses and drafted the manuscript; all authors edited, read and approved the final manuscript.

Declaration of competing interest

None of the authors has any conflict of interest to declare in relation to this quality improvement project.

References

[1] [Internet] Oesophageal cancer statistics. Cancer Research UK; 2020. Available from: https://about-cancer.cancerresearchuk.org/about-cancer/oesophageal-cancer/about. [Accessed 4 April 2020].
[2] van der Werf L, Busweiler L, van Sandick J, van Berge Henegouwen M, Wijnhoven B. Reporting national outcomes after esophagectomy and gastrectomy according to the esophageal complications consensus group (ECCG). Ann Surg 2020;271(6):1095–101.
[3] Garth A, Newsome C, Simmance N, Crowe T. Nutritional status, nutrition practices and post-operative complications in patients with gastrointestinal cancer. J Hum Nutr Diet 2010;23(4):393–401.
[4] Findlay M, Purvis M, Venman R, Luong R, Carey S. Nutritional management of patients with oesophageal cancer throughout the treatment trajectory: benchmarking against best practice. Support Care Canc 2020;28(12):5963–71.
[5] West M, Wischmeyer P, Grocott M. Prehabilitation and nutritional support to improve perioperative outcomes. Curr Anesthesiol Rep 2017;7(4):340–9.
[6] Filip B, Scarpa M, Cavallin F, Cagol M, Alfieri R, Saadeh L, et al. Postoperative outcome after oesophagectomy for cancer: nutritional status is the missing ring in the current prognostic scores. Eur J Surg Oncol 2015;41(6):787–94.
[7] Low D, Allum W, De Manzoni G, Ferri L, Immanuel A, Kuppusamy M, et al. Guidelines for perioperative Care in esophagectomy: enhanced recovery after surgery (ERAS®) society recommendations. World J Surg 2018;43(2):299–330.
[8] Norman K, Stobäus N, Gonzalez M, Schulzke J, Pirlich M. Hand grip strength: outcome predictor and marker of nutritional status. Clin Nutr 2011;30(2):135–42.
[9] Ordan M, Mazza C, Barbe C, Perrier M, Botsen D, Renard Y, et al. Feasibility of systematic handgrip strength testing in digestive cancer patients treated with chemotherapy: the FIGHTDIGO study. Cancer 2017;124(7):1501–6.
[10] Mendes J, Alves P, Amaral T. Comparison of nutritional status assessment parameters in predicting length of hospital stay in cancer patients. Clin Nutr 2014;33(3):466–70.
[11] Kilgour R, Vigano A, Trutschnigg B, Lucar E, Borod M, Morais J. Handgrip strength predicts survival and is associated with markers of clinical and functional outcomes in advanced cancer patients. Support Care Canc 2013;21(12):3261–70.
[12] Lakenman P, Ottens-Oussoren K, Witvliet-van Nierop J, van der Peet D, de van der Schueren M. Handgrip strength is associated with treatment modifications during neoadjuvant chemoradiation in patients with esophageal cancer. Nutr Clin Pract 2017;32(5):652–7.
[13] Chen C, Ho-Chang, Huang Y, Hung T. Hand-grip strength is a simple and effective outcome predictor in esophageal cancer following esophagectomy with reconstruction: a prospective study. J Cardiothorac Surg 2011;6(1).
[14] Sato S, Nagai E, Taki Y, Watanabe M, Watanabe Y, Nakano K, et al. Hand grip strength as a predictor of postoperative complications in esophageal cancer patients undergoing esophagectomy. Esophagus 2017;15(1):10–8.
[15] van Egmond M, van der Schaaf M, Klinkenbijl J, Engelbert R, van Berge Henegouwen M. Preoperative functional status is not associated with postoperative surgical complications in low risk patients undergoing esophagectomy. Dis Esophagus 2016:1–7.
[16] Drover J, Cahill N, Kutsogiannis J, Pagliarello G, Wischmeyer P, Wang M, et al. Nutrition therapy for the critically ill surgical patient. J Parenter Enteral Nutr 2010;34(6):644–52.
[17] Schier R, Levett D, Riedel B. Prehabilitation: The next challenge for anaesthesia teams. Eur J Anaesthesiol 2020;37:259–62.
[18] Le Roy B, Selvy M, Slim K. The concept of prehabilitation: what the surgeon needs to know? J Visc Surg 2016;153(2):109–12.
[19] Underwood T, Noble F, Madhusudan N, Sharland D, Fraser R, Owsley J, et al. The development, application and analysis of an enhanced recovery programme for major oesophagogastric resection. J Gastrointest Surg 2017;21(4):614–21.
[20] Chen L, Lee W, Peng L, Liu L, Arai H, Akishita M. Recent advances in sarcopenia research in asia: 2016 update from the asian working group for sarcopenia. J Am Med Dir Assoc 2016;17(8). 767.e1-e7.
[21] Clavien P, Barkun J, de Oliveira M, Vauthey J, Dindo D, Schulick R, et al. The clavien-dindo classification of surgical complications. Ann Surg 2009;250(2):187–96.
[22] Hynes O, Anandavadivelan P, Gossage J, Johar A, Lagergren J, Lagergren P. The impact of pre- and post-operative weight loss and body mass index on prognosis in patients with oesophageal cancer. Eur J Surg Oncol 2017;43(8):1559–65.
[23] van der Schaaf M, Tilanus H, van Lanschot J, Johar A, Lagergren P, Lagergren J, et al. The influence of preoperative weight loss on the postoperative course after esophageal cancer resection. J Thorac Cardiovasc Surg 2014;147(1):490–5.
[24] Skipworth J, Foster J, Raptis D, Hughes F. The effect of preoperative weight loss and body mass index on postoperative outcome in patients with esophagogastric carcinoma. Dis Esophagus 2009;22(7):559–63.
[25] D'Journo X, Ouattara M, Loundou A, Trousse D, Dahan L, Nathalie T, et al. Prognostic impact of weight loss in 1-year survivors after transthoracic esophagectomy for cancer. Dis Esophagus 2011;25(6):527–34.

[26] Kitagawa H, Namikawa T, Munekage M, Fukisawa K, Munekage E, Kawanishi Y, et al. Analysis of factors associated with weight loss after esophagectomy for esophageal cancer. Anticancer Res 2016;36(10):5409–12.
[27] Park S, Kim D, Suh J, Byun G. Risk factors for weight loss 1 Year after esophagectomy and gastric pull-up for esophageal cancer. J Gastrointest Surg 2018;22(7):1137–43.
[28] Ligthart-Melis G, Weijs P, te Boveldt N, Buskermolen S, Earthman C, Verheul H, et al. Dietician-delivered intensive nutritional support is associated with a decrease in severe postoperative complications after surgery in patients with esophageal cancer. Dis Esophagus 2012;26(6):587–93.
[29] Bozzetti F. Nutritional support in patients with oesophageal cancer. Support Care Canc 2009;18(S2):41–50.
[30] Odelli C, Burgess D, Bateman L, Hughes A, Ackland S, Gillies J, et al. Nutrition support improves patient outcomes, treatment tolerance and admission characteristics in oesophageal cancer. Clin Oncol 2005;17(8):639–45.
[31] Boshier P, Heneghan R, Markar S, Baracos V, Low D. Assessment of body composition and sarcopenia in patients with esophageal cancer: a systematic review and meta-analysis. Dis Esophagus 2018;31:193–4.
[32] Paireder M, Asari R, Kristo I, Rieder E, Tamandl D, Ba-Ssalamah A, et al. Impact of sarcopenia on outcome in patients with esophageal resection following neoadjuvant chemotherapy for esophageal cancer. Eur J Surg Oncol 2017;43(2):478–84.
[33] Elliott J, Doyle S, Murphy C, King S, Guinan E, Beddy P, et al. Sarcopenia prevalence, and impact on operative and oncologic outcomes in the multimodal management of locally advanced esophageal cancer. Ann Surg 2017;266(5):822–30.
[34] Gillis C, Buhler K, Bresee L, Carli F, Gramlich L, Culos-Reed N, et al. Effects of nutritional prehabilitation, with and without exercise, on outcomes of patients who undergo colorectal surgery: a systematic review and meta-analysis. Gastroenterology 2018;155(2):391–410. e4.
[35] Bolshinsky V, Li M, Ismail H, Burbury K, Riedel B, Heriot A. Multimodal prehabilitation programs as a bundle of Care in gastrointestinal cancer surgery. Dis Colon Rectum 2018;61(1):124–38.
[36] Doganay E, Moorthy K. Prehabilitation for esophagectomy. J Thorac Dis 2019;11(S5):S632–8.
[37] Allen S, Brown V, Prabhu P, Scott M, Rockall T, Preston S, et al. A randomised controlled trial to assess whether prehabilitation improves fitness in patients undergoing neoadjuvant treatment prior to oesophagogastric cancer surgery: study protocol. BMJ Open 2018;8(12). e023190.
[38] Le Roy B, Pereira B, Bouteloup C, Costes F, Richard R, Selvy M, et al. Effect of prehabilitation in gastro-oesophageal adenocarcinoma: study protocol of a multicentric, randomised, control trial—the PREHAB study. BMJ Open 2016;6(12). e012876. Study protocol.