An investigation into the nutritional status of patients receiving an Enhanced Recovery After Surgery (ERAS) protocol versus standard care following Oesophagectomy

Benton, Katie; Thomson, Iain ; Isenring, Elisabeth; Smithers, B. Mark ; Agarwal, Ekta

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Abstract

Purpose: Enhanced Recovery After Surgery (ERAS) protocols have been effectively expanded to various surgical specialities including oesophagectomy. Despite nutrition being a key component, actual nutrition outcomes and specific guidelines are lacking. This cohort comparison study aims to compare nutritional status and adherence during implementation of a standardised post-operative nutritional support protocol, as part of ERAS, compared to those who received usual care

Methods: Two groups of patients undergoing resection of oesophageal cancer were studied. Group 1 (n=17) underwent oesophagectomy between Oct 2014 and Nov 2016 during implementation of an ERAS protocol. Patients in group 2 (n=16) underwent oesophagectomy between Jan 2011 and Dec 2012 prior to the implementation of ERAS. Demographic, nutritional status, dietary intake and adherence data were collected. Ordinal data was analysed using independent t tests, and categorical data using chi square tests.

Results: There was no significant difference in nutrition status, dietary intake or length of stay following implementation of an ERAS protocol. Malnutrition remained prevalent in both groups at day 42 post surgery (n=10, 83% usual care; and n= 9, 60% ERAS). A significant difference was demonstrated in adherence with earlier initiation of oral free fluids *(p=<0.008),* transition to soft diet *(p= 0.004)* and continuation of jejunostomy feeds on discharge (*p=<0.000)* for the ERAS group.

Conclusion: A standardised post-operative nutrition protocol, within an ERAS framework, results in earlier transition to oral intake; however malnutrition remains prevalent post-surgery. Further large scale studies are warranted to examine individualised decision making regarding nutrition support within an ERAS protocol.

Keywords Oesophagectomy, Enhanced Recovery after Surgery, Nutrition, Early oral Feeding

Introduction

Although surgical resection for curable oesophageal cancer is the mainstay treatment for suitable patients, it greatly impacts nutritional status due to an altered gastrointestinal anatomy, early satiety, loss of appetite and reduced gastric volume [1,2]. Oesophagectomy is associated with significant morbidity and prolonged length of stay (LOS) ranging from 15-19 days in hospital [3,4]. Malnutrition and unintentional weight loss equal to or greater than 10% of preoperative body weight occurs in up to half of all oesophagectomy patients within the first post-operative year. Malnutrition has been shown to increase the incidence of post-operative complications, such as delayed wound healing and dehiscence of anatomises [5,6,2]. As such optimising nutritional management in this population is a well-established (refs).

In the past ten years there have been significant improvements in multimodal interventions for the peri-operative period, referred to as Enhanced Recovery after Surgery (ERAS) protocol which aims to expedite recovery without increasing morbidity and mortality [7]. ERAS was developed and implemented in colorectal surgery and has demonstrated reduction in LOS without a concurrent rise in complications or re-admissions [7,8]. More recently, ERAS protocols have been effectively expanded to various surgical sub-specialities including oesophagectomy [9-12]. ERAS protocols in oesophagectomy are an emerging area with data suggesting that optimised nutrition and metabolic care peri-operatively can minimise the stress response to surgery [7].

Implementing ERAS at an institutional level requires involvement of the multidisciplinary team including surgical, anaesthesia, nursing, physiotherapy and dietetic professionals [7]. The benefit associated with nutrition intervention in oesophageal cancer surgical patients has been reported [13]. Optimising nutrition is an important aspect of the ERAS protocol with early initiation of postoperative nutrition support and return to normal oral diet resulting in reduced LOS and incidence of infectious complications [14]. However, nutrition outcomes post ERAS implementation in patients with oesophagectomy have not been previously reported [11].

Therefore, this study aims to assess if patients undergoing oesophagectomy commencing on a standardised post-operative nutritional support protocol, as part of ERAS, have improved dietary intake

and nutritional status compared to those who received usual care. A secondary aim of the study was to evaluate adherence of the ERAS group to the nutrition support protocol.

Methods

Study setting, design and participants

This was a single site historical cohort-comparison trial. Patients undergoing oesophagectomy as treatment for oesophageal cancer at a tertiary hospital in Brisbane, Australia, were divided into two historical groups. Between October 2014 and November 2016, patients (Group 1) underwent surgery and their post-operative nutritional management based on the newly developed standardised ERAS protocol as described below. This group were compared with an historical comparative cohort of patients who had surgery between January 2011 and December 2012, when no formal ERAS protocol had been implemented (Group 2) in our setting. Patients were deemed ineligible if they were: <18 years old, underwent Salvage oesophagectomy or emergency oesophageal resection for malignancy, or required parental nutrition (see Figure 1). The current study received ethics approval from the Metro South Human Research Ethics Committee.

Data Collection

Eligible patients in Group 1 (ERAS) were approached to participate in the study at the weekly multidisciplinary outpatient clinic after surgeons had determined suitability for oesophagectomy. Patients in Group 2 (pre-ERAS usual care) were selected from a previous ethically approved NHMRC trial from a time period prior to the ERAS protocol. Both patient groups had completed the same standardised nutritional assessments. Assuming a clinically significant difference of 5 PGSGA units greater in one group relative to the other then complete data will be required on 20 patients per group to detect this difference with 90% power at the 95% significance level (2-tailed) [15]

Patients in both groups underwent assessment by the dietitian prior to surgery. Feeding jejunostomy tubes were placed intra-operatively and enteral nutrition support was commenced on day one following surgery. Data was collected at baseline and 42 days post-operatively regarding demographics, nutritional status (PG-SGA) [16,17], dietary intake by means of a 3 day food and fluid diary completed by the patient, dietitian-estimated energy and protein requirements based on post- operative

hypermetabolic state (125-145kJ/kg/d) of energy and (1.2-1.5g/kg/d) of protein [13], and post-operative LOS. Time points for the group 1 patients in the current study were selected as a comparison of time points used for the retrospective group 2. Adherence to, and maintenance of, the standardised ERAS post operative nutrition support pathway (Group 1) was examined retrospectively via chart review, and compared with the adherence in Group 2.

ERAS protocol – Group 1

The ERAS protocol in this study was developed on existing evidence regarding ERAS in patients undergoing upper gastrointestinal surgery [9,13]. A standardised post-operative nutrition support pathway was developed in conjunction with the surgical team, oncology dietitians, and the hospital foodservice dietitian. The nutrition support pathway included: upgrade to oral clear fluids at day X post-operatively, transition to a soft diet at day X, and continuation of supplementary jejunostomy feeds for one-week post-discharge (Table 1). The clinical nurse consultant and ward dietitian provided a follow-up phone review one week after discharge and conducted a face-to-face review in the upper gastrointestinal clinic in week 2 post-discharge. The post-operative management of both groups is detailed in Table 1.

Usual Care – Group 2

Patients in Group 2 underwent oesophagectomy and received usual care. The typical protocol was for jejunal feeding to commence on post-operative day 1 and calculated nutritional requirements would be met by day 3. Oral intake was initiated after day 4 or 5 following radiological assessment for anastomotic integrity. Patients were commenced on clear fluids and upgraded gradually to solid food, as per clinical tolerance. The jejunal feeding volume was tapered once the patient had commenced solid food intake. Jejunal feeds were ceased prior to discharge.

Statistical Analysis

Data were analysed on SPSS version 23.0. Categorical variables were presented as percentage; continuous variables not normally distributed were presented as median and range. Chi-square tests and non-parametric tests were used to evaluate associations at bivariate levels. P-values <0.05 were considered statistically significant.

Results

Twenty-five patients underwent oesophagectomy under the ERAS protocol. Of the 22 eligible patients, 2 did not attend the weekly clinic and two others declined (Figure 1). Eighteen patients provided consent and one patient withdrew in week one due to disease progression and cancellation of surgery. The complete data set included 17 patients who followed the ERAS protocol, with 16 matched historical participants in Group 2.

Patient Characteristics

Median age for both groups was above 60 years of age, with greater than 80% of patients being treated for adenocarcinoma. There were no statistically significant differences between the two groups for age, gender, histological tumour type or pre-operative neoadjuvant therapy (Table 2). Median LOS was 12.5 (days) for both groups.

Nutritional status and dietary intake

Patients in both groups were within a healthy BMI range (18.5-25.0kg/m^2) at baseline. Malnutrition defined by PG-SGA was prevalent in 6 patients (20%) (*p=0.383)* at baseline and this increased to 19 (70%) (*p=0.362)* at day 42 post surgery, which was not significant between groups. No patients in either group met their requirements for energy and protein at baseline or day 42 post- surgery (Table 3).

Adherence to the standardised ERAS post operative nutrition support pathway

Post-operative upgrade to clear fluids occurred on day 3 in 4 patients (33%) in Group 1 and one (8%) in Group 2 (*p= 0.343*). The number transitioning to free fluids by day 6 was 11 (69%) patients compared to 2 (15%) patients in Group 2 (*p=0.008).* The number transitioning from free fluid to soft diet by day 7 8 (50%) in Group 1 compared to 1 (8%) in Group 2 (*0.002).* Continuation of overnight supplementary jejunostomy feeds for one week post discharge occurred in 16 (100%) of patients in Group 1 compared with 1 (8%) in Group 2 *(p=<0.000)*(Table 4). No significant difference was identified when a subset analysis was performed, due to four patients being removed from the analysis in the ERAS group due to surgical complications preventing oral diet.

Discussion

This study reports that the implementation of a post-operative nutrition support pathway within an ERAS protocol in patients undergoing oesophagectomy is feasible. Patients on an ERAS protocol commenced oral fluids earlier, upgraded to solids more quickly, and were discharged home on supplemental nutrition via jejunonstomy feeding when compared with the usual care group. Despite a large number of well-nourished patients in both groups at baseline, more patients became malnourished (as defined by PG-SGA) and less than 50% of patients were meeting their calculated caloric requirements for energy and protein at day 42 post surgery.

There is concern amongst surgical teams that although ERAS protocols in oesophagectomy provide a framework, there is variation in relation to the exact timing of diet upgrade and length of time to continue jejunostomy feeding on discharge. Evidence-based guidelines on ERAS for oesophagectomy by Findlay et al. (2014) conclude that the optimal timing of oral intake after oesophagectomy is unclear and no recommendations have been provided for continuation of enteral feeds upon discharge due to inadequate research in the area [11]. Traditional dietary upgrade to early oral intake has been limited due to concern regarding anastomotic [11]. Despite this clinical expectation, the systematic review by Findlay et al (2014) identified no adverse outcomes in commencing early oral intake within 48 hours, with earlier discharge and fewer complications found with unrestricted intake, nil oral intake plus feeding jejunostomy [11]. In the current study, we were able to demonstrate adherence to the standardised ERAS post operative nutrition support pathway with more patients able to commence early oral clear fluids by day three in Group one , compared to usual care in Group 2. In addition, we demonstrated significant change in Group 1 in regards to dietary upgrade to free fluids and soft diet by day six and seven along with continuation of overnight jejunostomy feeds for one-week post discharge.

Despite the extended use (one-week post discharge) of supplementary jejunostomy feeding in the current study as per the ERAS protocol, a proportion of patients in both groups were malnourished at day-42 post-surgery. Therefore, it could be assumed that one week of ongoing enteral feeding via jejunostomy is insufficient to buffer the reduced oral intake expected post-surgery. There are no randomised studies investigating the effect of extended nutritional support post oesophagectomy either employing oral nutrition support as tailored dietary advice, or oral nutritional supplements, and the use

of enteral tube feeding [2]. Gupta et al (2009) found feeding jejunostomy to be a safe and an effective method to provide supportive nutrition care in the post-operative setting whilst a patient re-establishes oral intake [18]. However deterioration in nutritional status, weight loss and poorer QoL scores have been reported in a systematic review in this population irrespective of post-operative nutritional care provided [2]. This highlights the impact this surgery has on a patient's ability to consume adequate oral diet post surgery despite implementation of nutrition interventions. The results of the current study may provide preliminary evidence to support the ongoing use of jejunostomy feeding in the post-operative, post-discharge setting to optimise nutrition status within an ERAS protocol. However the exact time frame required for supplementary feeding is unknown.

Although LOS has been observed during implementation of ERAS protocols, the current study found no significant change in LOS. Similarly, Findlay et al. (2015) also reported no statistically significant difference in LOS during implementation of an ERAS protocol (18). The authors suggested focusing on optimizing the clinical components of ERAS pathways themselves [19]. It is important to emphasise that ERAS is a multimodal pathway including involvement of the multidisciplinary team, therefore challenging to make an associated between nutrition components and LOS.

Overall ERAS for oesophagectomy has been deemed safe and feasible however the evidence for individual components is often lacking [11]. The current study provides information regarding the nutrition status of patients undergoing an oesophagectomy on an ERAS protocol highlighting the feasibility of earlier postoperative nutrition support, return to normal diet and continuation of jejunostomy feeds. To our knowledge there were no direct complications associated with the postoperative related morbidity with the implementation of a standardised ERAS diet protocol which included earlier oral diet upgrade and continuation of jejunostomy feeds on discharge.

The current study highlights that despite ERAS protocol, malnutrition remains prevalent at day 42 post-operatively. Symptoms such as anorexia, reduced gastric volume and early satiety as a result of the surgery itself are unlikely to be influenced by an ERAS protocol. Surgical teams implementing ERAS should consider individualised decision-making regarding continuation of nutrition support in addition to ongoing specialised dietetic support and counselling. Simply targeting increasing nutritional intake

without consideration of the management to alleviate any gastrointestinal symptoms are likely to fail to improve overall nutrition status [2]. Additionally, the incorporation of evidence-based nutrition guidelines into an ERAS protocol may facilitate standardise evidenced-based care.

This study is limited by its small numbers. ERAS protocols traditionally include pre-operative supplementation of carbohydrate to optimise nutritional status during surgery however the current study focuses on post-operative management thus provides an area for future research included the pre-operative nutritional management of patients within an ERAS protocol.

Conclusion

To the best of our knowledge, this is the first study to report on the nutritional outcomes of patients undergoing oesophagectomy on an ERAS protocol when compared to usual care. The results of this study adds to the growing body of literature on ERAS for oesophagectomy demonstrating safety regarding the earlier dietary upgrade, continuation of jejunostomy feeds and adherence of an ERAS protocol. Malnutrition remained prevalent at day-42 post surgery despite an ERAS protocol, suggesting the need for further studies examining individualised decision making regarding continuation of nutrition support. Such studies will help to provide evidence based recommendations to optimise patient outcomes in context of the move towards standardised ERAS protocol implementation.

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