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

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1 **Abstract**

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

7 **Methods:** Two groups of patients undergoing resection of oesophageal cancer were studied. Group 1  
8 (n=17 ) underwent oesophagectomy between Oct 2014 and Nov 2016 during implementation of an  
9 ERAS protocol. Patients in group 2 (n=16) underwent oesophagectomy between Jan 2011 and Dec  
10 2012 prior to the implementation of ERAS. Demographic, nutritional status, dietary intake and  
11 adherence data were collected. Ordinal data was analysed using independent t tests, and categorical  
12 data using chi square tests.

13 **Results:** There was no significant difference in nutrition status, dietary intake or length of stay  
14 following implementation of an ERAS protocol. Malnutrition remained prevalent in both groups at day  
15 42 post surgery (n=10, 83% usual care; and n= 9, 60% ERAS). A significant difference was  
16 demonstrated in adherence with earlier initiation of oral free fluids ( $p < 0.008$ ), transition to soft diet  
17 ( $p = 0.004$ ) and continuation of jejunostomy feeds on discharge ( $p < 0.000$ ) for the ERAS group.

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

22

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

24

25 **Introduction**

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

35

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

44

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

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

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

56

## 57 **Methods**

### 58 *Study setting, design and participants*

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

69

### 70 *Data Collection*

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

78

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

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

89

#### 90 ***ERAS protocol – Group 1***

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

100

#### 101 ***Usual Care – Group 2***

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

108

#### 109 **Statistical Analysis**

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

114 **Results**

115 Twenty-five patients underwent oesophagectomy under the ERAS protocol. Of the 22 eligible patients,  
116 2 did not attend the weekly clinic and two others declined (Figure 1). Eighteen patients provided  
117 consent and one patient withdrew in week one due to disease progression and cancellation of surgery.  
118 The complete data set included 17 patients who followed the ERAS protocol, with 16 matched  
119 historical participants in Group 2.

120

121 ***Patient Characteristics***

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

126

127 ***Nutritional status and dietary intake***

128 Patients in both groups were within a healthy BMI range (18.5-25.0kg/m<sup>2</sup>) at baseline. Malnutrition  
129 defined by PG-SGA was prevalent in 6 patients (20%) ( $p=0.383$ ) at baseline and this increased to 19  
130 (70%) ( $p=0.362$ ) at day 42 post surgery, which was not significant between groups. No patients in  
131 either group met their requirements for energy and protein at baseline or day 42 post- surgery (Table 3).

132

133 ***Adherence to the standardised ERAS post operative nutrition support pathway***

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

142

143

144 **Discussion**

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

152

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

167

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

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

183

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

190

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

198

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



204 without consideration of the management to alleviate any gastrointestinal symptoms are likely to fail to  
205 improve overall nutrition status [2]. Additionally, the incorporation of evidence-based nutrition  
206 guidelines into an ERAS protocol may facilitate standardise evidenced-based care.  
207 This study is limited by its small numbers. ERAS protocols traditionally include pre-operative  
208 supplementation of carbohydrate to optimise nutritional status during surgery however the current  
209 study focuses on post-operative management thus provides an area for future research included the pre-  
210 operative nutritional management of patients within an ERAS protocol.

211

## 212 **Conclusion**

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

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