See corresponding editorial on page 10.

Protein intakes are associated with reduced length of stay: a comparison between Enhanced Recovery After Surgery (ERAS) and conventional care after elective colorectal surgery

Sophia E Yeung,[1] Leslee Hilkewich,[2] Chelsia Gillis,[3] John A Heine,[2,4] and Tanis R Fenton[1,3]

[1]Nutrition Services and [2]Surgery, Peter Lougheed Centre, Alberta Health Services, Calgary, Alberta, Canada; [3]Cumming School of Medicine, Community Health Sciences, Institute of Public Health, Alberta Children's Hospital Research Institute, and [4]Department of Surgery, University of Calgary, Calgary, Alberta, Canada

ABSTRACT

Background: Protein can modulate the surgical stress response and postoperative catabolism. Enhanced Recovery After Surgery (ERAS) protocols are evidence-based care bundles that reduce morbidity.

Objective: In this study, we compared protein adequacy as well as energy intakes, gut function, clinical outcomes, and how well nutritional variables predict length of hospital stay (LOS) in patients receiving ERAS protocols and conventional care.

Design: We conducted a prospective cohort study in adult elective colorectal resection patients after conventional (n = 46) and ERAS (n = 69) care. Data collected included preoperative Malnutrition Screening Tool (MST) score, 3-d food records, postoperative nausea, LOS, and complications. Multivariable regression analysis assessed whether low protein intakes and the MST score were predictive of LOS.

Results: Total protein intakes were significantly higher in the ERAS group due to the inclusion of oral nutrition supplements (conventional group: 0.33 g $\cdot$ kg^{-1} $\cdot$ d^{-1}; ERAS group: 0.54 g $\cdot$ kg^{-1} $\cdot$ d^{-1}; $P < 0.02$). This group difference in protein intake was maintained in a multivariable model that controlled for differences between baseline and surgical variables (P = 0.001). Oral food intake did not differ between the 2 groups. The ERAS group had shorter LOS (P = 0.049) and fewer total infectious complications (P = 0.01). Nausea was a predictor of protein intake. Nutrition variables were independent predictors of earlier discharge after potential confounders were controlled for. Each unit increase in preoperative MST score predicted longer LOSs of 2.5 d (95% CI: 1.5, 3.5 d; $P < 0.001$), and the consumption of ≥60% of protein requirements during the first 3 d of hospitalization was associated with a shorter LOS of 4.4 d (95% CI: −6.8, −2.0 d; $P < 0.001$).

Conclusions: ERAS patients consumed more protein due to the inclusion of oral nutrition supplements. However, total protein intake remained inadequate to meet recommendations. Consumption of ≥60% protein needs after surgery and MST scores were independent predictors of LOS. This trial was registered at clinicaltrials.gov as NCT02940665. *Am J Clin Nutr* 2017;106:44–51.

Keywords: colorectal surgery, Enhanced Recovery After Surgery, length of stay, oral nutrition supplement, dietary protein, energy, nutrition, diet, bowel surgery, malnutrition screening tool

INTRODUCTION

The surgical stress response induces a catabolic state. Patients undergoing uncomplicated elective surgery and recovery lose ∼2 kg total lean mass (1, 2). Nutrition, particularly protein, can modulate the surgical stress response. Whole-body protein balance (protein synthesis − breakdown) is dependent on amino acid supply in healthy individuals (3, 4) as well as in cancer and surgical patients (1, 5, 6).

Enhanced Recovery After Surgery (ERAS) protocols for elective colonic and rectal or pelvic surgery are evidence-based multimodal perioperative care bundles that reduce morbidity and shorten the length of hospital stay (LOS) (7, 8). ERAS protocols include nutrition-specific aspects, such as the following: preoperative nutrition risk screening, preoperative carbohydrate loading, minimizing postoperative nausea and vomiting, early feeding of normal food, fluid optimization, and inclusion of oral nutritional supplements (ONSs) (7, 8). The ERAS protocol has also been shown to stimulate the gastrointestinal tract, reduce insulin resistance, and enhance substrate utilization (7–10).

A previous study examined protein intakes of ERAS patients and found that patients were unable to meet their protein requirements (11). This study, however, did not compare protein intakes between ERAS patients with those receiving conventional care. Given the importance of protein intake on convalescence (12, 13), it is appropriate to evaluate whether the implementation of ERAS protocols positively affects protein intake. The primary objective of this study was to compare

Supported by a grant from the Canadian Foundation for Dietetic Research, Dietitians of Canada.

Supplemental Tables 1–3 are available from the "Online Supporting Material" link in the online posting of the article and from the same link in the online table of contents at http://ajcn.nutrition.org.

Address correspondence to SEY (sophia.yeung@ahs.ca).

Abbreviations used: ERAS, Enhanced Recovery After Surgery; HbA1c, glycated hemoglobin; LOS, length of hospital stay; MST, Malnutrition Screening Tool; ONS, oral nutrition supplement; POD, postoperative day.

Received November 4, 2016. Accepted for publication March 29, 2017.

First published online May 3, 2017; doi: https://doi.org/10.3945/ajcn.116.148619.

protein intake and adequacy between patients receiving ERAS protocols and patients receiving conventional care. The study also compared energy intakes, gut function, and clinical outcomes between groups. Finally, we assessed whether nutritional variables (preoperative malnutrition risk and postoperative protein intake) predicted LOS.

METHODS

A prospective cohort study was conducted at 2 tertiary care hospitals within Calgary, Alberta, Canada. The Foothills Medical Centre was designated the control site, providing conventional care, and the Peter Lougheed Centre was the ERAS site. ERAS protocols were implemented at the Peter Lougheed Centre 13 mo before the start of data collection. The study was approved by the Conjoint Health Research Ethics Board at The University of Calgary (clinicaltrials.gov; identifier: NCT02940665).

Study population

A consecutive convenience sample of patients ≥18 y of age admitted for elective colorectal resection from March 2014 to April 2015 were prospectively enrolled once written consent was obtained. Patients who lacked the ability to accurately record food intake or who had comorbidities that could have interfered with oral intake (e.g., dysphagia) or concurrent enteral or parenteral nutrition before surgery were excluded.

Data collection

Patients were screened for nutrition risk by using the validated Malnutrition Screening Tool (MST) (14). Malnutrition risk was defined as an MST score ≥2. The type of diet ordered as well as energy and protein intakes from food records on postoperative days (PODs) 1, 2, and 3 were recorded. Patients recorded the

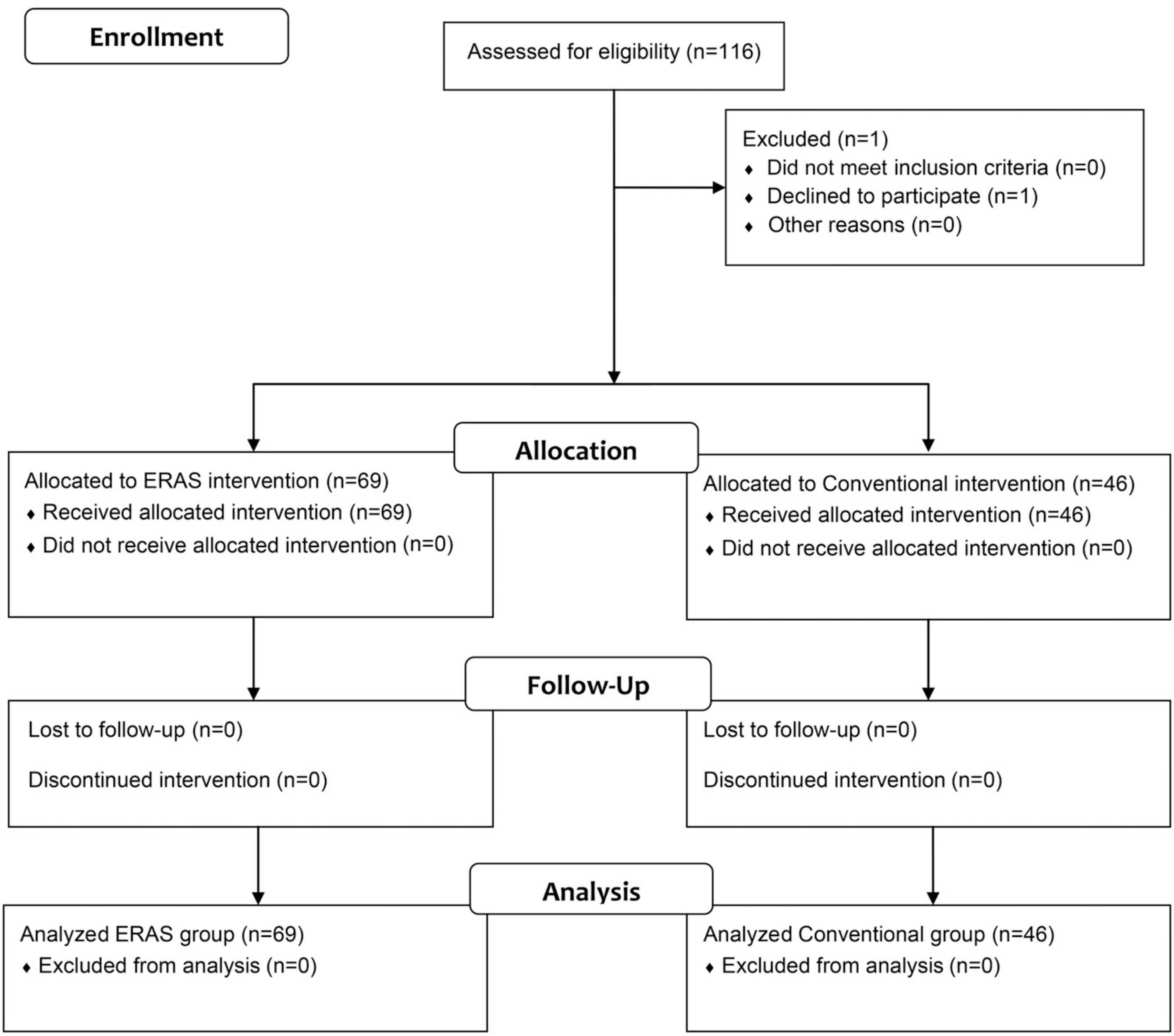

FIGURE 1 Flow diagram of the sequence through the stages of an observational trial of the ERAS and conventional care groups. ERAS, Enhanced Recovery After Surgery.

TABLE 1
Demographic, operative, and malnutrition screening characteristics of conventional care compared with ERAS patients[1]

Patient characteristics	Conventional (n = 46)	ERAS (n = 69)	P
Age, y	57 ± 13	61 ± 14	0.21
Female, n (%)	21 (46)	27 (39)	0.56
Charlson Comorbidity Index[2]	1.9 ± 1.6	1.8 ± 1.4	0.84
Diagnoses, n (%)			0.031
Colon cancer	12 (26)	34 (49)	
Rectal cancer	17 (37)	14 (20)	
Other diagnosis	17 (37)	21 (31)	
MST,[3] n (%)			0.043
At risk (2, 3, 4, or 5)	15 (33)	11 (16)	
Low risk (0 or 1)	31 (67)	58 (84)	
Laboratory measures (preoperative)			
Prealbumin	0.26 ± 0.02	0.26 ± 0.01	0.86
HbA1C	5.8 ± 0.7	5.8 ± 0.6	0.84
BMI, kg/m^2	27.3 ± 6.3	29.8 ± 6.3	0.044
Obese (BMI ≥30), %	12 ± 26	27 ± 39	0.17
Type of surgery, n (%)			0.70
Colon[4]	28 (61)	47 (68)	
Rectum[5]	14 (31)	19 (28)	
Small bowel resection	2 (4)	2 (3)	
Other stoma procedure	2 (4)	1 (1)	
Procedure type, n (%)			
New stoma creation	11 (24)	9 (13)	0.046
Laparoscopic procedures	26 (57)	57 (83)	0.003

[1] Statistical comparisons were made by using 2-sided t test and Fisher's exact tests. ERAS, Enhanced Recovery After Surgery; HbA1C, glycated hemoglobin; MST, Malnutrition Screening Tool.

[2] The Charlson Comorbidity Index (25) is a method of categorizing comorbidities of patients on the basis of the International Classification of Diseases diagnosis codes found in administrative data. A score of 0 indicates that no comorbidities were found.

[3] The MST is a valid and reliable tool to screen for malnutrition for adult acute hospitalized patients. A score of ≥2 indicates malnutrition risk.

[4] Includes right and left hemicolectomy, sigmoid resection, and subtotal/total colectomy.

[5] Includes anterior resection, proctocolectomy, and abdominoperineal resection.

amount of food and fluid consumed with the use of quartiles (none; one-quarter, one-half, three-quarters of a portion of food consumed; or all) on a food record (15), commencing on POD 1. Research staff were provided with detailed written instructions on data collection and completion of the food records. The research assistants were each instructed by the principal investigators on the method for accurate verification of the foods consumed by first viewing standard portions provided on a meal tray. Research assistants practiced estimating portions with a principal investigator before independently collecting the data. Research assistants verified the self-reported food records with the patients after each meal, and nursing staff recorded the quantity of ONS intake by ERAS patients. Dietitians assessed the energy and protein intakes from food records by using nutrition information on the hospital diets with the use of CBORD (The CBORD Group, Inc.). For patients who were discharged on a study day before receiving 3 hospital meals, food intakes (but not ONS intakes) for the missed hospital meals were estimated on the basis of the percentage of their intake of their last meal before discharge. For foods and fluids that were brought in from outside the hospital, the nutritional information was estimated by using the USDA's National Nutrient Database (16) or obtained from company website pages.

At the ERAS site as part of the ERAS guideline for preadmission education, all of the patients were provided with the option of attending a preoperative colorectal surgery education class, which included a nutrition component that emphasized the importance of ONS intake to supplement food intake. After surgery, patients were offered normal food and beverages from a nonselective menu starting on PODs 0 or 1, with a selective menu on POD 2 onward. The schedule for diet progression of the conventional group was at the surgeon's discretion and ranged from nil per os to a regular diet. The ERAS group was also offered 60 mL of ONS at 2 kcal/mL (TwoCal HN; Abbott Laboratories) 5 times/d starting on the day of surgery to meet energy intake goals as per the ERAS protocol.

Individualized resting energy requirements were calculated by using the Mifflin-St. Jeor equation (17). Protein requirements were estimated on the basis of the American Society of Parenteral and Enteral Nutrition and the European Society of Clinical Nutrition and Metabolism guidelines of 1.5 g/kg protein of ideal body weight for postsurgical patients (18, 19). Bloodwork included preoperative serum C-reactive protein, glycated hemoglobin (HbA1c), and prealbumin; on POD 2, bloodwork included C-reactive protein, random glucose, serum potassium, magnesium, calcium, and albumin. C-reactive protein was determined by immunoturbidimetric assay, and serum albumin, calcium, magnesium, and HbA1c were measured by calorimetric assay.

Surgical procedures were coded as per the ERAS Interactive Audit System's Patient Data Entry Manual (4.2a1), coding the main procedure performed at the primary operation unless it was not listed, in which case the procedure that most closely resembled the procedure was selected. The incidence of vomiting, first flatus, and first bowel movement from PODs 1–3 was assessed and recorded by nurses. To further assess gut function, research staff questioned patients about their level of nausea daily with the use of a verbal numeric rating scale of 0 (no nausea) to 10 (extreme nausea) (20, 21). Complications that occurred within 30 d of surgery were categorized by using the Clavien-Dindo Classification of Surgical Complications (22). Readmission within 30 d after surgery and total LOS were also recorded.

Statistical analysis

Statistical comparisons were made by using a 2-sided t test and Fisher's exact tests. To determine whether there was an impact of group imbalances in baseline and surgical variables on our primary outcome, protein intakes, we adjusted for these variables in multivariable regression. The association between nausea and protein intake was examined by using linear regression. To determine whether the MST score and a low protein intake were independently associated with LOS, a multivariable regression analysis in the combined ERAS and conventional patients was conducted, with potential confounders controlled for. First, each potential LOS predictor was examined to

TABLE 2
Compliance to the ERAS protocol within the ERAS group[1]

Compliance criteria	Compliance within ERAS (n = 69)
Overall compliance to all modalities of ERAS,[2] %	62
Compliance to nutrition modalities of ERAS, n/total n (%)	
Preoperative oral carbohydrate loading	43/69 (62)
Preadmission patient education	69/69 (100)
Preoperative malnutrition screening	69/69 (100)
Preoperative nutritional treatment[3]	1/10[4] (10)
Postoperative nausea and vomiting prophylaxis administered	25/26[5] (96)
Stimulation of gut motility (gum chewing)	52/69 (75)
Overall compliance to ONSs, n/total n (%)	
Energy intake on day of surgery, POD 0 (≥300 kcal from ONSs)	5/69 (7)
Energy intake on POD 1 (≥600 kcal from ONSs)	16/69 (23)
Energy intake on POD 2 (≥600 kcal from ONSs)	16/69 (23)
Energy intake on POD 3 (≥600 kcal from ONSs)	7/69 (10)
Overall intake of ONSs,[6] n/total n (%)	
POD 1	47/69 (68)
POD 2	50/59 (72)
POD 3	40/69 (58)

[1] Statistical comparisons were made by using Fisher's exact tests. ERAS, Enhanced Recovery After Surgery; ONS, oral nutrition supplement; POD, postoperative day.
[2] There were 22 modalities followed within the ERAS protocol.
[3] Personalized counseling by a dietitian for a Malnutrition Screening Tool score ≥2.
[4] Ten patients had a Malnutrition Screening Tool score ≥2 and therefore required nutrition treatment before surgery.
[5] Twenty-six patients met ERAS criteria to receive postoperative nausea and vomiting prophylaxis.
[6] Overall intake of ONSs refers to any amount of supplement taken when offered.

determine whether it was associated with LOS in our sample. Transfusion, protein intake of ≥60% of individual requirements, and Clavien-Dindo complications were included in the model as dichotomous variables; all other variables were continuous. Second, a full model was assessed; and third, variables with a P value >0.1 were removed one at a time to develop a parsimonious model. Stata/IC 13.1 (StataCorp) was used for the analysis.

We estimated that we would need to recruit 23 patients in each group to detect a difference between ERAS and control patients in the primary outcome variable, protein intake in the first 3 d after surgery, on the basis of mean protein intakes of 0.95 compared with 0.57 $g \cdot kg^{-1} \cdot d^{-1}$, by using an SD of 0.45 (23) and a 5% level of significance and 80% power. Because this study had a quasi-experimental design without randomization to the ERAS implementation, we increased our total sample size to 120 patients, with ethical approval by the Conjoint Health Research Ethics Board.

RESULTS

Forty-seven patients in the conventional group and 69 in the ERAS group were enrolled in the study. One patient in the conventional group requested to be excluded from the study on POD 2; thus, 46 patients completed the study (**Figure 1**) (24). There were no differences in pre-existing comorbidities between the 2 groups (**Supplemental Table 1**). The ERAS group had a lower risk of preoperative malnutrition before surgery than did the conventional care group (MST <2: 84% for ERAS and 67% for conventional; **Table 1**). The ERAS group underwent significantly more laparoscopic procedures, whereas the conventional group underwent more open procedures.

Compliance to ERAS

Before the implementation of ERAS in the city of Calgary, median overall compliance was assessed as 39% across 6 acute care hospital sites in Alberta, which included our conventional group (26). The overall compliance to the ERAS protocol in the ERAS arm was 62% (**Table 2**). Several nutrition-specific aspects of the ERAS protocol were implemented. There was a high level of compliance for most nutrition-related aspects of the ERAS protocol (Table 2); however, the compliance to the preoperative nutrition counseling intervention for high-nutrition-risk patients was low (10%). Overall consumption of any amount of ONS intake within the ERAS group was greatest on POD 2 at 72%, whereas compliance to the target for an energy intake of 300 kcal/d on POD 0 from supplements was only 7% and for an energy intake of 600 kcal/d on PODs 1, 2, and 3 was 23%, 23%, and 10%, respectively (Table 2). Patients being discharged home on POD 3 accounted for the decrease in ONS intake compliance. Eighty-seven percent of the conventional group and 94% of the ERAS group (P = 0.20) received solid foods on POD 1. The remaining patients were nil per os or received a fluid diet.

Protein and energy intakes

ERAS patients achieved a statistically greater average intake of 16 g protein/d (95% CI: 9, 24 g protein/d) and 370 kcal/d (95% CI: 211, 530 kcal/d) over the first 3 PODs compared with the conventional care group. Total protein intakes (food and ONSs) were significantly higher in the ERAS group on all 3 d (**Table 3**). The conventional group, on average, consumed 22% and the ERAS group consumed 36% of their estimated protein requirements during the first 3 d (P = 0.001) (**Figure 2**, Table 3).

TABLE 3
Protein and energy intakes between conventional care and ERAS patients[1]

	Conventional[2] (n = 46)	ERAS[3] (n = 69)	P
Total protein intake,[4] g/d			
POD 1	20.6 (15.4, 25.8)	38.4 (32.6, 44.1)	<0.0001
POD 2	20.5 (14.6, 26.2)	38.7 (32.3, 44.9)	0.0001
POD 3	24.0 (17.2, 30.8)	37.6 (31.7, 43.5)	0.004
Protein intake from food, g/d			
POD 1	20.6 (15.4, 25.8)	24.6 (20.3, 29.0)	0.24
POD 2	20.5 (14.6, 26.2)	26.1 (21.2, 31.0)	0.15
POD 3	24.0 (17.2, 30.8)	29.5 (24.0, 34.9)	0.21
Total energy intake,[4] kcal/d			
POD 1	544 (422, 665)	942 (810, 1073)	0.0001
POD 2	525 (391, 638)	917 (781, 1053)	0.0001
POD 3	585 (426, 743)	907 (782, 1032)	0.002
Energy intake from food, kcal/d			
POD 1	544 (422, 665)	625 (527, 724)	0.30
POD 2	525 (391, 638)	623 (523, 724)	0.23
POD 3	585 (426, 743)	716 (603, 829)	0.17

[1] Values are means (95% CIs). Statistical comparisons were made by using 2-sided *t* tests. ERAS, Enhanced Recovery After Surgery; POD, postoperative day.

[2] The conventional group received nil per os and diet progressed at the discretion of the surgeon.

[3] The ERAS group received solid food on POD 0 and 60 mL oral nutrition supplement offered 5 times/d.

[4] Refers to intakes of food and oral nutrition supplements.

Compared with estimated protein requirements of 1.5 g $\cdot$ kg^{-1} $\cdot$ d^{-1} with the use of ideal body weight (18, 19), both groups' intakes were low at 0.54 g $\cdot$ kg^{-1} $\cdot$ d^{-1} (ERAS group) compared with 0.33 g $\cdot$ kg^{-1} $\cdot$ d^{-1} (conventional group). Although ERAS patients consumed more total protein ($P < 0.02$), their protein intakes from food alone (not including ONSs) were not significantly higher on any of the 3 d.

In the multivariable regression that adjusted for group imbalances in baseline (MST, obesity rate) and surgical variables (open compared with laparoscopic procedures and whether ostomies were created) between the 2 groups on our primary outcome, the protein intake per kilogram remained statistically different between the ERAS and conventional groups by 0.20 g $\cdot$ kg^{-1} $\cdot$ d^{-1} ($P = 0.001$).

The ERAS group consumed more total energy than the conventional group ($P < 0.002$) (Table 3) and was able to achieve significantly higher proportions of estimated energy requirements on all 3 d: 62% (95% CI: 54%, 69%) compared with 39% (95% CI: 31%, 47%) ($P < 0.0001$). Similar to protein intakes, the higher energy intakes of the ERAS group were primarily due to the contribution of ONSs because the energy intakes from food did not differ significantly between the 2 groups (Table 3).

The numbers of patients who were discharged before receiving 3 hospital meals/d were as follows—on POD 2: 1 (1%) for the ERAS group; on POD 3: 4 (9%) for the conventional group and 26 (38%) for the ERAS group. Other than these food records missed due to early discharge, we had complete food records for all other meals.

Postoperative outcomes

Major postoperative complication rates were similar between the groups (4% compared with 7%; $P = 0.70$) (**Table 4**). The ERAS group had significantly fewer total complications (39% compared with 61%; $P = 0.04$) and significantly fewer minor complications (32% compared with 57%; $P = 0.01$) (Table 4). Total infectious complications were also fewer in the ERAS group (14% compared with 35%; $P = 0.01$), including wound infections (1% compared with 11%; $P = 0.04$).

The LOS for the ERAS group was significantly shorter than that of the conventional group (6.5 compared with 9.7 d; $P = 0.049$) (Table 4). There were no significant differences between the 2 groups for postoperative measures of gastrointestinal function (nausea, vomiting, day of first flatus, day of first bowel movement) or readmission within 30 d (Table 4).

Laboratory values

There were no significant differences in the preoperative laboratory values between the 2 groups. Postoperative potassium and magnesium were statistically lower, but not clinically different, in the conventional group compared with the ERAS group ($P = 0.02$ and 0.001, respectively) (**Supplemental Table 2**). There was no association between measures of gastrointestinal function and electrolyte concentrations (magnesium, potassium, and calcium) (data not shown).

Nausea and food intake

Nausea was a predictor of protein intake. For every unit of nausea on a scale from 0 to 10, protein intake was lower by 2.5 g/d (95% CI: −3.1, −1.9 g/d; $P < 0.001$) (**Supplemental Table 3**). The difference in protein intake between those with a reported level of extreme nausea (10) compared with no nausea (0) was estimated to be 19–31 g (95% CI) lower/d (**Figure 3**).

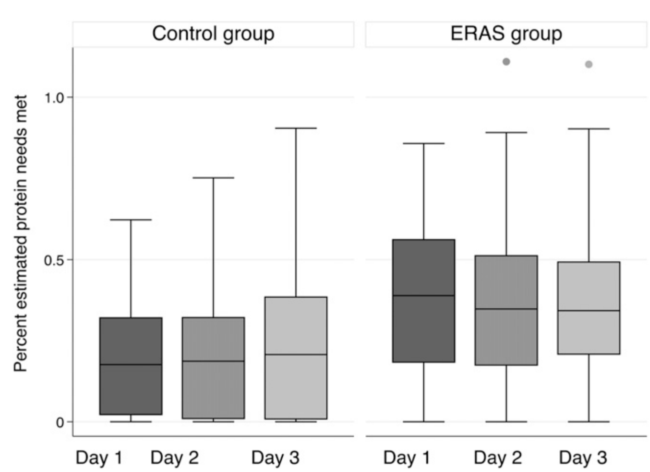

FIGURE 2 Boxplots showing that protein intakes, expressed as a percentage of estimated protein requirements (1.5 g $\cdot$ kg^{-1} $\cdot$ d^{-1}), were significantly higher in the ERAS group ($n = 69$) than in conventional care group ($n = 46$) on each of the 3 d postoperatively ($P < 0.04$). The median, IQR, and high adjacent values are shown. Gray dots indicate outlying values. The conventional group, on average, consumed 22% and the ERAS group consumed 36% of their estimated protein requirements during the first 3 d (2-sided *t* test, $P = 0.001$). ERAS, Enhanced Recovery After Surgery.

TABLE 4
Postoperative outcomes between conventional care and ERAS patients[1]

	Conventional (n = 46)	ERAS (n = 69)	P
Length of hospital stay	9.7 (7.2, 12.1)	6.5 (4.4, 8.5)	0.049
Readmissions within 30 d, n (%)	2 (4)	8 (12)	0.31
Self-reported nausea score[2]			
POD 1	3.4 (2.4, 4.5)	3.7 (2.7, 4.6)	0.74
POD 2	2.8 (1.8, 3.8)	3.5 (2.6, 4.4)	0.32
POD 3	2.4 (1.4, 3.3)	2.4 (1.5, 3.2)	0.98
Vomiting incidence first 3 postoperative days, n (%)	15 (33)	13 (19)	0.12
Day of first postoperative flatus	1.8 (1.4, 2.1)	1.6 (1.4, 1.8)	0.34
Day of first postoperative bowel movement	2.1 (1.6, 2.7)	1.8 (1.4, 2.1)	0.23
Total patients with complications, n (%)	21 (46)	22 (32)	0.17
Total number of complications, n (%)	28 (61)	27 (39)	0.036
Total major complications,[3] n (%)	2 (4)	5 (7)	0.70
Total minor complications,[4] n (%)	26 (57)	22 (32)	0.012
Total infectious complications, n (%)	16 (35)	10 (14)	0.013
Wound infection, n (%)	5 (11)	1 (1)	0.037

[1] Values are means (95% CIs) unless otherwise indicated. Statistical comparisons were made by using 2-sided t test and Fisher's exact tests. ERAS, Enhanced Recovery After Surgery; POD, postoperative day.

[2] Nausea was determined by verbal numeric rating scale between 0 (no nausea) and 10 (extreme nausea).

[3] Clavien-Dindo classification was used to grade postoperative complication rates. Higher scores represent greater severity of complications. Major complications refer to a Clavien-Dindo classification score of 3b-5.

[4] Refers to a Clavien-Dindo classification score ≤3a. Patients may have had >1 complication.

Regression analysis

Multivariable linear regression analysis was used to identify independent predictors of LOS after potential confounders were controlled for. The final model (R^2 = 0.576) identified independent predictors of LOS including the following: high MST score, low protein intake for the first 3 d of <60% of requirements, high preoperative and postoperative C-reactive protein concentrations, high HbA1C, complications-graded Clavien-Dindo score of 3b-5, and transfusions (**Table 5**). Notably, each unit increase in preoperative MST score was found to predict a longer mean LOS by 2.5 d (95% CI: 1.5, 3.5 d; P < 0.001) and each unit of preoperative HbA1C concentration predicted a longer mean LOS by 3.1 d (95% CI: 1.1, 5.2 d; P = 0.003). The consumption of ≥60% of protein requirements during the first 3 d of hospitalization was associated with a shorter LOS of 4.4 d (95% CI: −6.8, −2.0 d; P < 0.001). Blood transfusions predicted a longer LOS of 11.6 d (95% CI: 5.9, 17.2 d; P < 0.001). The following variables were not associated with LOS in the multivariable model: age, Charlson Comorbidity Index, ERAS group, length of surgery, presence of an ostomy, and open compared with laparoscopic surgery.

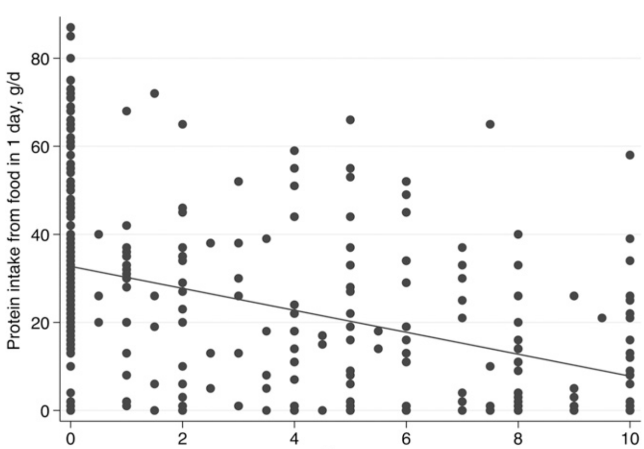

FIGURE 3 Association between nausea and protein intakes during days 1–3 after surgery in both the ERAS and conventional care groups combined (n = 115). Linear regression (as indicated by the regression line) showed that for every unit of nausea on a scale from 0 to 10, protein intake was lower by 2.5 g/d (95% CI: −3.1, −1.9 g/d; P < 0.001). The difference in protein intake between those with a reported level of extreme nausea (10) compared with no nausea (0) was estimated to be 19–31 g (95% CI) lower per day. ERAS, Enhanced Recovery After Surgery.

DISCUSSION

Optimizing nutrition status is an integral component of ERAS protocols. This is the first study, to our knowledge, to show that total oral intake of protein is greater in ERAS patients than in those receiving conventional care. The ERAS patients consumed significantly more protein and energy than the conventional care patients during the first 3 PODs as a result of the ERAS guideline to supplement with ONSs (7, 8). Total oral food intake was similar between the 2 groups, which suggests that ONS intake did not reduce patients' food consumption from meals, a finding that supports a similar result from a previous non-ERAS study (27).

Thus, ONS intake is an important nutritional component of the ERAS pathway. However, most of our ERAS patients did not consume ONS amounts recommended by ERAS guidelines. Given our patients' suboptimum protein intakes, further understanding of the barriers to meeting these targets and strategies to improve ONS intake is needed.

Our findings that a low food intake during the first week of hospitalization and a diagnosis of malnutrition at admission were independent predictors of longer LOS are in agreement with those of a large prospective multicenter cohort study in hospitalized patients, the Canadian Malnutrition Task Force (28) and other studies (29, 30). Similarly, Garth et al. (29) identified that a longer time to achieve adequate oral intake after gastrointestinal

TABLE 5
Independent predictors of LOS among both conventional care and ERAS patients[1]

		Univariate relations		Adjusted relations	
Independent variables	Sample size, *n*	LOS (95% CI), d	*P*	LOS (95% CI), d	*P*
Malnutrition Screening Tool	115	2.5 (1.2, 3.9)	<0.001	2.5 (1.5, 3.5)	<0.001
Preoperative HbA1C	114	2.9 (0.6, 5.2)	0.013	3.1 (1.1, 5.2)	0.003
Preoperative C-reactive protein	97	0.11 (0.04, 0.18)	0.003	0.06 (0.01, 0.11)	0.017
Transfusion	115	20.5 (13.1, 27.7)	<0.001	11.6 (5.9, 17.2)	<0.001
Postoperative C-reactive protein	115	0.10 (0.05, 0.10)	<0.001	0.03 (0.01, 0.05)	0.005
Protein intake of ≥60% of individual requirements	115	−7.8 (−11.0, −4.6)	<0.001	−4.4 (−6.8, −2.0)	<0.001
Clavien-Dindo complications of grade 3b or higher	115	16.8 (10.5, 23.1)	<0.001	6.8 (1.5, 12.1)	0.011

[1] Multivariable linear regression analysis was used to identify independent predictors of LOS in the full sample of ERAS and conventional care patients (R^2 = 0.576). Statistical analysis was performed by using multivariable regression. ERAS, Enhanced Recovery After Surgery; HbA1c, glycated hemoglobin; LOS, length of hospital stay.

surgery was correlated with longer LOS ($r = 0.493$, $P < 0.01$). It is thus becoming increasingly recognized that attention to perioperative nutrition status and oral intake is required to optimize recovery from surgery.

Our finding that lower protein intakes were associated with more nausea may at least in part explain the suboptimal protein intakes in colorectal surgery patients. In addition to adequate control of nausea, there are other factors to consider for improving protein intake. The protein content of reported standard hospital meals, from 67 to 95 g protein/d (15, 31–33), may not meet the enhanced protein needs of surgery patients. Hospital menu systems that allow for customized protein choices to better accommodate patients' food preferences may promote greater food intake (11, 32). A previous randomized trial found that patients who received ONSs preoperatively from ∼2 wk before surgery until 4 wk after discharge had less postoperative weight loss and fewer minor complications (27). Furthermore, a current systematic review showed that the provision of a high-protein ONS (≥20% of energy as protein) increased protein and energy intakes without decreasing usual food intake (34).

Most of our patients, independent of grouping, were discharged home before meeting their protein needs. Dietitian nutrition counseling after gastrointestinal surgery has been effective in achieving clinically important improvements in both energy and protein intakes (29). We recommend perioperative nutrition education by a dietitian with the goal of optimizing nutritional status (29, 35).

Our findings suggest that ERAS patients are able to achieve minimally acceptable energy intakes [i.e., ∼60% of energy requirements (19, 39)]; yet, protein intakes (36%) are far below this recommendation. Current ERAS publications do not include specific protein recommendations (7, 8). Currently, the ERAS Interactive Audit System is used to monitor the energy but not protein consumption of ONSs. ERAS protocols should be expanded to optimize the protein intake of surgical patients, to monitor and set minimum standards. The ERAS pathway should also include specific recommendations for nutrition education in the perioperative period. Our findings that the patients who received ERAS care were discharged earlier and experienced fewer complications than conventional care patients are consistent with the findings of meta-analyses that showed that the ERAS pathway shortens LOS by 2–3 d (37–39).

Several limitations of this study are related to the lack of randomization of the participants to the ERAS program and conventional care, which resulted in patient groups that were not identical. Although our multivariable regression found that the difference in protein intakes between the groups was maintained at 0.2 $g \cdot kg^{-1} \cdot d^{-1}$ (P = 0.001) when these intergroup differences were adjusted for, there is always the possibility of residual confounding by unmeasured variables. The possibility of residual confounding could have produced bias and inaccurate findings to either over- or underestimate the differences in nutrition intake. In addition, medical residents rotating between hospital sites were exposed to ERAS protocols during the data collection phase at the conventional site, which may have influenced ordering practices to include some ERAS components. This contamination of the groups would have diluted the effects. Finally, we acknowledge that the method of visual estimation of oral food intake may have resulted in inaccuracies of the quantity of food consumed.

In conclusion, ERAS patients consume more protein attributed to ONSs. However, neither ERAS nor conventional care patients consumed amounts of protein considered minimally acceptable in the first 3 d after surgery. The consumption of ≥60% of recommended protein needs and preoperative MST scores were found to be independent predictors of LOS. Future ERAS guidelines should therefore consider including a more specific, comprehensive nutrition component that promotes strategies for maintaining nutritional adequacy postoperatively.

We thank Melissa Mucenski, Ramia Elkadri, Eric Holmes, and Tammy Herda-Nelson for their valuable assistance with consultation, data collection, and administrative assistance.

The authors' responsibilities were as follows—SEY and LH: designed the research (project conception, development of the overall research plan, and study oversight) and had primary responsibility for the final content; CG: analyzed the data; TRF: designed the research and performed the statistical analysis; SEY, LH, CG, JAH, and TRF: wrote the paper; and all authors: read and approved the final manuscript. None of the authors reported a conflict of interest related to the study.

REFERENCES

1. Schricker T, Meterissian S, Donatelli F, Carvalho G, Mazza L, Eberhart L, Wykes L, Carli F. Parenteral nutrition and protein sparing after surgery: do we need glucose? Metabolism 2007;56:1044–50.
2. Phillips BE, Smith K, Liptrot S, Atherton PJ, Varadhan K, Rennie MJ, Larvin M, Lund JN, Williams JP. Effect of colon cancer and surgical resection on skeletal muscle mitochondrial enzyme activity in colon cancer patients: a pilot study. J Cachexia Sarcopenia Muscle 2013;4:71–7.
3. Gibson NR, Fereday A, Cox M, Halliday D, Pacy PJ, Millward DJ. Influences of dietary energy and protein on leucine kinetics during feeding in healthy adults. Am J Physiol 1996;270:E282–91.

4. Longland TM, Oikawa SY, Mitchell CJ, Devries MC, Phillips SM. Higher compared with lower dietary protein during an energy deficit combined with intense exercise promotes greater lean mass gain and fat mass loss: a randomized trial. Am J Clin Nutr 2016;103:738–46.
5. Deutz NEP, Safar A, Schutzler S, Memelink R, Ferrando A, Spencer H, van Helvoort A, Wolfe RR. Muscle protein synthesis in cancer patients can be stimulated with a specially formulated medical food. Clin Nutr 2011;30:759–68.
6. Carli F, Galeone M, Gzodzic B, Hong X, Fried GM, Wykes L, Eberhart L, Schricker T. Effect of laparoscopic colon resection on postoperative glucose utilization and protein sparing: an integrated analysis of glucose and protein metabolism during the fasted and fed states using stable isotopes. Arch Surg 2005;140:593–7.
7. Gustafsson UO, Scott MJ, Schwenk W, Demartines N, Roulin D, Francis N, McNaught CE, Macfie J, Liberman AS, Soop M, et al. Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS) Society recommendations. World J Surg 2013;37:259–84.
8. Nygren J, Thacker J, Carli F, Fearon KCH, Norderval S, Lobo DN, Ljungqvist O, Soop M, Ramirez J. Guidelines for perioperative care in elective rectal/pelvic surgery: Enhanced Recovery After Surgery (ERAS) Society recommendations. World J Surg 2013;37:285–305.
9. Nygren J, Soop M, Thorell A, Hausel J, Ljungqvist O. An enhanced-recovery protocol improves outcome after colorectal resection already during the first year: a single-center experience in 168 consecutive patients. Dis Colon Rectum 2009;52:978–85.
10. Svanfeldt M, Thorell A, Hausel J, Soop M, Rooyackers O, Nygren J, Ljungqvist O. Randomized clinical trial of the effect of preoperative oral carbohydrate treatment on postoperative whole-body protein and glucose kinetics. Br J Surg 2007;94:1342–50.
11. Gillis C, Nguyen TH, Liberman AS, Carli F. Nutrition adequacy in enhanced recovery after surgery: a single academic center experience. Nutr Clin Pract 2015;30:414–9.
12. Winter A, MacAdams J, Chevalier S. Normal protein anabolic response to hyperaminoacidemia in insulin-resistant patients with lung cancer cachexia. Clin Nutr 2012;31:765–73.
13. Gillis C, Carli F. Promoting perioperative metabolic and nutritional care. Anesthesiology 2015;123:1455–72.
14. Ferguson M, Capra S, Bauer J, Banks M. Development of a valid and reliable malnutrition screening tool for adult acute hospital patients. Nutrition 1999;15:458–64.
15. Olin AO, Osterberg P, Hådell K, Armyr I, Jerström S, Ljungqvist O. Energy-enriched hospital food to improve energy intake in elderly patients. JPEN J Parenter Enteral Nutr 1996;20:93–7.
16. USDA, Agricultural Research Service. National Agricultural Library [Internet]. [cited 2015 Oct 15]. Available from: https://ndb.nal.usda.gov/.
17. Mifflin MD, St. Jeor ST, Hill LA, Scott BJ, Daugherty SA, Koh YO. A new predictive equation for resting energy expenditure in healthy individuals. Am J Clin Nutr 1990;51:241–7.
18. Colliet BR, Cherry-Bukowiec JR, Millis M. Trauma, surgery, burns. In: Mueller C, editor. The ASPEN adult nutrition core curriculum. 2nd ed. Silver Spring (MD): American Society for Parenteral and Enteral Nutrition; 2012. p. 393–406.
19. Braga M, Ljungqvist O, Soeters P, Fearon K, Weimann A, Bozzetti F. ESPEN guidelines on parenteral nutrition: surgery. Clin Nutr 2009;28:378–86.
20. Meek R, Egerton-Warburton D, Mee MJ, Braitberg G. Measurement and monitoring of nausea severity in emergency department patients: a comparison of scales and exploration of treatment efficacy outcome measures. Acad Emerg Med 2015;22:685–93.
21. Diemunsch P, Gan TJ, Philip BK, Girao MJ, Eberhart L, Irwin MG, Pueyo J, Chelly JE, Carides AD, Reiss T, et al. Single-dose aprepitant vs ondansetron for the prevention of postoperative nausea and vomiting: a randomized, double-blind phase III trial in patients undergoing open abdominal surgery. Br J Anaesth 2007;99:202–11.
22. Dindo D, Demartines N, Clavien P-A. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205–13.
23. Henriksen MG, Hansen HV, Hessov I. Early oral nutrition after elective colorectal surgery: influence of balanced analgesia and enforced mobilization. Nutrition 2002;18:263–7.
24. Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux PJ, Elbourne D, Egger M, Altman DG. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. J Clin Epidemiol 2010;63:e1–37.
25. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–83.
26. Nelson G, Kiyang LN, Crumley ET, Chuck A, Nguyen T, Faris P, Wasylak T, Basualdo-Hammond C, McKay S, Ljungqvist O, et al. Implementation of Enhanced Recovery After Surgery (ERAS) across a provincial healthcare system: the ERAS Alberta colorectal surgery experience. World J Surg 2016;40:1092–103.
27. Smedley F, Bowling T, James M, Stokes E, Goodger C, O'Connor O, Oldale C, Jones P, Silk D. Randomized clinical trial of the effects of preoperative and postoperative oral nutritional supplements on clinical course and cost of care. Br J Surg 2004;91:983–90.
28. Allard JP, Keller H, Jeejeebhoy KN, Laporte M, Duerksen DR, Gramlich L, Payette H, Bernier P, Vesnaver E, Davidson B, et al. Malnutrition at hospital admission—contributors and effect on length of stay: a prospective cohort study from the Canadian Malnutrition Task Force. JPEN J Parenter Enteral Nutr 2016;40:487–97.
29. Garth AK, Newsome CM, Simmance N, Crowe TC. Nutritional status, nutrition practices and post-operative complications in patients with gastrointestinal cancer. J Hum Nutr Diet 2010;23:393–401.
30. Tsaousi G, Kokkota S, Papakostas P, Stavrou G, Doumaki E, Kotzampassi K. Body composition analysis for discrimination of prolonged hospital stay in colorectal cancer surgery patients. Eur J Cancer Care (Engl) 2016 Mar 16 (Epub ahead of print; DOI: 10.1111/ecc.12491).
31. Dupertuis YM, Kossovsky MP, Kyle UG, Raguso CA, Genton L, Pichard C. Food intake in 1707 hospitalised patients: a prospective comprehensive hospital survey. Clin Nutr 2003;22:115–23.
32. Munk T, Beck AM, Holst M, Rosenbom E, Rasmussen HH, Nielsen MA, Thomsen T. Positive effect of protein-supplemented hospital food on protein intake in patients at nutritional risk: a randomised controlled trial. J Hum Nutr Diet 2014;27:122–32.
33. Barton AD, Beigg CL, Macdonald IA, Allison SP. High food wastage and low nutritional intakes in hospital patients. Clin Nutr 2000;19:445–9.
34. Cawood AL, Elia M, Stratton RJ. Systematic review and meta-analysis of the effects of high protein oral nutritional supplements. Ageing Res Rev 2012;11:278–96.
35. Lithner M, Johansson J, Andersson E, Jakobsson U, Palmquist I, Klefsgard R. Perceived information after surgery for colorectal cancer—an explorative study. Colorectal Dis 2012;14:1340–50.
36. Weimann A, Braga M, Harsanyi L, Laviano A, Ljungqvist O, Soeters P, Jauch KW, Kemen M, Hiesmayr JM, Horbach T, et al. ESPEN guidelines on enteral nutrition: surgery including organ transplantation. Clin Nutr 2006;25:224–44.
37. Ni T-G, Yang H-T, Zhang H, Meng H-P, Li B. Enhanced Recovery After Surgery programs in patients undergoing hepatectomy: a meta-analysis. World J Gastroenterol 2015;21:9209–16.
38. Zhuang C-L, Ye X-Z, Zhang X-D, Chen B-C, Yu Z. Enhanced Recovery After Surgery programs versus traditional care for colorectal surgery: a meta-analysis of randomized controlled trials. Dis Colon Rectum 2013;56:667–78.
39. Greco M, Capretti G, Beretta L, Gemma M, Pecorelli N, Braga M. Enhanced recovery program in colorectal surgery: a meta-analysis of randomized controlled trials. World J Surg 2014;38:1531–41.