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RAPID COMMUNICATION

Perioperative artificial nutrition in malnourished gastrointestinal cancer patients

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Abstract

AIM: To investigate the potential role of perioperative nutrition in reducing complications and mortality in malnourished gastrointestinal cancer patients.

METHODS: Four hundred and sixty-eight elective moderately or severely malnourished surgical patients with gastric or colorectal cancers defined by the subjective global assessment (SGA) were randomly assigned to 7 d preoperative and 7 d postoperative parenteral or enteral nutrition *vs* a simple control group. The nutrition regimen included 24.6±5.2 kcal /kg per d non-protein and 0.23±0.04 g nitrogen /kg per d. Control patients did not receive preoperative nutrition but received 600±100 kcal non-protein plus or not plus 62 ± 16 g crystalline amino acids postoperatively.

RESULTS: Complications occurred in 18.3% of the patients receiving nutrition and in 33.5% of the control patients ($P = 0.012$). Fourteen patients died in the control group and 5 in those receiving nutrition. There were significant differences in the mortality between the two groups (2.1% *vs* 6.0%, $P = 0.003$). The total length of hospitalization and postoperative stay of control patients were significantly longer (29 *vs* 22 d, $P = 0.014$) than those of the studied patients (23 *vs* 12 d, $P = 0.000$).

CONCLUSION: Perioperative nutrition support is beneficial for moderately or severely malnourished gastrointestinal cancer patients and can reduce surgical complications and mortality.

Key words: Malnutrition; Perioperative nutrition; Parenteral nutrition; Enteral nutrition; Mortality; Complications

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INTRODUCTION

Malnutrition is common in gastrointestinal cancer patients and the causes are often complex and multi-factorial. Although it is widely accepted that malnutrition adversely affects the postoperative outcome of patients, there is little evidence that perioperative nutrition support can reduce surgical risk in malnourished cancer patients. Early retrospective studies suggested that perioperative nutrition support may effectively reduce postoperative complications[1,2]. Subsequent prospective, randomized clinical trials (RCTs) demonstrated that the benefits of perioperative nutrition support are limited to severely malnourished patients undergoing major surgery[3,4]. Most RCTs of perioperative nutritional support in patients with gastrointestinal cancer have shown that the degree of malnutrition varies considerably, ranging from no weight loss to weight loss exceeding 10 % and the results obtained by these studies are different in malnourished and non-malnourished patients[1-4]. Unfortunately, studies in really malnourished gastrointestinal cancer patients are not available. Meanwhile, parenteral and enteral nutrition is till controversial in perioperative malnourished gastrointestinal cancer patients[5].

The aim of this study was to evaluate the efficacy of optimal perioperative nutrition support in reducing complications and mortality in malnourished gastrointestinal cancer patients.

MATERIALS AND METHODS

This prospective study was carried out from May 2002 to July 2004 at the General Surgical Department of Zhongshan Hospital. All patients who underwent surgery for gastrointestinal (stomach, colon and rectum) malignancies were eligible for inclusion. Patients were excluded if they were admitted for emergency surgery. Within 48 h of admission, patients underwent nutritional assessment by the subjective global assessment. (SGA) performed with a standardized questionnaire including the patient's history (weight loss, changes in dietary intake, gastrointestinal symptoms, and functional capacity), physical examination (muscle, subcutaneous fat, sacral

Table 1 Preoperative characteristics of the patients

	Study group ($n=235$)	Control group ($n=233$)
Mean age (yr)	57.3	56.5
Male/ female	162/95	166/89
Body weight (kg)	59.4±15.2	61.1±14.9
SGA score		
B	147	153
C	88	80
Gastric carcinoma	124	129
Colon carcinoma	65	61
Rectum carcinoma	46	43

SGA: subjective global assessment; B: moderately- malnourished; C: severely-malnourished.

and ankle edema, ascites) and the clinician's overall judgment of the patient's status (normal, moderately or severely malnourished). On the basis of these data, the patients were classified as well-nourished, moderately- or severely-malnourished. A total of 512 moderately- and severely-malnourished gastrointestinal cancer patients were included in this study. The Ethical Committee of the Institution approved this clinical study.

After stratified for age, sex and tumor localization (gastric, colorectal), patients were randomly divided into study group ($n=257$, 95 women, 162 men) and control group ($n=255$, 89 women, 166 men). The mean ages were 57.3 years (range 21 - 84 years) and 56.5 years (range 24 - 86 years) in the study group and control group, respectively.

Perioperative nutrition was administered in the study group by parenteral or enteral route or a combination of the two based on a clinical assessment of intestinal function. Patients due to permanent or temporary intestinal failure were given parenteral nutrition (PN). If the clinician felt that the patients had a functioning gastrointestinal tract, they received enteral nutrition (EN).

Most patients (68%) received PN support during the preoperative and postoperative periods. The PN regimen consisted of 25 kcal/kg per d non-protein and 0.25 g nitrogen /kg per d. The non-protein calorie source included glucose and fat, accounting for 60% and 40% respectively of the energy intake. The protein source was supplied by crystalline amino acid solutions. Electrolytes, vitamins, and trace elements were administered according to the current recommendations. PN mixture was delivered through a central venous catheter or peripheral veins using an "all in one" bag. In addition, the patients receiving preoperative PN had free access to food they preferred.

EN was given to 75 patients (32%) in whom GI function was adequate through a fine bore silicone feeding tube. Where appropriate, EN was alternatively administered via a nasogastric tube or a feeding jejunostomy catheter. Similar target intake of non-protein (25 kcal/kg per d) and protein (0.25 g nitrogen/kg per d) was provided using commercially available enteral formulas. The initial rate of delivery was 40-60 mL/h, increasing stepwise to full intake for 48 h according to patient tolerance. Foods were usually given as a continuous infusion using a volumetric pump for 24 h. Nutritional support was started 8-10 d before surgery and continued for more than a week after surgery.

Patients in the control group were given a standard hospital oral diet before surgery and a hypocaloric parenteral solution (600 kcal non-protein and 60 g amino acid) in the postoperative period until gastrointestinal function recovered completely.

After surgery, patients were monitored daily for postoperative complications including septicemia, intra-abdominal abscess, wound infection, wound dehiscence, fistula formation, urinary tract infection, pneumonia, respiratory insufficiency and phlebitis. Rigid objective criteria were established defining each complication to avoid subjective bias. A diagnosis of septicemia was based on a positive blood culture, hypotension and hypoperfusion. An intra-abdominal abscess was defined as an intra-abdominal purulent collection requiring operative drainage. Fistulae were radiographically documented. A diagnosis of urinary tract infection required a quantitative culture of greater than 100 000 organisms. Pneumonia was documented by an abnormal chest x-ray, positive sputum culture, and treatment with antibiotics. The presence of a wound infection was defined by culture and operative or spontaneous drainage of purulent materials. A wound dehiscence required operative re-closure of the wound. The occurrence and cause of death during hospitalization and the length of hospitalization were recorded.

Statistical analysis

Data were analyzed using standard statistical software (SPSS 10.0). For normally distributed data, a paired Student's t test was used for statistical analysis. $P \leqslant 0.05$ was considered statistically significant. Data were expressed as mean $\pm$ SE.

RESULTS

A total of 512 malnourished patients gave their consent to participate in the study and 16 declined. Of the 512 patients, 28 were not randomized after surgery because of un-resectability. Four hundred and sixty-eight patients were assigned at random to study group ($n=235$, 87 women, 148 men) and control group ($n=233$, 90 women, 143 men). Patient demographics and preoperative parameters of the two groups are presented in Table 1. There were no significant differences in mean age, sex distribution and nutrition status between the two groups. Operative data are listed in Table 2. The mean length of the surgical procedure and the volume of intraoperative blood transfusions were similar in two groups. The volume of postoperative blood transfusions was larger in control group. However, none of these differences was statistically significant. The number of patients requiring albumin infusions and the volume of infused albumin were comparable between the groups.

The number of postoperative complications per study group is shown in Table 3. Forty-three complications occurred in 31 patients in the study group, and five patients died due to major complications. Seventy-eight complications occurred in 64 patients of the control group, and 14 patients died. There were significant

Table 2 Operative data of the patients (mean ± SE)

	Study group (*n* = 235)	Control group (*n* = 233)
Mean operating time (min)	210±84	196±102
Operative blood loss (mL)	540±150	525±120
Mean blood transfused (mL)		
Intraoperative	420±80	400±100
Postoperative	200±60	280±120
Patients with albumin infusion (*n*)	156	173
Mean albumin infusion (g)	45±22	55±30
Kind of operation		
Partial gastrectomy	82	90
Total gastrectomy	42	39
Colon resection	65	61
Rectum resection	46	43

Table 3 Postoperative complications in two groups

	Study group (*n* = 235)	Control group (*n* = 233)
Pneumonia	12	23
Urinary tract infection	6	10
Wound infection	11	20
Septicemia	2	5
Intra-abdominal abscess	4	7
Wound dehiscence	3	4
Fistula	2	4
Respiratory insufficiency	2	3
Phlebitis	1	2
Total	43 in 31 patients	78 in 64 patients

differences in the mortality and complications between the two groups (2.1% *vs* 6.0%, $P = 0.003$ for mortality; 18.3% *vs* 33.5%, $P = 0.012$ for complications). In both groups, the most frequent complication was infection related to muscle weakness and/or prolonged immobilization (respiratory insufficiency, phlebitis).

Table 4 summarizes the incidence of septic complications between PN and EN groups. No significant differences were found in the incidence of septic complications between the two groups of nonrandomized patients. In addition, there was no significant difference in the number of septic complications between the two groups.

The total perioperative and postoperative median length of hospitalization was 22 *vs* 29 d in the study group and 12 *vs* 23 d in the control group, respectively. The total length of hospitalization and postoperative stay of the control patients were significantly longer than those of the study patients ($P = 0.014$, $P = 0.000$).

Table 4 Incidence of septic complications in PN or EN group

	PN group (*n* = 160)	EN group (*n* = 75)	*P*
Incidence of septic complications	25 -15.60%	10 -13.30%	0.36
Mean No. of complications per patient (±SE)	0.22±0.03	0.20±0.04	0.19
Mean No. of complications per infected patient (±SE)	1.33±0.05	1.26±0.06	0.22

PN: parenteral nutrition; EN: enteral nutrition.

DISCUSSION

Malnutrition in hospitalized patients is a critical issue associated with a significant increase in morbidity and mortality. Recent surveys have demonstrated that 30 - 50% of hospitalized patients have a certain degree of malnutrition[6,7]. Malnutrition is closely associated with increased morbidity and mortality after major gastrointestinal surgery. Perioperative nutrition support can restore many of biochemical and immunologic abnormalities in malnourished or normal state. However, it is difficult to demonstrate that perioperative nutrition support can significantly reduce surgical complications except in the most severely malnourished patients[8]. Early retrospective studies from 1970s to 1980s suggested that perioperative nutrition support can reduce surgical complications. Subsequent prospective, randomized trials demonstrated that the benefits of perioperative nutrition support are limited to severely malnourished patients undergoing major surgery[3,4]. Most RCTs of perioperative nutritional support in patients with gastrointestinal cancer have shown that the degree of malnutrition varies considerably, ranging from no weight loss to weight loss exceeding 10%, and that the complication rate decreases from 56% in the control arm to 34% in the TPN arm, with no deaths in the latter group[4,9]. Because nutrition support can only ameliorate but not reverse the catabolic response to trauma, it may effectively improve nutritional state and reduce postoperative complications when started preoperatively[10].

This study represented a large randomized clinical trial to explore the role of perioperative nutrition support in moderately- and severely-malnourished gastrointestinal cancer patients. In these patients nutritional support was started 8 ± 10 d before surgery and continued for more than a week after surgery. Nutrition was given by parenteral or enteral routes or a combination of these two. Postoperative complications were defined by rigid objective criteria to avoid subjective bias. This prospective study demonstrated that adequate perioperative nutritional support could effectively reduce the incidence of postoperative complications in moderately- and severely-malnourished gastrointestinal cancer patients. In perioperative nutrition support patients, there was a two-fold reduction in complications ($P = 0.012$) and a three-fold reduction in death ($P = 0.003$). The most dramatic decrease was noted in major septic complications (14.9% *vs* 27.9%, $P = 0.011$) such as pneumonia and wound infection. In addition, the mortality was statistically lower in artificial nutrition support group than in the control group (2.1% *vs* 6.0%, $P = 0.003$). As a consequence of the lower infection rate, the length of hospital stay of the study group was shorter. These results indicate that malnutrition has a negative impact on postoperative outcomes, which may be efficiently controlled by a perioperative nutrition support

that is adequate in quality, quantity, and duration.

Perioperative nutritional support can be administered by PN or EN or their combination. PN has the advantage of easy administration and essentially immediate provision of optimal nitrogen and caloric requirements once the central venous access is established. A major concern with PN in hospitalized patients is the increased risk of septic complications related to immune dysfunction after PN. Unlike PN, EN is not associated with increased infectious complications. In fact, enteral feeding can maintain structural and functional integrity of the gastrointestinal tract and reduce septic complications in critically ill patients. The major disadvantages of EN support are the time delay when attempting to provide complete nutrition by the enteral route and the inability of patients with postoperative abdominal complications to tolerate enteral feeding. Early postoperative EN has fewer septic complications compared to early postoperative PN [11, 12]. Unfortunately, studies in really malnourished cancer patients are not available. The present prospective study demonstrated that there was no statistically significant difference in the incidence of septic complications between PN and EN (15.6% *vs* 13.3%, $P = 0.36$). In addition, there was no significant difference in the number of septic complications per patient or complications per infected patient between PN and EN between the two groups. The results of our study are different from other prospective randomized trials[13-15]. There are several possible explanations for the discrepancies. First, patients are quite different in terms of age, physiologic and nutritional status. Second, the relative protein and energy intake in previous studies are often not comparable, usually being much higher in patients receiving PN than in those receiving EN[16,17]. Excessive energy intake may result in hyperglycaemia and lead to increased septic complications and mortality[18,19]. In the present study, the prescribed target intake for both PN and EN patients was the same (25 kcal /kg per d and 0.25 g N/kg per d). Third, in previous studies, all patients were randomized to receive either PN or EN, with no consideration given to the issue of gut function. Therefore some patients able to tolerate EN were given PN. In the present study, the route of feeding was dictated by an assessment of gut function, ensuring EN was administered only to patients with adequate intestinal function. The results of this study are in accord with the recent studies[20, 21].

In conclusion, perioperative nutrition support can decrease the incidence of postoperative complications in moderately- and severely-malnourished gastrointestinal cancer patients. In addition, it is effective in reducing mortality. Both parenteral support and enteral nutrition support, or their combination can be used in the management of malnourished patients undergoing gastrointestinal surgery.

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