



Enteral nutrition provides favorable postoperative outcomes for patients with pseudomyxoma peritonei: a retrospective study

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Background: Pseudomyxoma peritonei (PMP) is a rare malignancy, and many uncertainties regarding its treatment and prognosis still remain. The main treatment for PMP is cytoreductive surgery (CRS) combined with heated intraperitoneal chemotherapy (HIPEC), which can lead to intra-abdominal trauma and systemic reactions. Enteral nutrition (EN) is an important and beneficial perioperative option for major complicated abdominal surgery compared with total parenteral nutrition (TPN). However, the role of EN in PMP after surgery is still unknown. The purpose of this study was to analyze the effects of EN on postoperative outcomes in PMP patients.

Methods: The perioperative clinical data of PMP patients from Xiangya Hospital of Central South University who accepted CRS plus HIPEC from January 2011 to December 2018 were collected and analyzed. The effects of EN on the nutritional status, postoperative complications, and hospital stay time of patients with PMP were studied. We further analyzed the risk factors affecting hospital stay and complications in PMP patients after surgery.

Results: A total of 51 PMP patients accepted CRS and were enrolled in this study, including 25 cases in the EN group and 26 patients in the TPN group. The baseline demographic characteristics and preoperative nutritional status were not significantly different between the two groups. The postoperative absolute lymphocyte count ($P<0.001$), hemoglobin ($P=0.016$), and albumin ($P<0.001$) levels of the EN group were higher than those of the TPN group, but the postoperative hospital stay time ($P=0.008$) and the complication rate ($P=0.03$) in the EN group were less than those in the TPN group. Logistic regression analysis showed that age ($P=0.031$), American Society of Anesthesiologists (ASA) score ($P=0.008$), and EN ($P=0.024$) were independent risk factors for postoperative hospital stay in PMP patients. ASA score ($P=0.006$), number of prior operations ($P=0.021$), and EN ($P=0.035$) were independent risk factors for postoperative complications in PMP patients.

Conclusions: EN support results in better outcomes and is an independent protective factor for the postoperative hospital stay time and complications of PMP patients.

Keywords: Pseudomyxoma peritonei (PMP); enteral nutrition (EN); parenteral nutrition (TPN); postoperative complications

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Introduction

Pseudomyxoma peritonei (PMP) is a rare disease with mucinous ascites as the main clinical symptom, and is frequently associated with perforation of the appendix or ovary mucinous tumors (1,2). Although PMP rarely occurs in extra-abdominal metastasis, mucus exocrine cells are widely planted in the peritoneal cavity to form a large amount of jelly-like mucus ascites, causing death due to intestinal obstruction and cachexia (3). It is currently believed that cytoreductive surgery (CRS) combined with heated intraperitoneal chemotherapy (HIPEC) is the standard treatment option for patients with PMP (4–6). Because of the extensive abdominal and pelvic lesions, PMP patients who accept CRS can experience huge surgical trauma and a long operation time. In addition, postoperative HIPEC may be beneficial for selected PMP patients, but it might increase adverse events within the perioperative period, such as intra-abdominal infection, ileus, and anastomotic leakage (7,8). Therefore, smooth recovery is a challenge in the clinical treatment of PMP patients after CRS plus HIPEC.

One of the most important therapeutic progression for severe abdominal illnesses or major abdominal surgery in the past years is nutritional support (9,10). The effect of nutritional support on postoperative outcomes is especially important (11). Total parenteral nutrition (TPN) and enteral nutrition (EN) are the major nutritional support options for postoperative patients, and both of them have been shown to accelerate wound healing and prevent immunosuppression (9). EN is a type of nutritional support which is performed via an oral or nasogastric tube or jejunum tube. EN has the advantages of protecting immunity, balancing metabolic responses, and alleviating stress reactions, which finally improves the patient's clinical outcome compared to TPN (12). However, there is still controversy between the choice of postoperative EN or TPN for patients undergoing major abdominal surgery, mainly due to the potential complications of EN, including nausea, vomiting, and ileus (13). Moreover, there are few studies regarding the application of EN in PMP after CRS plus HIPEC.

The purpose of this study was to explore the application of EN in PMP patients and analyze the effects of EN and TPN on postoperative outcomes, and finally provide the appropriate postoperative nutritional support option for PMP patients. We present the following article in accordance with the STROBE reporting checklist (available

at <https://gs.amegroups.com/article/view/10.21037/gS-22-170/rc>).

Methods

Patient selection

This retrospective study was conducted in the Department of Gynecology Surgery of Xiangya Hospital of Central South University in China. We collected clinical data from all PMP patients who underwent CRS plus HIPEC in Xiangya Hospital of Central South University from January 2011 to December 2018. The inclusion criteria for the study were as follows: (I) all patients were diagnosed as PMP by postoperative pathological examination by at least 2 experienced pathologists; (II) the patient's surgical approach was CRS, and the generic surgical approach involved peritonectomy procedures and visceral resections as described by Sugarbaker (14). In this study, all patients underwent partial or total colectomy and partial omentectomy; (III) postoperative EN or TPN was feasible for the patient. The exclusion criteria were defined as patients with conditions involving difficulties in tumor identification, or patients in which EN or TPN was not performed. There was a total of 51 patients recruited in this study. Among the total of 51 patients with PMP enrolled in the study, 25 patients accepted EN and 26 patients accepted TPN therapy. This study was approved by the Ethics Committee of the Xiangya Hospital of Central South University (No. 202112173). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Since this study was retrospective and did not involve personal privacy, informed consent of previous patients could not be obtained objectively.

EN and TPN nutritional support

EN support was defined as the start of EN on the second day after surgery. The patients were given 30 kcal/kg per day after 2 or 3 days until the patient recovered and was discharged. The enteral nutrient solution was intact protein EN powder. The solution contained 1,000 kcal energy per 1,000 mL and consisted of 126 g carbohydrates, 50 g protein, and 33 g fat. The EN supplement method was tube feeding in addition to oral intake. TPN support was defined as a total parenteral venous infusion, which included glucose, amino acids, and fat emulsion, immediately after surgery until the patient recovered and was discharged.

Patients who received TPN were also given 30 kcal/kg per day, and the carbohydrates, proteins, and fats were provided as 50%, 20%, and 30% proportion of the overall energy, respectively.

Data collection

For each patient, we collected the general demographic characteristics and clinical data, including age, sex, histopathological subtype, number of prior operations, preoperative American Society of Anesthesiologists (ASA) physical status classification (0 point was given for normal health, no systemic diseases except local lesions and mild or moderate systemic diseases; 1 point was given for serious systemic diseases that limited daily life, but not incapacitated to work; serious systemic disease that lost the ability to work, life threatening; a dying patient who was critically ill and unable to sustain life), preoperative body mass index (BMI), preoperative absolute lymphocyte count, preoperative hemoglobin, preoperative albumin, postoperative absolute lymphocyte count, postoperative hemoglobin, postoperative albumin, postoperative BMI, postoperative hospital stay, and postoperative complications. Blood data was derived from clinical treatment blood sampling data. Weight and height were measured on admission and on the 10th day after surgery.

All patients were monitored during hospitalization until discharge in the hospital. Postoperative complications were graded as follows: grade 0 refers to no complications; grade 1 refers to self-resolving complications (such as gastrointestinal motility disorder); grade 2 refers to complications requiring medical treatment (such as abdominal, urinary, and pulmonary infections); grade 3 refers to complications requiring interventional radiology or minimally invasive procedural treatment (such as mild intestinal fistula or mild bleeding); grade 4 refers to complications requiring a return to the operating room for management (such as uncontrolled abdominal bleeding); and grade 5 refers to a 30-day stay in hospital or mortality [such as serious systemic inflammatory response syndrome (SIRS) or multiple organ dysfunction syndrome (MODS)]. Grade 0–2 was considered as a mild complication, and grade 3–5 was considered as a serious complication.

Statistical analysis

Data analysis was performed using SPSS version 22 software (SPSS Inc., Chicago, IL, USA). Continuous

variables were presented as mean \pm standard deviation (SD). Student's *t*-test, the Chi square test, one-way analysis of variance (ANOVA), and Fisher's exact tests were used to analyze differences in demographic and clinical data between the EN and TPN groups. The associations between demographic and clinical variables and postoperative outcomes were analyzed by odds ratios with their confidence intervals. Logistic regression analysis was used to explore the risk factors affecting hospital stay and complications after CRS in patients with PMP. A *P* value <0.05 was considered statistically significant.

Results

Baseline demographic characteristics and preoperative nutritional status of the two groups of patients

There were 32 female patients (62.7%) and 19 male patients (37.3%) in this study, and the median age was 58 years (59.06 \pm 11.09; range, 27 to 84 years). According to the nutritional support methods, there were 25 patients in the EN group and 26 patients in the TPN group. The general demographic characteristics and preoperative nutritional status of the two groups of patients were shown in *Table 1*. There were no significant differences between the EN and TPN groups in terms of age (*P*=0.833), gender (*P*=0.856), number of prior operations (*P*=0.931), ASA score (*P*=0.692), histopathological subtype (*P*=0.723), preoperative BMI (*P*=0.806), absolute lymphocyte count (*P*=0.619), hemoglobin (*P*=0.681), and albumin level (*P*=0.123). These results indicated that the baseline information of the two groups were comparable.

Postoperative nutritional status

The nutritional status of patients after CRS plus HIPEC in the EN and TPN groups was analyzed and compared. The dynamic curves of nutrition-related blood indicators on the 1st, 3rd, 5th, 7th, and 10th day after surgery in both groups are shown in *Figure 1*. The results showed that the postoperative absolute lymphocyte count of the EN group was superior to that of the TPN group (*P* <0.001 , *Figure 1A*). The postoperative hemoglobin and postoperative albumin levels in the EN group were also higher than those in the TPN group (*P*=0.016; *P* <0.001 , respectively, *Figure 1B, 1C*). At the same time, we compared the BMI of the two groups on the 10th day after surgery, and the results showed that the BMI of the EN group was significantly higher than that

Table 1 Baseline demographic characteristics and preoperative nutritional status of the two groups

Characteristics	EN	TPN	P
Age (years) , mean \pm SD	58.72 \pm 12.75	59.38 \pm 9.48	0.833
Preoperative BMI (kg/m ²), mean \pm SD	21.77 \pm 3.20	21.53 \pm 3.54	0.806
Preoperative absolute lymphocyte count (10 ⁶ /L), mean \pm SD	1.66 \pm 0.77	1.56 \pm 0.67	0.619
Preoperative hemoglobin (g/dL), mean \pm SD	11.84 \pm 1.55	12.03 \pm 1.75	0.681
Preoperative albumin (g/L), mean \pm SD	39.49 \pm 5.75	37.18 \pm 4.75	0.123
Time of operation (hours), mean \pm SD	4.61 \pm 1.31	4.55 \pm 1.13	0.426
Intraoperative bleeding (mL), mean \pm SD	473.34 \pm 24.56	484.57 \pm 38.87	0.233
Sex, n (%)			0.856
Male	9 (36.0)	10 (38.5)	
Female	16 (64.0)	16 (61.5)	
Histopathological subtype, n (%)			0.723
DPAM	16 (64.0)	19 (73.1)	
PMCA	7 (28.0)	6 (23.1)	
Hybrid	2 (8.0)	1 (3.8)	
ASA score, n (%)			0.692
I-II	16 (64.0)	18 (69.2)	
III-IV	9 (36.0)	8 (30.8)	
No. of prior operations, n (%)			0.931
0-1	18 (72.0)	19 (73.1)	
\geq 2	7 (28.0)	7 (26.9)	

EN, enteral nutrition; TPN, total parenteral nutrition; SD, standard deviation; BMI, body mass index; DPAM, diffuse peritoneal adenomucinosis; PMCA, peritoneal mucinous carcinomatosis; ASA, American Society of Anesthesiologists.

of the TPN group (21.27 \pm 2.87 *vs.* 19.74 \pm 3.94, P=0.029). These results demonstrated that EN could provide better nutritional support compared with TPN in patients with PMP after surgery.

Postoperative hospital stay and complications

Length of hospital stay and complications were the main markers for the fast recovery of patients after surgery. We compared the incidence of complications and the length of postoperative hospital stay of PMP patients after CRS plus HIPEC in the EN and TPN groups (Table 2). The results showed that the operation time (P=0.426) and intraoperative bleeding (P=0.233) were similar between the EN group and TPN group. However, the EN group had a shorter postoperative hospital stay than that in the TPN group (P=0.008). Furthermore, the incidence of

postoperative complications in the EN group was also lower than that in the TPN group (P=0.030). Our results showed that only 2 cases of SIRS and 1 case of celiac hemorrhage occurred in the EN group, while 5 cases of SIRS, 2 cases of celiac hemorrhage, 2 cases of intestinal fistula, and 1 case of pulmonary embolism occurred in the TPN group. These results indicated that EN could decrease postoperative complications and shorten the time of postoperative hospital stay in patients with PMP after surgery, which also indicated potentially greater economic efficiency.

The risk factors for postoperative hospital stay and complications

Finally, we further analyzed the potential risk factors for hospitalization time and complications after CRS plus HIPEC in patients with PMP by logistic regression

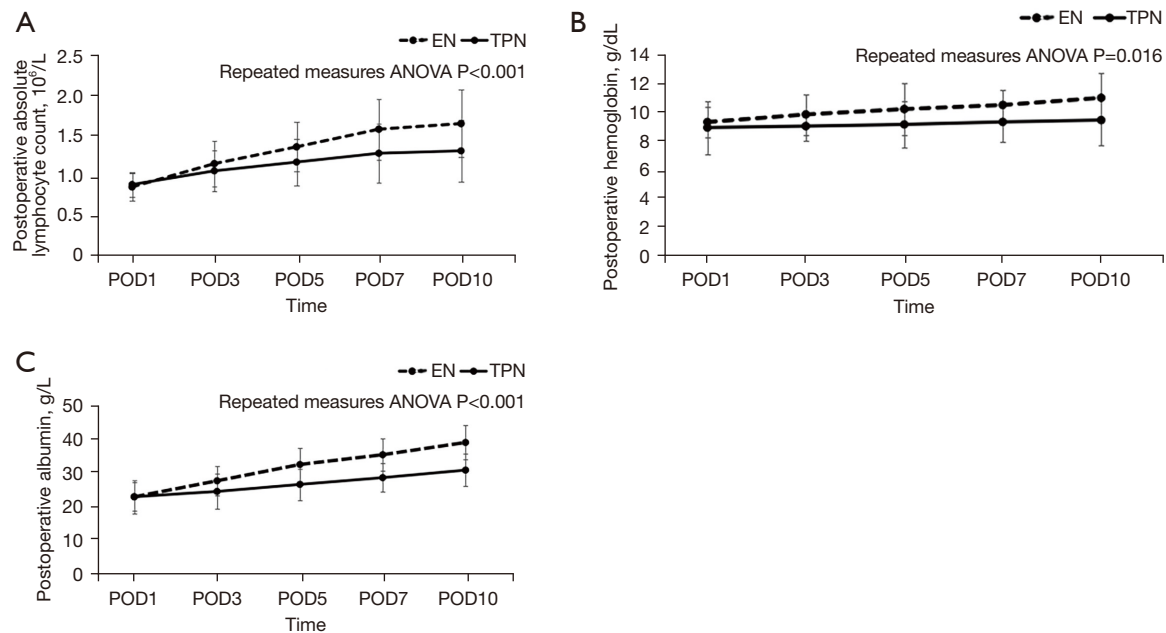


Figure 1 The nutritional status of PMP patients after surgery in the EN and TPN groups. The Y-axis of (A-C) represented absolute lymphocyte count, hemoglobin, and albumin level, and the X-axis represented day 1, 3, 5, 7 and 10 after operation. (A) The postoperative absolute lymphocyte count of the EN group was higher than that in the TPN group ($P < 0.001$); (B) the postoperative hemoglobin level of the EN group was higher than that in the TPN group ($P = 0.016$); (C) the postoperative albumin level of the EN group was higher than that in the TPN group ($P < 0.001$). PMP, pseudomyxoma peritonei; EN, enteral nutrition; TPN, total parenteral nutrition; ANOVA, analysis of variance; POD, day after operation.

Table 2 Postoperative hospital stay and complications after CRS in the two groups

Variables	EN	TPN	P
Postoperative hospital stay (days), mean \pm SD	14.34 \pm 2.03	17.34 \pm 2.67	0.008
Postoperative complications, n (%)			0.03
Grade 0 to 2	22 (88.0)	16 (61.5)	
Grade 3 to 5	3 (12.0)	10 (38.5)	

CRS, cytoreductive surgery; EN, enteral nutrition; TPN, total parenteral nutrition; SD, standard deviation.

analysis. The univariate analyses showed that older age (OR = 1.287, $P = 0.039$) and higher ASA score (OR = 1.327, $P = 0.003$) were risk factors, while EN (OR = 0.578, $P = 0.013$) was a protective factor for hospital stay time (Table 3). The multivariate analyses showed that older age (OR = 1.193, $P = 0.031$) and higher ASA score (OR = 1.301, $P = 0.008$) were independent risk factors for hospital stay time, while EN (OR = 0.628, $P = 0.024$) was an independent protective factor for hospital stay time (Table 3).

The univariate analyses for postoperative complications showed that older age (OR = 1.156, $P = 0.045$), higher ASA

score (OR = 1.164, $P = 0.001$), and operation history ≥ 2 (OR = 1.754, $P = 0.018$) were risk factors for postoperative complications, while EN (OR = 0.774, $P = 0.027$) was a protective factor for postoperative complications in PMP patients after CRS plus HIPEC (Table 3). Furthermore, multivariate analysis showed that higher ASA score (OR = 1.184, $P = 0.006$) and operation history ≥ 2 (OR = 1.703, $P = 0.021$) were independent risk factors for postoperative complications, while EN (OR = 0.887, $P = 0.035$) was an independent protective factor for postoperative complications (Table 3).

Table 3 Logistic regression analysis factors affecting postoperative hospital stay and complications

Variables	Postoperative hospital stay						Postoperative complications					
	Univariate analysis			Multivariate analysis			Univariate analysis			Multivariate analysis		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
Age (years)	1.287	1.034–1.534	0.039	1.193	1.021–1.501	0.031	1.156	1.003–1.234	0.045	1.093	0.987–1.247	0.073
Sex (male)	0.867	0.453–3.458	0.346	–	–	–	0.743	0.458–3.444	0.643	–	–	–
Preoperative BMI	0.983	0.876–5.356	0.738	–	–	–	1.042	0.881–3.222	0.334	–	–	–
Preoperative absolute lymphocyte count	2.123	0.894–5.557	0.548	–	–	–	1.352	0.793–1.983	0.226	–	–	–
Preoperative hemoglobin	1.474	0.993–1.653	0.737	–	–	–	0.834	0.362–8.342	0.822	–	–	–
Preoperative albumin	1.667	0.378–4.355	0.653	–	–	–	2.124	0.231–9.924	0.092	–	–	–
ASA score	1.327	1.123–1.735	0.003	1.301	1.204–1.802	0.008	1.164	1.034–1.214	0.001	1.184	1.042–1.337	0.006
Histopathological subtype	1.834	0.934–6.358	0.883	–	–	–	1.083	0.892–6.23	0.777	–	–	–
No. of prior operations	1.536	0.731–4.982	0.634	–	–	–	1.754	1.004–1.809	0.018	1.703	1.045–1.826	0.021
Time of operation	0.646	0.444–2.226	0.556	–	–	–	1.923	0.734–2.124	0.194	–	–	–
Intraoperative bleeding	1.863	0.323–7.433	0.759	–	–	–	1.782	0.432–7.328	0.872	–	–	–
Nutritional support methods	0.578	0.234–0.764	0.013	0.628	0.398–0.987	0.024	0.774	0.585–0.874	0.027	0.887	0.764–0.921	0.035

OR, odds ratio; CI, confidence interval; BMI, body mass index; ASA, American Society of Anesthesiologists.

These results indicated that ASA score was an independent risk factor, but EN was an independent protective factor both for hospital stay time and complications.

Discussion

Although the pathological morphology of PMP is relatively benign or low malignant, its biological behavior is malignant. It has the tendency to relapse and chronic consumption, which finally results in cachexia (15,16). Patients with PMP always undergo multiple operations or prolonged treatment, and cachexia is the main cause of death in advanced patients with PMP (17). As a result, good nutritional status after surgery is critical for the recovery of patients with PMP. Although TPN is still an important nutritional support method for serious illnesses, there are many drawbacks. For example, intravenous albumin does not provide enough glucose for energy to prevent the use of protein (18). Excessive albumin infusion can lead to thrombosis, renal leakage, fever, nausea, and vomiting (19–21). Therefore, there have been many studies on the benefits of EN for patients undergoing major operations, demonstrating that this approach can facilitate the recovery of intestinal function, improve postoperative nutritional status, and enhance immunity, among others (22–24). Most

PMP patients still retain enough functional gastrointestinal tract after CRS plus HIPEC, indicating that EN can be implemented. However, the effect of EN on postoperative nutritional support has rarely been reported for patients with PMP. The present study was the first report on EN applied in PMP patients, which identified the hypothesis.

Postoperative nutritional status is the most important criterion for selecting a nutritional support method. Through this study, we found better postoperative absolute lymphocyte count, postoperative hemoglobin, and postoperative albumin in the EN group, which indicated that EN was a rational method for PMP patients after surgery. This may be potentially explained by the fact that EN is more closely related to the form of nutrition uptake of healthy people, though little is known about how the intestine maintains a normal nutritional state. Wang *et al.* found that early EN could lead to better nutritional status in patients with esophageal cancer (25). This was consistent with our conclusions, which indicated that EN played a similar role in PMP patients after surgery.

Another important finding of our study was that the incidence of postoperative complications in the EN group was significantly lower than that in the TPN group, especially major complications such as SIRS and pulmonary embolism. A possible explanation is that EN can effectively

promote the recovery of gastrointestinal function. Previous studies identified that good nutritional status was beneficial to the healing of surgical wounds, enhancing immunity (26), and increasing the ability to resist the risk of postoperative complications (27-29).

Moreover, our study suggested that EN might improve the long-term prognosis of PMP patients, as the univariate and multivariate analyses showed that EN was an independent protective factor both for hospital stay time and complications. These findings were consistent with previous studies in that favorable nutritional status brought by EN was a positive predictor for postoperative mortality and prognosis in cancer patients (30,31). The improvement of nutritional status by EN also shortened the hospital stay time in this study, which saves on hospitalization costs and is beneficial to the physical and mental health of PMP patients.

In conclusion, our study provided the first evidence of EN in the perioperative management of the rare disease PMP. EN could provide better postoperative nutritional status, less complications, and a shorter postoperative hospital stay for PMP patients, and was an independent protective factor both for hospital stay time and complications. These findings suggested that EN was the appropriate nutritional support method for PMP patients after surgery and is worthy of further study.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://gs.amegroups.com/article/view/10.21037/gc-22-170/rc>

Data Sharing Statement: Available at <https://gs.amegroups.com/article/view/10.21037/gc-22-170/dss>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://gs.amegroups.com/article/view/10.21037/gc-22-170/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all

aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of the Xiangya Hospital of Central South University (No. 202112173). Since this study was retrospective and did not involve personal privacy, informed consent of previous patients could not be obtained objectively.

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