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Effect of early enteral nutrition on postoperative outcomes in pancreatic cancer patients with diabetes.

Xinjie Wang[1], Xianglong Wang[1], Yang Zhang[1], Zhenyang Wang[1], Ying Jiang[1] and Long Ling[2]

[1]Department of Hepatobiliary Surgery, The First Affiliated Hospital of Guizhou University of traditional Chinese medicine, Guiyang, Guizhou, China.
[2]Department of Metabolic Endocrinology, The Second Affiliated Hospital of Guizhou University of traditional Chinese medicine, Guiyang, Guizhou, China.

Keywords: diabetes mellitus; early enteral nutrition; gastrointestinal function; pancreatic cancer.

Abstract. This study aimed to evaluate the impact of early enteral nutrition support in pancreatic cancer patients with diabetes mellitus following total pancreatectomy. Ninety-six patients were randomly divided into control and research groups, each with 48 patients. Both groups received parenteral nutrition, while the research group received additional enteral nutrition within the first 48 hours post-surgery. Results showed that the research group experienced faster recovery of bowel sounds, earlier first defecation, and shorter gastric tube retention times compared to the control group ($p<0.05$). Postoperative gastrointestinal function, immune function, and nutritional status were significantly better in the research group, with higher levels of gastrin, motilin, immunoglobulins G, A, and M, CD4/CD8 ratio, albumin, prealbumin, and transferrin ($p<0.05$). Furthermore, the research group had better blood glucose control from 48 hours to seven days post-surgery ($p<0.05$). The above results demonstrated a promoting impact of early nutrition support on postoperative physical functioning recovery of pancreatic cancer patients with diabetes mellitus. In conclusion, early enteral nutrition support in pancreatic cancer patients with diabetes mellitus significantly improved nutritional status, postoperative gastrointestinal recovery, gastrointestinal and immune function, and blood glucose control, leading to a better overall prognosis.

Corresponding author: Long Ling, Department of Metabolic Endocrinology, The Second Affiliated Hospital of Guizhou University of Traditional Chinese Medicine, Guiyang 550000, Guizhou, China. E-mail: LLYLHD358@163.com

Efecto de la nutrición enteral temprana en los resultados postoperatorios en pacientes con cáncer de páncreas y diabetes.

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Palabras clave: diabetes mellitus; nutrición enteral temprana; función gastrointestinal; cáncer de páncreas.

Resumen. Este estudio tuvo como objetivo evaluar el impacto del apoyo nutricional enteral temprano en pacientes con cáncer de páncreas y diabetes mellitus después de una pancreatectomía total. Noventa y seis pacientes fueron divididos aleatoriamente en grupos de control y de investigación, cada uno con 48 pacientes. Ambos grupos recibieron nutrición parenteral, mientras que el grupo de investigación recibió nutrición enteral adicional dentro de las primeras 48 horas posteriores a la cirugía. Los resultados mostraron que el grupo de investigación experimentó una recuperación más rápida de los ruidos intestinales, una primera defecación más temprana y tiempos de retención del tubo gástrico más cortos en comparación con el grupo de control ($p<0,05$). La función gastrointestinal posoperatoria, la función inmunológica y el estado nutricional fueron significativamente mejores en el grupo de investigación, con niveles más altos de gastrina, motilina, inmunoglobulinas G, A y M, relación CD4/CD8, albúmina, prealbúmina y transferrina ($p<0,05$). Además, el grupo de investigación tuvo un mejor control de la glucemia desde las 48 horas hasta los siete días posteriores a la cirugía ($p<0,05$). Los resultados anteriores demostraron un efecto promotor del apoyo nutricional temprano en la recuperación de la función física posoperatoria de pacientes con cáncer de páncreas y diabetes mellitus. En conclusión, el apoyo nutricional enteral temprano en pacientes con cáncer de páncreas y diabetes mellitus mejoró significativamente el estado nutricional, la recuperación gastrointestinal posoperatoria, la función gastrointestinal e inmunitaria y el control de la glucemia, lo que condujo a un mejor pronóstico general.

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INTRODUCTION

As a common malignancy, pancreatic cancer (PC) majorly occurs in the exocrine glands of patients' pancreas [1,2] we assessed serum trace element concentrations in patients with pancreatic cancer and compared the results to those of healthy controls and patients with chronic pancreatitis. We evaluated the association between trace element concentrations during cancer treatment and the risk of cancer progression and mortality in pancreatic cancer patients. Methods A retrospective cohort study was conducted at a tertiary center in Korea. Serum trace element concentrations of cobalt (Co. Generally, PC develop pretty rapidly, and patients' prognosis is unfavorable, with high morbidity and mortality in China. Moreover, PC has become a common disease that endangers

the health of the body and the quality of daily life [3,4] consequently raising the pancreatic cancer surgery rate. This study aimed to determine whether advanced age is a risk factor for morbidity and mortality following pancreaticoduodenectomy (PD. Diabetes mellitus (DM) is a metabolic disease resulting from insulin secretion or use defects [5]. Once it co-occurs with PC, it can enhance the severity and complexity of the disease and bring severe consequences to patients [6].

Currently, surgery is usually used to treat pancreatic cancer, which can effectively clear focus, prevent metastasis of focus, and prolong the survival period of patients. Total pancreatectomy refers to reconstruction and anastomosis of the digestive tract after removing the entire pancreas, duodenum, a significant part of the stomach, lower segment of common bile duct, gallbladder, large and small omentum and spleen [7]. PC patients suffer from malnutrition and poor immune function, and surgical trauma can put patients in a state of stress and immunosuppression; thus, their nutritional status and immune function will further deteriorate [8,9] due to the complexity of nutrition assessment, only 30-60% of patients with nutritional risks receive nutritional treatment at present. It is important to identify biomarkers that may be used to improve management of PDAC-associated malnutrition. Serum insulin-like growth factor binding protein 2 (IGFBP2. Enteral nutrition (EN) and parenteral nutrition (PN) are fundamental nutritional methods for postoperative PC patients [10]. Early EN has received wide recognition in clinical practice; early administration of nutrients in the gastrointestinal tract after surgery can stimulate intestinal peristalsis and related cytokine secretion, which helps protect intestinal mucosal barrier function [11]. Due to the loss of pancreatic endocrine and exocrine function in patients after total pancreatectomy, severe glucose metabolism disorders occur; coupled with surgical trauma stress, blood glucose control has become a crucial issue worthy of medical attention [12]. Clinical research demonstrates that for PC patients with DM, timely and reasonable nutrition support in the early postoperative period can ameliorate insulin tolerance, facilitate reasonable blood glucose control, and elevate postoperative recovery [13].

This research aimed to elucidate the clinical influence of early EN support in treating PC complicated with DM in terms of nutritional status, postoperative gastrointestinal recovery, gastrointestinal and immune function, and blood glucose control, which may provide a favorable basis for patients to recover better.

PATIENTS AND METHODS

General data

The 96 patients selected with PC who underwent total pancreatectomy in our hospital from January 2021 to May 2023 were randomly divided into a control group (CG) and a research group (RG), with 48 cases each. **Inclusion criteria:** 1) Primary PC confirmed by pathological examination; 2) age ranging 18-80 years old; 3) meeting surgical indications for total pancreatectomy and undergoing surgery under general anesthesia; 4) research subjects were informed and agreed to surgical, anesthesia, nursing, and blood glucose control plans, and signed informed consent. **Exclusion criteria:** 1) DM patients (type 1 and type 2); 2) those complicated with severe organic diseases such as heart, lung, liver, and kidney; 3) those complicated with primary malignancies of other organs and systems; 4) pregnant or lactating women; 5) those with severe postoperative biliary and abdominal inflammation. The research received approval from our hospital's ethics committee.

Methods

Both groups received conventional nursing. Postoperative conventional nursing included vital sign monitoring, assisted sputum drainage, oral nursing, skin nursing, drainage nursing, and parenteral nutrition

(PN). On the day after surgery, both groups received PN support via intravenous route, with a total calorie intake of approximately 110 kj/(kg • d). Administered enteral nutrition through the NJT (nasojejunal tube) from the second day after surgery, with an initial volume of 500 mL (1 Kcal/mL, protein 4.5 g/100 mL, carbohydrate 14.3 g/100 mL, lipid 2.8 g/100 mL). Both groups received conventional blood glucose monitoring and blood glucose control.

The RG received an enteral nutrition (EN) solution to prevent infection and correct electrolyte balance. Patients were given normal saline via a nasogastric tube two days after surgery. The nursing staff observed patients' reactions and continued to provide infusion if there was no abdominal discomfort. Three days after surgery, patients received Enteral Nutrition Suspension total protein-medium chain triglycerides (TP-MCT) via a nasogastric tube, with a dose gradually increasing from 250 mL. Nursing staff controlled the amount of nutrient solution used between 1000-1500 mL/d based on the patient's condition. The EN supply was reduced gradually after patients returned to a regular diet.

Observation indicators

1. Nutritional status: The serum albumin (ALB), prealbumin (PA), and transferrin (TF) levels between both groups before and seven days after surgery were compared.
2. Postoperative recovery: The bowel sound recovery time, anus exhaust time, defecation time, and gastric tube retention time between both groups after surgery received comparison.
3. Gastrointestinal function: A 5 mL venous blood sample was extracted from both groups at dawn before and seven days after surgery. The levels of gastrin (GAS) and motilin (MTL) were detected with radioimmunoassay.
4. Immune function: A 5 mL venous blood sample was extracted from both groups at dawn before and seven days after surgery. The serum immunoglobulin G (IgG), serum immunoglobulin A (IgA), and serum immunoglobulin M (IgM) levels were detected with immunoturbidimetry. Before and seven days after surgery, 5 mL of peripheral venous blood was extracted from both groups at dawn. The ratio of $CD4^+$ cells to $CD8^+$ cells (CD4/CD8) was detected with flow cytometry.
5. Blood glucose level: The fasting blood glucose (FBG) levels in both groups before surgery, 12 h, 24 h, 36 h, 48 h, 72 h, five days and seven days after surgery were compared.

Statistical analysis

The IBM® SPSS® 27.0 software was used for analyzing data. Quantitative data following a normal distribution received expression as mean ± standard deviation (mean ± SD), followed by t-tests for intergroup comparisons. Counting data received expression in percentages (%), followed by χ^2 test for intergroup comparisons, $p<0.05$ indicated a statistically significant difference.

RESULTS

General data shows no differences between the control group and the research group

RG: 24 males and 24 females; mean age of 56.30 ± 6.20 years old; body mass index (BMI): 23.10 ± 2.30 kg/m^2; tumor types: 27 cases of total pancreatic cancer, and 21 cases of pancreatic head cancer invading the pancreatic body. CG: 28 males and 20 females; mean age of 55.00 ± 6.70 years old; BMI: 23.30 ± 2.00 kg/m^2; tumor types: 30 cases of total pancreatic cancer and 18 cases of pancreatic head cancer invading the pancreatic body. Both groups exhibited no statistical significance in general data ($p>0.05$; Table 1).

Table 1
General data in both groups.

Groups	N	Gender [n (%)]		Age (years)	BMI (kg/m^2)	Tumor types [n (%)]	
		Male	Female			Total pancreatic cancer	Pancreatic head cancer invading pancreatic body
CG	48	24 (50.00)	24 (50.00)	56.30±6.20*	23.10±2.30*	27 (56.25)	21 (43.75)
RG	48	28 (58.33)	20 (41.67)	55.00±6.70*	23.30±2.00*	30 (62.50)	18 (37.50)
$\chi 2/t$		0.671		0.167	1.047	0.389	
p		0.413		0.868	0.298	0.533	

Abbreviations: CG = Control Group; RG = Research Group; BMI = Body Mass Index; * mean ± standard deviation. χ^2 test was used for categorical variables (gender, tumor types), while an independent-samples t -test was used for continuous variables (age, BMI).

Enteral nutrition ameliorates nutritional status in the research group

Before surgery, there were no statistically significant differences in ALB, PA, and TF levels between both groups ($p>0.05$); seven days after surgery, ALB, PA, and TF levels in both groups were elevated relative to those in the same group before surgery; and ALB, PA, and TF levels in the RG were elevated relative to those in CG during the same period, indicating statistical significance ($p<0.05$; Fig. 1).

Enteral nutrition accelerates postoperative gastrointestinal recovery in the research group

The bowel sound recovery time, anus exhaust time, defecation time, and gastric tube retention time in RG exhibited depletion relative to those in CG, indicating statistical significance ($p<0.05$; Fig. 2).

Enteral nutrition enhances gastrointestinal function in the research group

Before surgery, there was no statistical significance in GAS and MTL levels between both groups ($p>0.05$); seven days after surgery, GAS and MTL levels in both groups exhibited elevation relative to those in the same group before surgery, and GAS and MTL levels in RG exhibited elevation relative to those in CG during the same period, indicating statistical significance ($p<0.05$; Fig. 3).

Enteral nutrition enhances immune function in the research group

Before surgery, there was no statistical significance in IgG, IgA, IgM, and CD4/CD8 levels between both groups ($p > 0.05$); seven days after surgery, IgG, IgA, IgM, and CD4/CD8 levels in both groups exhibited elevation relative to those in the same group before surgery, and IgG, IgA, IgM, and CD4/CD8 levels in RG exhibited elevation relative to those in CG during the same period, indicating statistical significance ($p<0.05$; Fig. 4).

Enteral nutrition attenuates fasting blood glucose levels in the research group

Before surgery and 12-24 h after surgery, there were no statistically significant differences in FBG levels exhibited between SG and CG during the same period ($p< 0.05$); 48 h to seven d after surgery, FBG level in RG exhibited depletion relative to that in CG during the same period, indicating statistical significance ($p<0.05$; Fig. 5).

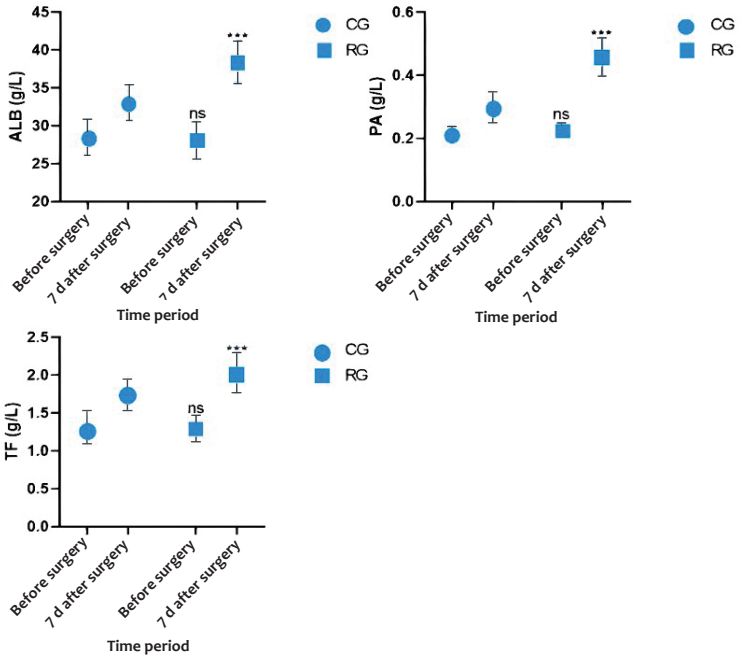

Fig. 1. Nutritional indicators in both groups.
RG versus CG, ns = no significance, ***p<0.05. CG = Control Group; RG = Research Group.
Values are mean ± SD. Statistical analyses were conducted using paired t-tests for within-group comparisons and independent-sample t-tests for between-group comparisons. **Abbreviations:** ALB: Serum Albumin, PA: Prealbumin, TF: Transferrin.

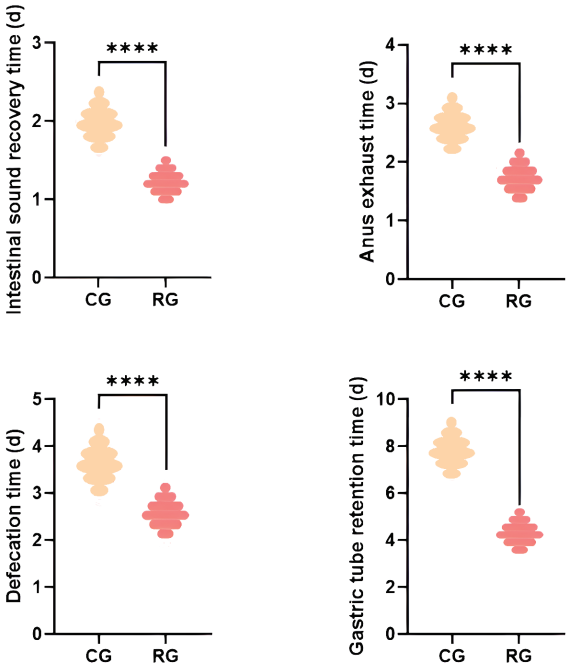

Fig. 2 Postoperative recovery indicators between both groups.
RG versus CG, RG = Research Group; CG = Control Group. ****p<0.05.
Values are mean ± SD. All statistical analyses were performed using Mann-Whitney U tests because of the non-normal distribution of the data.

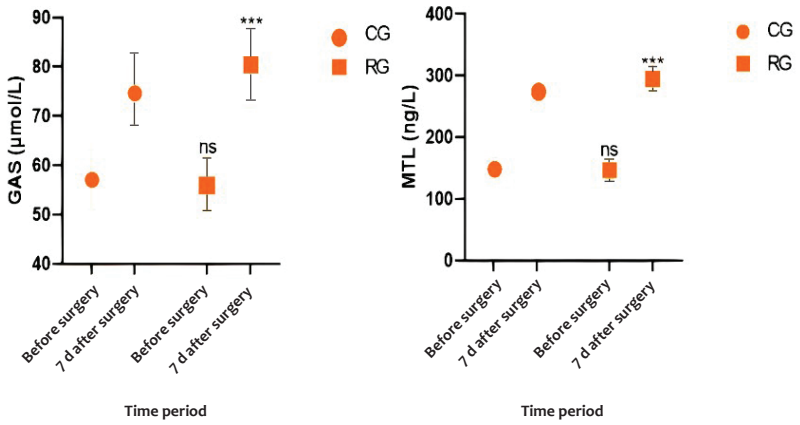

Fig. 3. Gastrointestinal function indicators in both groups.
RG versus CG, RG = Research Group; CG = Control Group. ns = no significance, ***p<0.05.
Values are expressed as mean ± SD. Statistical analyses were conducted using paired t -tests for within-group comparisons and independent-sample t-tests for between-group comparisons. **Abbreviations:** GAS: Gastrin, MTL: Motilin.

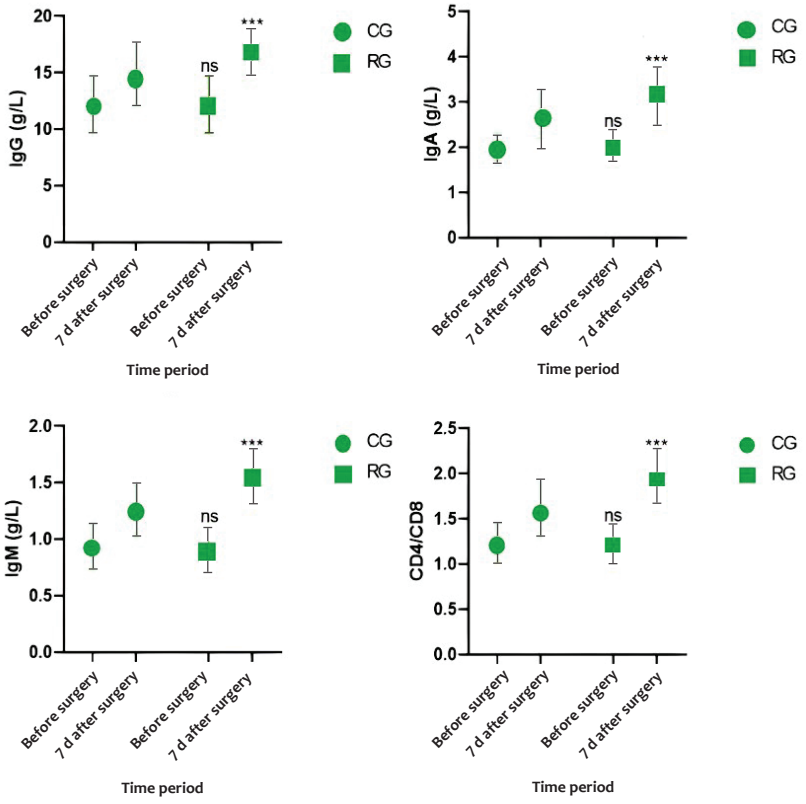

Fig. 4. Immune function indicators in both groups.
RG versus CG, RG = Research Group; CG = Control Group. ns = no significance, ***p<0.05.
All values are shown as mean ± SD. Statistical analyses were conducted using paired t-tests for within-group comparisons and independent-sample t-tests for between-group comparisons.

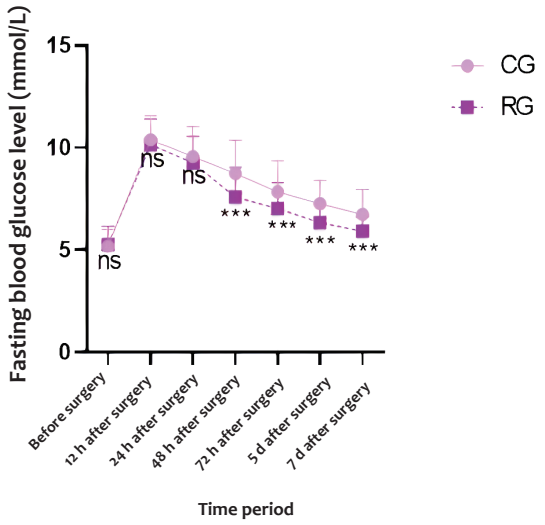

Fig. 5. Changes in blood glucose level in both groups.

RG versus CG, ns = no significance, ***p<0.05.

All values are presented as mean ± SD. Repeated-measures ANOVA and Bonferroni post hoc tests were used for statistical analyses.

DISCUSSION

PC is a common digestive system malignancy, and total pancreatectomy is the most effective treatment for early PC [14]. Nevertheless, due to the complexity of radical resection of PC, which involves resection of multiple organs and reconstruction of the digestive tract, it will cause more serious injuries to patients, and the risk of postoperative complications for patients is high, which may affect life safety in severe cases [15]. Thus, it is particularly crucial to implement effective postoperative nutritional treatment for PC patients undergoing total pancreatectomy.

All life activities and physical functions of living organisms are inseparable from the support of amino acids. The crucial physiological active substances in the human body, including enzymes, hormones, antibodies, and others, are proteins. Lack of protein can lead to malnutrition. Serum protein levels are the most commonly applied indicators reflecting the nutritional status of patients, including ALB, PA, and TF, among others [16]. Herein, after surgery, ALB, PA, and TF levels in both groups exhibited elevation relative to those in the same group before surgery, and ALB, PA, and TF levels in RG were elevated relative to those in CG during the same period, indicating that early EN support can facilitate visceral protein synthesis and elevate the overall nutritional status of patients. In the study by Mękal *et al.* [17], which confirmed the results of the present study, it was shown that Early Enteral can improve the nutritional status of patients after surgery. PC patients are often accompanied by severe gastrointestinal dysfunction, which can easily lead to malnutrition [18]. Nutritional intervention is one of the critical factors affecting the prognosis of surgical treatment. EN has gradually become a preferred method of clinical nutrition due to its advantages, such as economy, ease of maintenance, and compatibility with patients' physical characteristics. Early EN support can overcome PN deficiency, meet patients' early postoperative nutritional needs, and have advantages such as protecting the intestinal mucosal barrier, facilitating recovery of intestinal peristalsis function, and enhancing gastrointestinal hormone secretion [19]. In the study by ME Hamaker *et al.* [20], similar to this study, it was shown that EN can improve the patient's bowel function and nutritional status. Clinical reports have depicted that patients who receive early EN after surgery have a lower incidence of long-term related intestinal complications, indicating that early EN after surgery is more in line with patients' nutritional and gastrointestinal needs [21]. Herein, bowel sound recovery time, anus exhaust time, defecation time, and gastric tube retention time in RG exhibited depletion relative to those in the CG; after surgery, GAS and MTL levels in both groups exhibited elevation relative to those in the same group before surgery, and GAS and MTL levels in RG exhibited elevation relative to those in

CG during the same period. This indicates that early EN support can accelerate postoperative recovery and ameliorate patients' gastrointestinal function. The study by Yuan and Xiu 22 also showed that EN can reduce intestinal complications and problems in patients. The reasons are that early EN support can facilitate recovery of intestinal motility and absorption function in patients, accelerate organ blood circulation, improve mucosal blood flow, and prevent occurrence of mucosal acidosis and osmotic disorders; enteral nutrients can protect integrity of patients' intestinal mucosa, avoid dysbiosis of gastrointestinal microbiota, and facilitate regeneration of intestinal mucosal cells, enhance secretion of gastrointestinal hormones, thereby elevating patients' gastrointestinal function and enabling rapid recovery of gastrointestinal activity [23]. The study by Chakaroun *et al.* 24 also showed that EN favors the gastrointestinal microbiota and facilitates the regeneration of intestinal mucosal cells.

Due to the influence of PC itself and the trauma of pancreatectomy, the postoperative immune function of patients will be reduced to varying degrees, and postoperative malnutrition will also aggravate the degree of their immune dysfunction [25]. Herein, after surgery, IgG, IgA, IgM, and CD4/CD8 levels in both groups exhibited elevation relative to those in the same group before surgery, and IgG, IgA, IgM, and CD4/CD8 levels in RG exhibited elevation relative to those in CG during the same period. This indicates that early EN can enhance the immune function of patients, may be because early EN support can facilitate the absorption of nutrients in the body, enhance patient's physical fitness, and elevate their postoperative immunity; enteral nutrients can protect damaged gastrointestinal tissue, maintain the function of gastrointestinal microbiota, reduce the impact of gastrointestinal microbiota on damaged tissue, and block occurrence of inflammatory responses, thereby effectively elevating patients' immune function [26]. Negative nitrogen balance during the perioperative period, elevated insulin resistance due to surgical trauma, depleted glucose absorption in peripheral tissue, and elevated endogenous glucose production, coupled with stress hyperglycemia due to nutrition, fasting, hunger, pain, and long-term bed rest, can lead to complications such as wound infection and delayed wound healing, affecting patient prognosis [27]. Herein, 48 h to 7 d after surgery, FBG level in RG exhibited depletion relative to that in CG during the same period, indicating that EN intervention strategies effectively elevated blood glucose control efficacy 48 h after surgery. The study by Liu *et al.* (2025) [28] also showed that Early Enteral can improve immune system strengthening and blood sugar control. Thus, based on PN, combined with EN, improving short-term prognosis is vital.

Early postoperative EN support for PC patients complicated with DM can elevate the nutritional status of patients after surgery, speed up the recovery of patients, improve their gastrointestinal function and immune function, and facilitate more reasonable blood glucose control, which is conducive to a better prognosis of patients. The clinical application effect is significant.

Conflict of interest

The authors declare no conflict of interest.

Founding

None

Author's ORCID numbers

- Xinjie Wang (XW): 0000-0001-5359-1164
- Xianglong Wang (XLW): 0000-0002-3283-5606
- Yang Zhang (YZ): 0000-0003-4313-110X
- Zhenyang Wang (ZW): 0009-0004-7980-1800

- Ying Jiang (JJ): 0000-0002-5703-4653
- Long Ling (LL): 0000-0001-6968-5800

Authors' Participation

All authors participated in this study; XW, XLW: Contributed to the conception of the work, data collection, conducting the study, and data analysis. YZ, ZW: Contributed to the conception of the work, conducting the study, revising the draft, and approving the final version of the manuscript. YJ, LL: manuscript writing, translation and editing. Final approval of the manuscript.

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