

ORIGINAL ARTICLE

Effect of early oral feeding on gastrointestinal function recovery in postoperative gastric cancer patients: a prospective study

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Summary

Purpose: To prospectively compare the early and late postoperative oral feeding of operated gastric cancer patients on the gastrointestinal function recovery.

Methods: 198 gastric cancer patients treated in our hospital from June 2015 to June 2017 were enrolled. Patients were randomized into two groups, early feeding group and late feeding group. All patients underwent the same surgical procedure, which was laparoscopic radical gastrectomy. Time of the first postoperative exhaust and defecation was recorded. Fasting venous blood samples were collected on the day of surgery and 1, 3, and 5 days after surgery. Serum levels of gastrin and motilin were assessed.

Results: Time of the first postoperative exhaust and defecation in the early feeding group was 2.05 ± 0.71 days and 3.58 ± 0.92 days, respectively. In the late feeding group they were 2.50 ± 0.91 days and 5.17 ± 1.0 days, respectively ($p=0.008$, $p=0.002$). Serum levels of gastrin and motilin in

the early feeding group were remarkably higher than those of the late feeding group on the 3rd and 5th postoperative day. Univariate analysis showed that time of the first postoperative feeding, operation time and postoperative gastrin level on the 3rd day were factors remarkably affecting the time of the first postoperative exhaust ($p=0.003$, $p=0.043$, $p=0.032$, respectively). Multivariate analysis revealed that the time of postoperative feeding was an independent factor affecting the time of the first postoperative exhaust (Odds ratio/OR=0.986, 95%CI=0.974-0.997, $p=0.027$).

Conclusions: Early oral feeding promotes the recovery of postoperative gastrointestinal function in gastric cancer patients, and doesn't increase the incidence of related complications and adverse events.

Key words: early feeding, gastric cancer, gastrointestinal function, gastrin, motilin

Introduction

Gastric cancer is the second leading cause of cancer mortality in the world [1]. Although surgical resection of primary lesions or metastases can save or prolong life, it may also promote cancer cells to enter the blood circulation. Suppressed anti-tumor immunity, upregulated adhesion molecules in target organs and recruited immune cells all lead to tumor recurrence [2-5]. Currently, surgical resec-

tion of tumor is still the major treatment. In 1994, Kitano et al. [6] firstly reported the use of laparoscopic radical gastrectomy for the treatment of early gastric cancer. Compared with the traditional radical gastrectomy for gastric cancer, laparoscopic surgery has obvious advantages. In 1997, Goh et al. [7] performed laparoscopic radical gastrectomy for advanced gastric cancer for the first time. With

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the improvement of surgical skills and the development of endoscopic procedures, the commonly used Billroth I, Billroth II and Roux-en-Y gastrointestinal reconstruction could all be performed under laparoscopy [8-10]. However, postoperative stress usually results in decreased gastrointestinal function, hypoxemia, muscle atrophy, cognitive impairment and cardiopulmonary complications. Complications of gastric cancer lead to prolonged hospital stay and postoperative recovery time, and even affect the clinical outcomes [11]. In the traditional surgical treatment of gastric cancer, patients undergo regular fasting for 7 days after surgery and gastrointestinal decompression for 5-7 days for anastomosis recovery. Gastrointestinal decompression makes about 70% of patients feel unwell. A recent meta-analysis also showed that gastrointestinal decompression could not reduce the complications of abdominal surgery [12,13]. Accumulated evidence has suggested that early oral feeding after colorectal surgery, gynecologic surgery and gastrectomy was safe and effective [14-16].

This study aimed to investigate the effect of early oral feeding on gastrointestinal function recovery in patients undergoing laparoscopic radical gastrectomy. We also aimed to analyze the influencing factors affecting the recovery of gastrointestinal function after gastric cancer surgery.

Methods

Patients

In total, 198 gastric cancer patients aged 44-80 years treated in the Affiliated Jiangyin Hospital of Southeast University Medical College from June 2015 to June 2017 were enrolled in this study. Among them, 101 patients who received early postoperative feeding were considered as the experimental group, and another 97 patients who received conventional treatment were considered as the control group.

The inclusion criteria were as follows: 1) Patient age 18-80 years (male or female); 2) Patients were diagnosed as gastric cancer by gastroscopy and biopsy, without invasion of surrounding organs and distant metastasis; 3) All patients underwent laparoscopic radical gastrectomy in the same surgical department.

The exclusion criteria were as follows: 1) Patients that had severe malnutrition; 2) Patients with diabetes or other serious organ dysfunction; 3) Patients with preoperative neoadjuvant treatment; 4) Patients with emergency surgery with perforation and hemorrhage; 5) Patients whose operation time was longer than 5 hrs; 6) Patients with intraoperative blood transfusion products because of large amount of intraoperative blood loss; 7) Patients who were transferred to intensive care units on the day after surgery.

All enrolled patients signed informed consent and the study was approved by the ethics committee of the

Affiliated Jiangyin Hospital of Southeast University Medical College.

Treatment strategy

In this study, both groups of patients underwent general anesthesia for surgery. For patients who had not indwell nasogastric tube placement preoperatively, no nasogastric tube was placed during surgery if the estimated stomach size did not affect the surgical procedure. During the operation, distal gastrectomy or radical gastrectomy were performed according to the tumor site and intraoperative conditions. The operation time was 5 hrs. No additional blood products were given if the intraoperative bleeding was less than 800 mL. Abdominal drainage tube was placed next to the anastomosis after the surgery. Nonsteroidal anti-inflammatory drugs were routinely administered for analgesia. Rehydration or anti-infective treatment was given to patients based on their conditions. For the experimental group, the oral fluid diet started on the 2nd postoperative day. Semi-liquid food and soft food were given on the 3rd postoperative day. Insufficient intake of oral nutrition was supplemented by intravenous fluids. Patients in the control group were indwelled with nasogastric tube 30 min before surgery until the recovery of gastrointestinal function. Nasogastric tube extubation was performed until exhaust occurrence and a small amount of white gastric fluid was found in the tube.

Data collection

General data of gastric cancer patients in the two groups were carefully recorded, including age, gender, body mass index (BMI), operation time, preoperative albumin level, tumor stage, etc. Serum levels of gastrin and motilin before surgery and 1, 3 and 5 days after surgery were recorded. The clinical indicators mainly included time of the first postoperative exhaust and defecation (days). In addition, complications such as anastomotic bleeding, anastomotic leakage, abdominal infection and wound infection were recorded.

Statistics

SPSS 22.0 software (IBM, Armonk, NY, USA) was used for statistical analysis. The percentage data were analyzed using chi-square (χ^2) test. Quantitative data with normal distribution were expressed as mean±standard deviation. *t*-test was performed according to the homogeneity of variance. Binary logistic regression analysis was performed for single-factor analysis and multivariate analysis. $P < 0.05$ was considered statistically significant (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$).

Results

Baseline information

A total of 198 patients were enrolled in our study. There were 101 patients aged 48-79 years in the experimental group, including 168 males and 33 females. The control group included 97 pa-

tients (55 males and 42 females aged 44-80 years). No significant differences were observed in gender, age, BMI, preoperative albumin, operation time and tumor stage between the two groups ($p>0.05$, Table 1).

Comparison of gastrointestinal function recovery

Mean times to first exhaust and defecation in the experimental group were 2.05 ± 0.71 and 3.58 ± 0.92 days, respectively. In the late feeding group, mean time to first exhaust and defecation were 2.50 ± 0.91 and 5.17 ± 1.0 days, respectively ($p=0.008$, $p=0.002$), respectively.

Comparison of serum gastrointestinal hormone levels

The preoperative serum levels of gastrin before surgery and 1, 3 and 5 days after surgery in the experimental group were 198 ± 53.3 ng/L, 226 ± 54.3 ng/L, 244.3 ± 58.1 ng/L and 248.0 ± 55.1

ng/L, respectively. In the control group, gastrin levels were 197.7 ± 54.2 ng/L, 218.7 ± 43.2 ng/L, 217.2 ± 43.4 ng/L and 221.6 ± 55.7 ng/L, respectively. Serum levels of motilin before surgery and 1, 3 and 5 days after surgery in the experimental group was 420.6 ± 65.6 ng/L, 431.3 ± 76.3 ng/L, 435.4 ± 68.1 ng/L and 445.0 ± 79.4 ng/L, respectively, while in the late feeding group, motilin levels were 419.0 ± 68.1 ng/L, 421.0 ± 72.3 ng/L, 423.1 ± 66.1 ng/L and 430.6 ± 63.8 ng/L, respectively. Both excitatory gastrointestinal hormones on the 3rd and 5th day after operation in the early feeding group were significantly higher than those of the late feeding group (Figures 1 and 2).

Univariate and multivariate analyses of the first postoperative exhaust time

Univariate analysis showed that the time of postoperative feeding, operation time and gastrin level on the 3rd day after operation were significant

Table 1. General patient and disease characteristics

Characteristics	Test group(n=101)	Control group(n=97)	p value
Age, years	56.3 ± 10.2	53.9 ± 11.6	0.367
Gender (n)			0.123
Male	68	55	
Female	33	42	
BMI	22.36 ± 2.37	21.96 ± 2.48	0.421
Tumor stage (n)			0.236
I	30	23	
IIa	42	40	
IIb	29	34	
Serum albumin	42.08 ± 6.32	42.31 ± 5.68	0.768
Operation time	210.62 ± 56.97	215.68 ± 61.23	0.721

BMI: body mass index

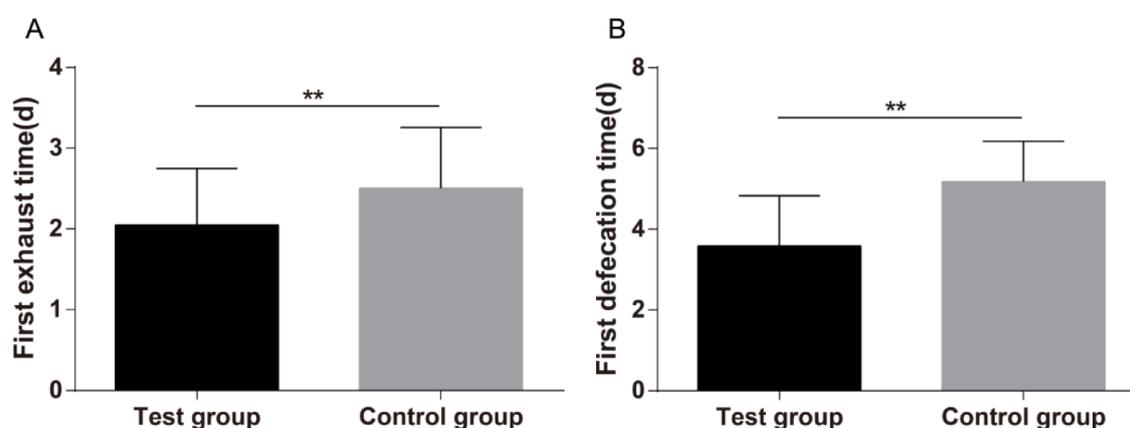


Figure 1. Comparison of postoperative exhaust and defecation time. **A:** The postoperative exhaust time in the experimental group was earlier than that of control group ($p=0.008$). **B:** The postoperative defecation time in the experimental group was earlier than that of the control group (** $p=0.002$).

factors affecting the first postoperative exhaust time. Variables with $p < 0.1$ were included in the multivariate analysis, which showed that the first feeding time was an independent factor for the first postoperative exhaust time ($p < 0.05$, Tables 2 and 3).

Comparison of adverse events

After extubation of nasogastric tube and oral feeding was given, a total of 8 patients in the experimental group experienced gastrointestinal intolerance featured by abdominal distention, nausea and vomiting. Fasting, saline enema and moderate exercise could help relieve the above symptoms. There were 6 patients in the control group who de-

veloped the abovementioned symptoms. No death cases happened in the two groups during the trial. No significant differences in the main complications were observed between the two groups, including anastomotic bleeding, anastomotic leakage, incision infection and abdominal infection ($p > 0.05$, Table 4).

Discussion

Rehabilitation of operated gastric cancer patients poses great challenge for general surgeons. The recovery of gastrointestinal function is an important part of postoperative rehabilitation. Se-

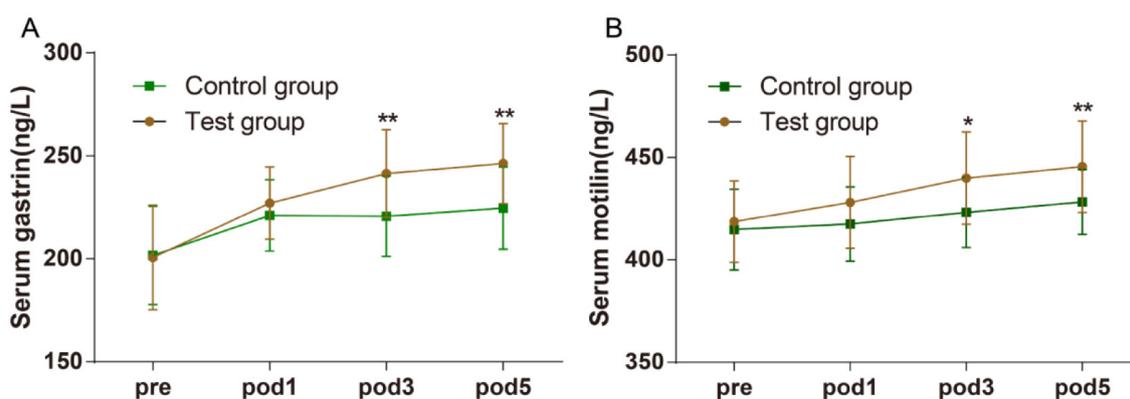


Figure 2. Comparison of gastrin and motilin levels. **A:** Gastrin level in the experimental group on the 3rd and 5th postoperative day were significantly higher than those in the control group. **B:** Motilin levels in the experimental group on the 3rd and 5th postoperative day were significantly higher than those of the control group. pre: preoperative day; pod: postoperative day. * $p < 0.05$, ** $p < 0.01$.

Table 2. Single factor analysis of first exhaust time in 198 patients with gastric cancer after operation

Clinical data	B	S.E.	Wald	OR	95%CI	p value
Age, years (<60 vs>60)	0.936	0.688	2.012	2.312	0.214~1.156	0.168
Gender	-1.045	0.877	1.838	0.598	0.771~4.124	0.186
BMI (<25 vs>25)	2.935	1.623	3.426	18.753	0.045~1.068	0.076
Tumor stage (I vs. IIa vs IIb)	-0.512	0.647	0.764	0.681	0.742~2.124	0.428
Pre- serum albumin	0.082	0.072	1.368	1.124	0.875~1.312	0.322
Operation time, min (>200 vs<200)	4.021	1.635	8.567	0.025	1.008~1.132	0.043
Early oral feeding	-6.257	0.986	45.158	0.005	16.312~165.125	0.003
GAS pod3	-0.023	0.006	5.212	0.895	0.925~0.989	0.032
MOT pod3	-0.003	0.008	0.624	0.997	0.995~1.003	0.486

BMI: body mass index, Pre: preoperative, GAS: serum gastrin, pod: postoperative day, MOT: serum motilin

Table 3. Multivariate analysis of 198 cases of postoperative first exhaust time in patients with gastric cancer

Clinical data	B	S.E.	Wald	OR	95%CI	p value
Operation time, min (>200 vs<200)	0.028	0.010	3.366	1.126	0.996~1.048	0.074
Early oral feeding	-0.011	0.005	5.100	0.986	0.974~0.997	0.027
GAS pod3	-0.006	0.008	0.254	0.993	0.981~1.012	0.538
BMI (<25 vs>25)	-0.314	1.286	0.068	0.785	0.069~7.102	0.736

For abbreviations see footnote of Table 2

Table 4. Complications

Complications	Test group(n=101) n (%)	Control group(n=97) n (%)	p value
Anastomotic bleeding	5 (4.95)	4 (4.12)	0.78
Infection of incisional wound	4 (3.96)	4 (4.12)	0.95
Anastomotic fistula	1 (0.99)	1 (1.03)	0.98
Abdominal infection	1 (0.99)	1 (1.03)	0.98

vere gastrointestinal dysfunction can result in a series of complications such as anastomotic leakage, malnutrition, delayed wound healing, etc. In order to restore the postoperative gastrointestinal function of patients with gastric cancer and to avoid the occurrence of a series of complications, postoperative treatments have been well studied. However, with the development of minimally invasive surgery, the concept of Fast Track Surgery (FTS) has gradually been accepted and applied to surgical treatment of colorectal, gastric and esophageal cancer. Early oral feeding, as an essential part of FTS, mainly includes nasal feeding and oral feeding.

A large number of studies have confirmed that early oral feeding is safe and feasible after minimally invasive surgery. Early oral feeding could accelerate patient recovery, shorten the length of hospital stay and reduce hospitalization costs [17-19]. In addition, early oral feeding after colorectal surgery and gastrectomy was also proved to be safe [14,20,21]. In the upper gastrointestinal surgery, early oral feeding was not only safe, but also accelerated disease recovery. A meta-analysis showed that early recovery diets (intravenous food feeding 4 hrs after surgery) reduced the incidences of postoperative complications such as abdominal distention and intra-abdominal infections. It also shortened hospital stay and did not increase the incidence of anastomotic leakage. However, this study mainly included gastric cancer patients undergoing gastrointestinal surgery [22]. A prospective randomized controlled trial found that early oral feeding after esophagectomy achieves a better gastrointestinal function recovery and shorter length of stay than those with traditional treatment [19]. Gastrin and motilin, as two major excitatory gastrointestinal hormones, were reported to be increasingly secreted after surgery, which stimulated peristalsis and accelerated gastrointestinal function recovery [23,24].

This study mainly observed and analyzed gastrointestinal function recovery in gastric cancer patients, including clinical indicators and laboratory indicators. Our data showed that time to first

exhaust and defecation in early oral feeding group was earlier than that of late oral feeding group. Excitatory gastrointestinal hormones exhibited a significant increase after surgery. The increase trend was more obvious in the early feeding group than in the late feeding group, suggesting that early oral feeding regulates the physiological function of the intestinal tract and accelerates the recovery of intestinal function by stimulating excitatory gastrointestinal hormones secretion. Levels of various hormones after surgery were also related to the stimulation of postoperative wounds and regulation of the nervous system. However, since the surgical processes were similar, the different treatment methods during the perioperative period, especially the feeding time, were the main reason affecting the levels of gastrointestinal hormones.

We also performed univariate and multivariate analyses of the first postoperative exhaust time. The results indicated that the first feeding time, operation time and gastrin level on the 3rd day after surgery remarkably affected the first exhaust time after surgery. In particular, the first feeding time was an independent factor affecting the postoperative exhaust time.

According to our data, symptoms of abdominal distention, nausea and vomiting were observed in both groups. However, no remarkable difference in the incidence of complications was found between the two groups. None of the patients died. Early feeding was reported to increase the probabilities of anastomotic leakage, wound infection and intra-abdominal infection, which were not observed in our study. A great number of studies have now confirmed the benefits of early postoperative oral feeding in gastric cancer [25-27].

Yet, some limitations are present in this study. Although it was a prospective randomized controlled study, a small sample size might lead to biased results. Furthermore, the short length of stay restricted the monitor of serum gastrointestinal hormonal changes over time. In addition, we only detected the serum levels of gastrin and motilin as the gastrointestinal function indicators.

Other significant substances were also needed to be further detected and evaluated.

Conclusions

Early oral feeding promotes the recovery of postoperative gastrointestinal function in operated gastric cancer patients, and does not increase the incidence of related complications and adverse events.

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Conflict of interests

The authors declare no conflict of interests.

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