

# Enhanced recovery after surgery decreases intestinal recovery time and pain intensity in patients undergoing curative gastrectomy

Weiping Ji,<sup>1-3,\*</sup> Arvine Chandoo,<sup>1,\*</sup> Xiaoling Guo,<sup>1</sup> Tao You,<sup>1</sup> Zhuo Shao,<sup>2</sup> Kailian Zheng,<sup>2</sup> Juan Wang,<sup>4</sup> Jianwei Bi,<sup>2</sup> Fang Gao Smith,<sup>3</sup> Olga N Tucker,<sup>5</sup> Xian Shen<sup>1</sup>

<sup>1</sup>Department of General Surgery, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Zhejiang, People's Republic of China; <sup>2</sup>Department of General Surgery, Changhai Hospital, The Second Military Medical University, Shanghai, People's Republic of China; <sup>3</sup>Institute of Inflammation and Dental Sciences, University of Birmingham, Birmingham, UK; <sup>4</sup>Department of General Surgery, Xi Jing Hospital, Fourth Military Medical University, Xi'an, People's Republic of China; <sup>5</sup>Department of Upper Gastrointestinal Surgery, Heart of England NHS Foundation Trust, Birmingham, UK

\*These authors contributed equally to this work

Correspondence: Weiping Ji; Xian Shen  
Department of General Surgery,  
Vice-President of the Second Affiliated  
Hospital and Yuying Children's Hospital  
of Wenzhou Medical University, No.109  
Xueyuan Road, Wenzhou, Zhejiang  
325003, People's Republic of China  
Tel +86 577 8800 2709  
Fax +86 577 8800 2709  
Email jiwpeiping19841022@126.com;  
1396888872@163.com

**Background:** Enhanced recovery after surgery (ERAS) reduces postoperative stress, increases patient satisfaction, and reduces postoperative stay and cost. In this study, we evaluated the feasibility and effectiveness of ERAS protocols compared with conventional perioperative care group and their effect in gastric cancer patients undergoing gastrectomy.

**Methods:** A cohort of 366 patients were analyzed from a prospectively maintained database. The patients' characteristics, tumor profile, surgical information data and postoperative complications were evaluated.

**Results:** Patients in the ERAS had a faster gastrointestinal function recovery and first flatus ( $3.26 \pm 0.64$ ;  $P < 0.001$ ). Pain intensity of patients in the ERAS group was significantly lower than that of patients in the conventional care group on postoperative days 1 ( $2.33 \pm 0.98$ ;  $P < 0.001$ ) and 3 ( $1.06 \pm 0.63$ ;  $P < 0.001$ ). Postoperative hospital stays were significantly shorter in patients receiving ERAS program ( $6.66 \pm 3.36$ ;  $P < 0.001$ ), than in those patients who received conventional perioperative care ( $9.02 \pm 2.61$ ).

**Conclusion:** ERAS can reduce postoperative stress, enhance the recovery of the gut, reduce the pain intensity, and increase satisfaction in gastric cancer patient undergoing curative gastrectomy.

**Keywords:** enhanced recovery after surgery, postoperative stress, pain intensity, postoperative complications, gastric cancer

## Introduction

Enhanced recovery after surgery (ERAS) was implemented by Wilmore and Kehlet in the mid-1990s.<sup>1</sup> Its multidisciplinary interventions aim to attenuate the surgical stress response and organ dysfunction, thereby enhancing recovery of intestinal mobility and accelerating full recovery, reducing the morbidity associated with postoperative complications, minimizing the length of postoperative hospitalization and reducing health care costs, all without compromising patient safety and ultimately leading to patients' satisfaction.<sup>2</sup>

In recent years, ERAS has been successfully implemented in several surgical diseases, such as colorectal surgery.<sup>3</sup> Previous prospective and retrospective studies have proven the feasibility of ERAS protocols in gastrectomy patients.<sup>2,4</sup> Gastric cancer (GC) is among the most common cancers worldwide, especially in China, and the second leading cause of cancer-related death.<sup>5</sup> Approximately 400,000 cases of GC are diagnosed in China annually.<sup>6</sup> A radical gastrectomy with D2 lymphadenectomy is the most appropriate treatment of GC. However, gastric cancer surgery is a complicated surgery that has high risk and is associated with postoperative stress, complications, and sequelae.

The rates of postoperative morbidity and mortality after conventional radical gastrectomy and perioperative care range from 10% to 46% and 0.8% to 10%, respectively.<sup>7</sup> Postoperative complications such as anastomotic leakage, pulmonary disease, pancreatitis, digestive fistulas, internal bleeding, and bowel obstruction prolong the duration of hospital stays and increase the hospital costs.<sup>7</sup> The aim of the present study was to evaluate the feasibility and effectiveness of our ERAS protocols compared with gastric cancer patients with conventional perioperative care undergoing gastrectomy.

## Methods

### Patients

Some 366 patients with gastric cancer who underwent gastrectomy with a curative intent at the Department of Gastrointestinal Surgery, Changhai Hospital affiliated to the Second Military Medical University from January 2011 to April 2014 were enrolled in the study. The conventional patients were added from a well-maintained retrospective database, whereas the ERAS group was prospectively enrolled. The Ethics Committee of the Changhai Hospital of the Second Military Medical University approved this study. Only one team with a standard surgical principle performed all surgeries.

### Study criteria

The inclusion criteria were as follows: 1) diagnosis of gastric adenocarcinoma confirmed by a preoperative gastroscopy and pathological biopsy and 2) curative gastrectomy without simultaneous resection of other organs. Patients with preoperative complete digestive tract obstruction or digestive tract perforation were not included in this study. Clinical staging was determined according to the American Joint Committee on Cancer 7th edition – TNM (tumor, node, metastasis) staging of I–III for postoperative pathological diagnosis. Written informed consent was obtained from the patient and the family to receive perioperative care.

### Data collection

All data were retrieved from the patients' database and clinical records. The items studied were the patients' characteristics, tumor profile, surgical information, postoperative data and postoperative complications. Patient characteristics evaluated includes age, gender, body mass index (BMI), Nutritional Risk Screening (NRS) 2002 score, and the risk grade of the American Society of Anesthesiologists (ASA) score. The tumor profile included the pathological T and N factors and pathological tumor stage (TNM classification). Surgical-related data included the kind of procedure and

the type of reconstruction, operation time and intraoperative blood loss. Postoperative data included the time of the first flatus or defecation, maximum pain on a visual analog scale (VAS, evaluated at postoperative day [POD] 1 and 3), the number of additional doses of analgesics, postoperative hospital stays, 30-day readmission. The recovery of bowel function was evaluated by the time of first flatus. Blood samples were collected 1 day before surgery and POD 1 and 3. Postoperative complications, 30-day readmissions and mortality were used to assess the safety of ERAS.

### ERAS program

The ERAS program can be divided into preoperative, intraoperative and postoperative phases. Detailed information about the treatment and perioperative care was explained to the patients on admission.<sup>8,9</sup> Patients could eat a normal diet until midnight of the day before surgery and were allowed to drink up to 500 mL of a carbohydrate-rich drink (18.0 g carbohydrate per 100 mL) until 4 hours before surgery. There was no bowel and nasogastric tube decompression.<sup>10</sup> The body temperature was strictly monitored and kept above 36°C. Anesthesia consisted a combination of general anesthesia and local preemptive analgesia. Surgical incisions sites were pre- and postoperatively injected with 0.25% bupivacaine hydrochloride solution. Intraoperatively, the fluid therapy was closely monitored and the anesthesiologist avoided sodium and fluid overload.<sup>11</sup> All patients received 8 mg of intravenous dexamethasone and 8 mg of ondansetron as prophylaxis to avoid any postoperative nausea and vomiting.

Postoperative pain was managed with a combination of intravenous patient-controlled analgesics (PCA, contained fentanyl citrate [15 mcg/kg] and ondansetron hydrochloride dehydrate [16 mg] with normal saline in 100 mL of total volume) and nonsteroidal anti-inflammatory drug (NSAID), 50 mg flurbiprofen axetil.<sup>12</sup> Additional analgesics were administered only when the patient complained about pain. If additional pain control was required, demerol 25 mg was intravenously injected. Oral feeding was initiated at day 1 after surgery, following a stepwise program. On the first POD, patients were allowed to drink water. On the second POD, a clear liquid diet was given unless patients had a high temperature (38.5°C or higher). A full liquid diet was started on POD 3. The patients began to eat solid food on POD 4, starting with rice gruel and soft food. During the first 1–4 days intravenous infusion of fat emulsion, amino acids, and glucose was administered according to daily physiological need, postoperatively.<sup>13</sup> Urinary catheters were removed at 6 hours after the surgery when patients were fully conscious.<sup>14</sup>

Drains were not routinely used and in the cases they were used, tubes were removed on the second or third POD if the drainage fluid was clear and the amount of drainage discharge was less than 100 mL/day.<sup>14</sup> Patients were encouraged to sit out of bed for more than 6 hours on the day of surgery and ambulation was encouraged on the evening of the day of surgery. All patients were mobilized on the POD 1.<sup>15</sup>

## Conventional perioperative care

Patients in the conventional surgery group received conventional perioperative care. The traditional radical gastrectomy perioperative procedure: 1) fasting for 10 hours prior to surgery and stopping fluid intake 6 hours prior to surgery, 2) bowel preparation (enemas and oral antibiotics), 3) nasogastric tube and peritoneal drainage tube placement, 4) administration of general anesthesia, 5) resumption of diet after the first flatus, and 6) resumption of ambulation 2–3 days after surgery.

Patients in the traditional perioperative care group were allowed to have a liquid diet until lunch of the day before surgery and after dinner no further food intake was allowed. Intensive bowel preparation (10 mL 0.75% sodium picosulfate hydrate and 34 g magnesium citrate) was administered the day before surgery. The operation was carried out under general anesthesia with endotracheal intubation. Anesthesia was general anesthesia without combination of local pre-emptive analgesia. Postoperative pain was managed by PCA only. The use of PCA was similar to that of the conventional care (CC) group. NSAIDs were not routinely used in the CC group. Additional painkillers were not routinely given and additional analgesics were administered only when the patient complained about pain. Nasogastric tube was used for stomach decompression before surgery and removed after the bowel function recovered completely.

Postoperative treatment consisted of parenteral nutrition of fat emulsion, amino acids and glucose (11%) injection, which was administered until flatus. At that time, the nasogastric tube was removed and the patients were advised to drink water. After full intestinal recovery, the diet consisted of a clear liquid diet, then a full liquid diet, and finally a soft diet (Table 1). The patients received nutritional support of 0.20 g/kg/day nitrogen and 25–30 kcal/kg/day calories. In the CC group, the urinary catheters were removed at 2–3 day after surgery. Drains routinely were used and the drainage tubes were removed on POD 5 or 6 if the drainage fluid was clear and the amount of drainage discharge was less than 100 mL/day. Ambulation was encouraged 24 hours after surgery in this group and all patients were mobilized on the POD 1–2 in CC group.

**Table 1** Comparison of clinicopathologic characteristics between the ERAS and CC groups

Characteristics	ERAS group (n=102)	CC group (n=264)	P-value
Age			0.733
≤60	54	145	
>60	48	119	
Mean	58	58	
Median	57	56	
Years	34–79	37–79	
Gender			0.074
Male	62	133	
Female	40	131	
BMI (kg/m <sup>2</sup> )	22.18±3.55	21.81±3.20	0.338
NRS 2002 score			0.866
I	40	101	
2	62	163	
ASA score			0.107
I	58	74	
II	44	90	
TNM classification			0.837
I	39	105	
II	32	87	
III	31	72	

**Abbreviations:** ERAS, enhanced recovery after surgery; CC, conventional care; ASA, American Society of Anesthesiologists; BMI, body mass index; NRS, nutritional risk screening; TNM, tumor node metastasis.

## Discharge criteria

Patients were discharged based on the following criteria: 1) normal body temperature; 2) adequate pain control with oral medication; 3) absence of nausea and/or vomiting; 4) good flatus and/or defecation; 5) ability to tolerate non-elemental diet and soft food without intravenous nutritional support; 6) mobilization without assistance; 7) normal laboratory data; 8) no postoperative complications; and 9) acceptance of discharge by the patient.

## Follow-up

In the ERAS group the patients kept in touch with us by an outpatient service or telephone after discharge within the first 24 hours and once weekly for 4 weeks. The patients could also contact us if they had any discomfort. Readmission was considered if any of the following occurred: hyperpyrexia, abdominal pain, bowel obstruction, gastrointestinal hemorrhage, infection or poor healing of the wound.

## Statistical analysis

Comparisons between the study groups were performed using Student's *t*-test, Chi-squared test, Mann–Whitney *U* test, or Fisher's exact test as appropriate. Continuous variables are represented as the mean ± standard deviation (SD) and were

analyzed using Student's *t*-test or Mann–Whitney *U*-test. Categorical variables are presented as counts and percentages and were analyzed using the Chi-squared test or the Fisher's exact test. All statistical tests were two-tailed, and a value of  $P < 0.05$  was considered statistically significant. All statistical analyses were performed using SPSS 17.0 statistics software (SPSS Inc., Chicago, IL, USA).

## Patient characteristics

A total of 366 patients were included in the study, 171 females and 195 males, with a mean age of 57.93 years ( $57.93 \pm 10.69$  years) and mean body mass index of  $21.91 \text{ kg/m}^2$  (range:  $14.38\text{--}30.86 \text{ kg/m}^2$ ) (Table 1). There were 232 patients (63.39%) in ASA class I and 134 patients (36.61%) in ASA class II. The procedures performed were total gastrectomy in 162 patients (44.26%) and distal gastrectomy in 204 patients (55.74%). Digestive continuity was restored by a Billroth I gastroduodenostomy or Billroth II gastrojejunostomy after partial gastrectomy, and a Roux-en-Y jejunal loop after total gastrectomy (esophagojejunostomy). Evaluation of tumor stages revealed 144 (39.34%) patients at stage I, 119 (32.51%) patients at stage II, and 103 (28.14%) patients at stage III. The ERAS group comprised 102 patients including 53 patients undergoing laparoscopic gastrectomy and 49 patients undergoing open surgery with routine use of ERAS protocol. The CC group comprised 264 patients including 128 patients undergoing laparoscopic gastrectomy and 136 patients undergoing open surgery with conventional care.

## Clinicopathological features with malnourishment

### Clinicopathological features

After statistical analysis, we found that there were no significant differences between the ERAS group and the CC group in terms of age ( $P=0.733$ ), gender ( $P=0.074$ ), BMI ( $P=0.338$ ), NRS 2002 score ( $P=0.866$ ), ASA score ( $P=0.107$ ) and TNM classification ( $P=0.837$ ) (Table 1).

## Surgical procedures and outcomes

### Operation time

Operation time was statistically associated with the ERAS and CC groups ( $P=0.007$ ) (Table 2). The mean time used to complete the surgery in the ERAS group was  $186.00 \pm 43.03$  and  $169.20 \pm 56.54$  minutes in the CC group.

### Intraoperative blood loss

There was no statistical significance in intraoperative blood loss between the ERAS and CC groups ( $P=0.3406$ ) (Table 2).

**Table 2** Comparison of surgical procedures and outcomes between the ERAS and CC groups

Characteristics	ERAS group (n=102)	CC group (n=264)	P-value
Surgical approach			
Laparoscopic assisted	53	128	0.551
Open	49	136	
Type of operation			
Distal gastrectomy	58	146	0.788
Total gastrectomy	44	118	
Type of reconstruction			
Billroth I	27	55	0.484
Billroth II	31	91	
Roux-en-Y	44	118	
Operation time (minutes)	$186.00 \pm 43.03$	$169.20 \pm 56.54$	0.007 <sup>a</sup>
Blood loss	$142.6 \pm 45.27$	$147.3 \pm 41.05$	0.341

**Note:** <sup>a</sup>Statistically significant ( $P < 0.05$ ).

**Abbreviations:** ERAS, enhanced recovery after surgery; CC, conventional care.

On the other hand, the median amount of bleeding was less in the laparoscopic surgery patients than in the open surgery patients in the ERAS and CC groups, respectively ( $114.58 \pm 19.5 \text{ mL}$  vs  $162.50 \pm 32.9 \text{ mL}$ ,  $107.65 \pm 42.49 \text{ mL}$  vs  $147.06 \pm 39.80 \text{ mL}$ ). The difference was not statistically significant ( $P > 0.05$ ).

## Comparison of postoperative recovery

### Gastrointestinal function recovery

Compared with the CC group, the patients in the ERAS group showed significantly accelerated recovery of gastrointestinal function in terms of time to first flatus ( $P < 0.001$ ) (Table 3). The mean time to first flatus was  $3.26 \pm 0.64$  postoperative days in the ERAS group and  $4.68 \pm 0.49$  postoperative days in the CC group. In subgroup analysis, first flatus in patients undergoing laparoscopic surgery was earlier than patients undergoing open surgery in the CC group, but the difference was not statistically significant ( $4.65 \pm 0.51$  vs  $4.71 \pm 0.47$  post-operative days), ( $P=0.3439$ ). Compared with patients undergoing laparoscopic surgery in the ERAS group, the duration of first flatus was similar to those patients receiving open surgery ( $3.17 \pm 0.67$  vs  $3.35 \pm 0.60$  postoperative days), ( $P=0.1637$ ). There was no statistical significance between the patients undergoing Billroth I, Billroth II, Roux-en-Y and between patients who received partial or total gastrectomies in the meantime to first flatus in the CC group or in the ERAS group, respectively.

### Pain control

VAS analysis showed that pain intensity of patients in the ERAS group was significantly lower than that of patients in the CC group on postoperative days 1 and 2 ( $P < 0.05$ ).

**Table 3** Comparison of postoperative clinical outcomes between ERAS and CC groups

Characteristics	ERAS group (n=102)	CC group (n=264)	P-value
Time to first flatus (h)	3.26±0.64	4.68±0.49	<0.001 <sup>a</sup>
VAS POD 1	2.33±0.98	4.17±0.99	<0.001 <sup>a</sup>
VAS POD 2	1.06±0.63	2.35±0.71	<0.001 <sup>a</sup>
Number of additional doses of analgesics	2(1.96%)	20(7.58%)	0.043 <sup>a</sup>
Postoperative hospital stays (days)	6.66±3.36	9.02±2.61	<0.001 <sup>a</sup>
Postoperative death	0	0	
Readmissions (n)	4 (3.92%)	14 (5.30%)	0.584

**Notes:** The values given are number of patients unless indicated otherwise. <sup>a</sup>Statistically significant ( $P<0.05$ ).

**Abbreviations:** ERAS, enhanced recovery after surgery; CC, conventional care; POD, postoperative day; VAS, visual analog scale.

(Table 3). Additional pain control was more frequently needed in the CC group than in the ERAS group.

### Postoperative surgical stress and inflammatory response

The response induced by systemic surgical stress was assessed by measuring the white blood cell (WBC) count and C-reactive protein levels. When comparing the WBC count before surgery between the groups, there was no statistical significance ( $P=0.223$ ) (Table 4). The WBC count in both groups was elevated on POD 1 but compared to ERAS group on POD 1 the WBC in the CC group was significantly lower ( $P<0.025$ ); however the WBC count in the ERAS group began to drop on POD 3 while the WBC count in the CC group continued to rise ( $P<0.01$ ).

For the inflammatory marker C-reactive protein, there was no statistical significance between the ERAS and CC groups before surgery ( $P=0.289$ ) (Table 4). There was statistical significance for C-reactive protein on POD 1 ( $P<0.01$ ) (Table 4). The median CRP (range) level increased from 22.07±6.70 mg/dL to 57.77±15.88 mg/dL at day 3 after surgery in the ERAS group and from 23.96±6.76 mg/dL to 61.50±16.30 mg/dL at day three after surgery in the conventional perioperative care group. Furthermore, compared with the conventional perioperative care group, the level of CRP in the ERAS group was also lower on POD 3 ( $P=0.049$ ). Similarly, the median lymphocyte count (range) decreased from 1.83±0.53 to 2.20±0.73 in the ERAS group and from 1.35±0.59 to 1.50±0.72 in the CC group at POD 3, which was also statistically significant ( $P<0.01$ ).

### Nutritional status

The postoperative nutritional status was assessed by measuring albumin serum concentrations and total lymphocyte count. There was no statistical significance between the

**Table 4** Comparison of laboratory findings between the ERAS and CC groups

Characteristics	ERAS group (n=102)	CC group (n=264)	P-value
White blood cell count			
Before surgery	6.36±1.58	6.58±1.48	0.223
POD 1	12.03±1.46	12.44±1.62	0.025 <sup>a</sup>
POD 3	10.30±2.23	12.61±2.37	<0.01 <sup>a</sup>
Albumin (g/L)			
Before surgery	40.05±2.54	39.82±2.58	0.441
POD 1	28.63±2.27	26.11±1.82	<0.01 <sup>a</sup>
POD 3	27.67±2.76	25.63±2.05	<0.01 <sup>a</sup>
Lymphocyte count			
Before surgery	2.52±0.45	2.44±0.49	0.180
POD 1	1.83±0.53	1.35±0.59	<0.01 <sup>a</sup>
POD 3	2.20±0.73	1.50±0.72	<0.01 <sup>a</sup>
CRP (mg/dL)			
Before surgery	5.05±0.51	5.11±0.49	0.289
POD 1	22.07±6.70	23.96±6.76	0.017 <sup>a</sup>
POD 3	57.77±15.88	61.50±16.30	0.049 <sup>a</sup>
Postoperative hospital stays (days)	5.56±0.50	7.94±0.75	<0.001 <sup>a</sup>

**Note:** <sup>a</sup>Statistically significant ( $P<0.05$ ).

**Abbreviations:** ERAS, enhanced recovery after surgery; CC, conventional care; CRP, C-reactive protein; POD, postoperative day.

groups before surgery ( $P=0.441$ ) (Table 4). The median albumin (range) level decreased from 28.63±2.27 mg/dL to 27.67±2.76 mg/dL in the ERAS group and from 26.11±1.82 mg/dL to 25.63±2.05 mg/dL in the CC group at POD 3, which was statistically significant ( $P<0.01$ ).

### Postoperative hospital stays

Postoperative hospital stays were significantly shorter in patients receiving ERAS treatment than in those patients who received conventional perioperative care 6.66±3.36 vs 9.02±2.61 days;  $P<0.001$ ) (Table 4).

### Postoperative complications

No statistical significance was found between the incidences of postoperative complications in the ERAS and CC groups ( $P=0.915$ ) (Table 5). A total of 15 (14.71%) patients experienced postoperative complications in the ERAS group and 40 (15.15%) patients in the CC group developed postoperative complications (Table 5). The operative complications were anastomotic leakage ( $n=8$ ;  $P=0.855$ ), intra-abdominal infection ( $n=7$ ;  $P=0.418$ ), surgical incision infection ( $n=12$ ;  $P=0.379$ ), incision fat liquefaction ( $n=18$ ;  $P=0.993$ ), and gastroparesis ( $n=9$ ;  $P=0.061$ ).

### The 30-day mortality and readmission rate

No deaths occurred within the first 30 days after surgery in either group (Table 3). No significant differences in 30-day

**Table 5** Comparison of postoperative complications between the ERAS group and CC groups

Characteristics	ERAS group (n=102)	CC group (n=264)	P-value
Postoperative complications	15 (14.71%)	40 (15.15%)	0.915
Anastomotic leakage	2 (1.96%)	6 (2.27%)	0.855
Intra-abdominal infection	1 (0.98%)	6 (2.27%)	0.418
Surgical-incision infection	2 (1.96%)	10 (3.79%)	0.379
Incision fat liquefaction	5 (4.90%)	13 (4.92%)	0.993
Gastroparesis	5 (4.90%)	4 (1.52%)	0.061

**Abbreviations:** ERAS, enhanced recovery after surgery; CC, conventional care.

readmission rates were recorded between the ERAS group with three patients (2.94%) readmitted compared to five patients (1.89%) in the CC group ( $P=0.539$ , Table 3). The main reasons for readmission were anastomotic leakage, infection and intestinal obstruction.

## Discussion

In the present study, we demonstrated the effectiveness and feasibility of our ERAS program in gastric cancer patients who underwent radical gastrectomy (distal subtotal, proximal subtotal, or radical total gastrectomy) by open surgery or laparoscopy. Compared with the conventional perioperative care group, the ERAS group had a faster postoperative bowel recovery ( $P<0.001$ ), patients experienced lesser pain ( $P<0.001$ ) and had a shorter postoperative hospitalization time ( $P<0.001$ ). How to effectively reduce the perioperative stress response and accelerate the postoperative recovery has become a key point in the field of gastric surgery. The trauma and stress that patients suffer are not only because of the surgery itself, but also come from anxiety, tension, pain, hypothermia, hypoxia, hunger, nausea, vomiting, sleep disorders, a variety of drainage tubes, catheter placement and movement disorder. All these factors could cause organ dysfunction and ultimately affect the wound healing and postoperative rehabilitation.<sup>16</sup>

ERAS encompassed a combination of preoperative, intraoperative and postoperative measures to enhance the postoperative recovery in surgical procedures. Compared with conventional care, ERAS could reduce the stress response and organ dysfunction, shorten the duration to flatus and defecation, accelerate the decrease in CRP and WBC, and thereby greatly shorten the postoperative stay, fasten the recovery of gut function, shorten the time required for overall recovery and increase patients' satisfaction.<sup>4,7,17,18</sup> Our results were consistent with the findings of other studies.<sup>2,4</sup> We found that in our study ERAS was able to reduce postoperative

stress and inflammation ( $P<0.001$ ). ERAS aims to improve outcomes and promote early discharge by emphasizing preoperative patient education, shortening the duration of preoperative fasting, supplying preoperative carbohydrates, no bowel preparation, active prevention of hypothermia, no routine use of nasogastric tubes, controlling pain sufficiently without opioids, providing early ambulation, and quickly advancing the return to a normal diet. Studies have found that some procedures in gastrectomy for example routine nasogastric decompression were unnecessary because early oral feeding enhances the postoperative gastrointestinal tract recovery and decreased the duration of hospital stay without increasing complications.<sup>20</sup> In the present study we found that patients after gastrectomy in the ERAS group had a shorter hospital stay ( $P<0.001$ ) and postoperative complications had no statistical significance ( $P=0.915$ ).

Preoperative patient education through contact between patients and staff can avoid the anxiety and perioperative stress reactions, which promotes faster recovery. Optimal pain control plays a fundamental role in postoperative care. Postoperative pain is one of the most important factors that delays postoperative recovery by not only increasing surgical stress, but also affecting the mobilization of patients.<sup>21,22</sup> The results showed that pain intensity in the ERAS group was significantly lower than that of the CC group ( $P<0.001$ ). Usage of analgesics was significantly less in the ERAS group. Wang et al<sup>7</sup> reported that the first day of flatus after gastrectomy was faster in patients who received ERAS care than in those who received conventional care. Our result is similar to his findings ( $P<0.001$ ), times to first flatus in the ERAS group were  $3.26\pm 0.64$  days and  $4.68\pm 0.49$  days in the CC group. Prolonged perioperative fasting, preoperative bowel preparation, and nasogastric tube intubation were likely to delay bowel-function recovery. Previous studies have shown that the small intestine might return to normal enterocinesia 6 hours after abdominal surgery, and that liquid can be easily absorbed in the small intestine in early postoperative recovery.<sup>23</sup>

Early oral feeding was safe.<sup>17,21</sup> Early postoperative enteral nutrition with dietary fiber could accelerate recovery of peristalsis, protect gut mucosal barrier function, alleviate intestinal barrier dysfunction, decrease incidence of bacterial translocation and enhance the recovery of gut function.<sup>24</sup> In the present study, most patients who underwent ERAS tolerated early oral diet well. Although gastroparesis occurred in some patients, the symptoms mostly occurred in the initial stage of oral diet and did not develop into severe complications ( $P=0.061$ ). Several studies showed that ERAS resulted

in significantly reduced postoperative hospital stays for gastrectomy.<sup>7</sup> It was reported that the postoperative hospital stay in gastric cancer patients could be decreased to 3.8 days in the ERAS group.<sup>25</sup> In the present study, ERAS patients had a mean postoperative hospital stay of  $6.66\pm 3.36$  days and  $9.02\pm 2.61$  days in the CC group. The results of our study suggested that postoperative recovery was significantly enhanced by our ERAS protocol in gastric cancer patients undergoing gastrectomy.

## Conclusion

ERAS can reduce postoperative stress, enhance the recovery of the gut, reduce pain intensity, shorten hospital stays and increase satisfaction in gastric cancer patients undergoing curative gastrectomy.

## Ethics

Ethical approval was obtained from the ethics committee of The Second Military Medical University of Shanghai.

## Consent to publish

Written informed consent form was obtained from patients participating in this study and to preserve patients' data confidentiality, the data were de-identified.

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## Disclosure

The authors report no conflicts of interest in this work.

## References

- Wilmore DW, Kehlet H. Recent advances: Management of patients in fast track surgery. *BMJ*. 2001;322(7284):473–476.
- Yamada T, Hayashi T, Aoyama T, et al. Feasibility of enhanced recovery after surgery in gastric surgery: a retrospective study. *BMC Surg*. 2014;14(1):41.
- Zhuang CL, Ye XZ, Zhang XD, Chen BC, 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(5):667–678.
- Kim JW, Kim WS, Cheong JH, Hyung WJ, Choi SH, Noh SH. Safety and efficacy of fast-track surgery in laparoscopic distal gastrectomy for gastric cancer: a randomized clinical trial. *World J Surg*. 2012;36(12):2879–2887.
- Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer*. 2015;136(5):E359–E386.
- G-C, Zhang Y-L, LI, Zhang M. An analysis of global cancer incidence and mortality tendency from 1999 to 2002 [J]. *China Cancer*. 2008;8:003.
- Wang D, Kong Y, Zhong B, Zhou X, Zhou Y. Fast-track surgery improves postoperative recovery in patients with gastric cancer: a randomized comparison with conventional postoperative care. *J Gastrointest Surg*. 2010;14(4):620–627.
- Mortensen K, Nilsson M, Slim K, et al. Consensus guidelines for enhanced recovery after gastrectomy. *Br J Surg*. 2014;101(10):1209–1229.
- Kehlet H, Wilmore DW. Multimodal strategies to improve surgical outcome. *Am J Surg*. 2002;183(6):630–641.
- Ljungqvist O, Scott M, Fearon KC. Enhanced recovery after surgery: a review. *JAMA Surg*. 2017;152(3):292.
- Kitayama M. Role of regional anesthesia in the enhanced recovery after surgery program. *J Anesth*. 2014;28(1):152–155.
- van Boerum DH, Smith JT, Curtin MJ. A comparison of the effects of patient-controlled analgesia with intravenous opioids versus Epidural analgesia on recovery after surgery for idiopathic scoliosis. *Spine*. 2000;25(18):2355–2357.
- Andersen HK, Lewis SJ, Thomas S. Early enteral nutrition within the first 24 hours post colorectal surgery seems to lower complications and enhance recovery. *Cochrane Database Syst Rev*. 2006;(4):CD004080.
- Pędziwiatr M, Matłok M, Kisialewski M, et al. Short hospital stays after laparoscopic gastric surgery under an Enhanced Recovery After Surgery (ERAS) pathway: experience at a single center. *Eur Surg*. 2014;46(3):128–132.
- Ding J, Sun B, Song P, et al. The application of enhanced recovery after surgery (ERAS)/fast-track surgery in gastrectomy for gastric cancer: a systematic review and meta-analysis. *Oncotarget*. 2017;8(43):75699–75711.
- Wilmore DW. From Cuthbertson to fast-track surgery: 70 years of progress in reducing stress in surgical patients. *Ann Surg*. 2002;236(5):643–648.
- Feng F, Ji G, Li JP, et al. Fast-track surgery could improve postoperative recovery in radical total gastrectomy patients. *World J Gastroenterol*. 2013;19(23):3642.
- Grantcharov TP, Kehlet H. Laparoscopic gastric surgery in an enhanced recovery programme. *Br J Surg*. 2010;97(10):1547–1551.
- Yang Z, Zheng Q, Wang Z. Meta-analysis of the need for nasogastric or nasojejunal decompression after gastrectomy for gastric cancer. *Br J Surg*. 2008;95(7):809–816.
- Hur H, Kim SG, Shim JH, et al. Effect of early oral feeding after gastric cancer surgery: a result of randomized clinical trial. *Surgery*. 2011;149(4):561–568.
- Doig GS, Heighes PT, Simpson F, Sweetman EA, Davies AR. Early enteral nutrition, provided within 24 h of injury or intensive care unit admission, significantly reduces mortality in critically ill patients: a meta-analysis of randomised controlled trials. *Intensive Care Med*. 2009;35(12):2018–2027.
- Park WY, Thompson JS, Lee KK. Effect of epidural anesthesia and analgesia on perioperative outcome: a randomized, controlled Veterans Affairs cooperative study. *Ann Surg*. 2001;234(4):560.
- Nelson R, Tse B, Edwards S. Systematic review of prophylactic nasogastric decompression after abdominal operations. *Br J Surg*. 2005;92(6):673–680.
- Hou H, Ping X, Zhu Y, Zhao Z, Li Y, Li J. Dietary fiber alleviates intestinal barrier dysfunction in post-trauma rats. *Clin Invest Med*. 2010;33(2):117–123.
- Yu G, Tang B, Yu PW, Peng ZH, Qian F, Sun G. Systemic and peritoneal inflammatory response after laparoscopic-assisted gastrectomy and the effect of inflammatory cytokines on adhesion of gastric cancer cells to peritoneal mesothelial cells. *Surg Endosc*. 2010;24(11):2860–2870.

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