Enhanced recovery after surgery with laparoscopic radical gastrectomy for stomach carcinomas

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Abstract

AIM: To study the efficacy of the enhanced recovery after surgery (ERAS) program in laparoscopic radical gastrectomy for stomach carcinomas.

METHODS: From June 2010 to December 2012, 61 gastric cancer patients who underwent laparoscopic-assisted radical gastrectomy with D2 lymphadenectomy at First Hospital of Jilin University were enrolled in this randomized controlled trial. (Clinical Trials.gov, registration ID: NCT01955096). The subjects were divided into the ERAS program group and the conventional control group. The clinical characteristics, recovery variables, and complications of patients were analyzed.

RESULTS: The time to first ambulation, oral food intake, and time to defecation were significantly shorter in the ERAS group (n = 30), compared to the conventional group (n = 31; \( P = 0.04, 0.003, \) and \( 0.01, \) respectively). The postoperative hospital stay was less in the ERAS group (6.8 \( \pm \) 1.1 d) compared to the conventional group (7.7 \( \pm \) 1.1 d) (\( P = 0.002 \)). There was no significant difference in postoperative complications between the ERAS (1/30) and conventional care groups (2/31) (\( P = 1.00 \)). There were no readmissions or mortality during the 30-d follow-up period.

CONCLUSION: The ERAS program is associated with a shorter hospital stay in gastric cancer patients undergoing laparoscopic radical gastrectomy. The ERAS protocol is useful in the treatment of gastric cancer.

Key words: Enhanced recovery after surgery; Laparoscopic; Gastrectomy; Gastric cancer
INTRODUCTION

Annually, almost one million cases of gastric cancer are diagnosed worldwide, of which, 400,000 cases alone are diagnosed in China. Surgical resection of gastric cancer and regional lymphadenectomy are the only options for curability in these patients. However, it is sometimes associated with significant morbidity, mortality, and has an impact on the quality of life of patients after surgery.

Since its introduction in 1994 by Kitano et al., laparoscopic-assisted gastrectomy (LAG) has become the standard treatment for early gastric cancer. LAG has significant advantages over conventional open gastrectomy such as faster recovery, shorter hospital stay and an overall improvement in quality of life. In recent years, as a result of advancements in the design of surgical instruments and increased surgeon experience, LAG is increasingly being used in the treatment of advanced gastric cancer, although there is still controversy surrounding the extent of lymphadenectomy that should be performed.

The combination of LAG with Enhanced Recovery After Surgery (ERAS), an evidence based multi-disciplinary perioperative and postoperative care program, leads to additional improvements in outcome such as decreased complications, length of hospital stay and hospital cost. ERAS constitutes components such as optimized pain control, restricted intravenous fluids, early oral nutrition and enforced mobilization with the aim of reducing surgical stress response hence optimizing patient recovery.

Despite the successful adoption of ERAS by several centers in the United Kingdom, Scandinavia and Germany, for colorectal cancer, this is not the case with gastric cancer. Studies reporting on fast track rehabilitation for gastric cancer are scarce. Thus, we undertook this study to evaluate the efficacy and safety of the ERAS program in patients undergoing elective laparoscopic gastric resection for advanced cancer.

MATERIALS AND METHODS

Patient population

This prospective study was conducted in the First Hospital of Jilin University, Department of Gastric and Colorectal Surgery between 2010 and 2012 (Trial registration number: NCT01955096). Only those diagnosed with advanced gastric cancer were enrolled into the study after undergoing a diagnostic workup consisting of endoscopy with biopsy, total-body CT scan, and endoscopic ultrasound in selected patients. Inclusion criteria were as follows: diagnosis of advanced gastric cancer, elective laparoscopic surgery and age under 75 years. Patients with early gastric cancer received neoadjuvant chemotherapy, and those with pyloric obstruction or with distant metastasis were excluded from the study.

After obtaining written consent from all patients, we randomly assigned them into two groups: 30 patients underwent LAG with the ERAS program and 31 underwent LAG, but received conventional postoperative care (Table 1). All operations were performed by an independent surgical group and the study protocol was approved by the hospital’s ethical committee.

Laparoscopic procedure

There was no difference in the surgical procedures between the two groups. Laparoscopy-assisted gastrectomy was carried out and depending on the location of the primary tumor, total, proximal subtotal, or distal subtotal gastrectomy was performed. After resection, a supraumbilical midline incision was made for restoration of intestinal continuity and tumor retrieval. Lymph node dissection was performed according to the Guidelines of Japanese Gastric Cancer Association with D2.

Postoperative care

Briefly, during the postoperative period, fluid intake was from POD 1 or POD 2 in the ERAS group, patients were advised to begin cautiously and increase intake according to tolerance. Furthermore, they were encouraged to take full semi-liquid diet on POD 2, and normal food as soon as possible after surgery. In the conventional group, postoperative oral intake was restricted. In the ERAS group, patients were encouraged to mobilize early from POD 1, and meet daily targets for mobilization. The conventional group received traditional postoperative care including bed rest. Urinary bladder drainage was routinely used in the conventional group, but limited to POD 1 in the ERAS group (Table 1).
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Table 1  Perioperative protocols in the enhanced recovery after surgery and conventional groups

| ERAS group                                                                 | Conventional group                                                                 |
|---------------------------------------------------------------------------|-----------------------------------------------------------------------------------|
| **PreOp**                                                                 |                                                                                                                                 |
| Patient education regarding FTS                                           | Patient education                                                                  |
| Solid food allowed until 6 h before surgery and carbohydrate drinks       | No solid food 24 h before surgery and no liquids 12 h before surgery                |
| until 2 h before surgery                                                   | Mechanical bowel preparation and nasogastric placement performed                   |
| No bowel preparation                                                       |                                                                                                                                 |
| **Intraoperative**                                                        |                                                                                   |
| 5-trocar laparoscopy-assisted procedure. Non-opioid analgesia after induction of anesthesia. No nasogastric tube or drainage tube used. I.V. fluids were restricted (Ringer’s lactate 20 mL/kg in the first h, after that 6 mL/kg per hour). Vasoactive drugs used if needed | 5-trocar laparoscopy-assisted procedure. Routine use of abdominal drainage tubes and placement of catheters I.V. fluids not restricted (Ringer’s lactate 20 mL/kg in the first h, then at the rate of 10-12 mL/kg per hour) |
| **1st PostOp Day**                                                        |                                                                                                                                 |
| Soluble contrast swallow study is done to check the anastomosis. If intact, fluids are started. Adequate pain control maintained | Keep NPO                                                                          |
| Urinary catheter removed                                                   | Removal of urinary catheter                                                        |
| Patient mobilized out of bed                                              | Mobilization in bed                                                                 |
| **2nd PostOp Day**                                                        |                                                                                                                                 |
| Patient started on soft food                                              | Patient is advised to get out of bed                                               |
| Continue and increase ambulation. Pain control maintained                 |                                                                                                                                 |
| **3rd PostOp Day**                                                        |                                                                                                                                 |
| Patient progresses to solid food                                          | Remove nasogastric tube and liquids started                                        |
| Epidural stopped and acetaminophen started                                 | Encouraged to walk in the ward                                                     |
| Mobilization continued                                                     | Drains removed                                                                     |
| **4th PostOp Day**                                                        | Solid food intake                                                                  |
| Check discharge criteria                                                  |                                                                                                                                 |

FTS: Fast-track surgery; PostOp: Postoperative; ERAS: Enhanced recovery after surgery.

Outcome parameters (data collection)
Collected data included: age, sex, tumor location, type of gastrectomy and reconstruction, T stage, number of lymph nodes retrieved, duration of operation, complications and postoperative outcomes (time to return to diet, first defecation and ambulation). Patients were monitored for the next 30 d for readmission.

Discharge criteria
The criteria for discharge were as follows: tolerance of solid diet, return of bowel habits and ability to walk on their own. To avoid influences from the clinicians, the discharge administration was managed by independent clinicians who were not involved in the study.

Statistical analysis
Measurement data are expressed as mean ± SD. The data were analyzed using the Independent Student’s t test, whereas categorical data were calculated using the $\chi^2$ test or Fisher’s exact test. Data analysis was performed using SPSS® software package version 16.0 (SPSS Inc., Chicago, IL, United States). $P < 0.05$ was considered statistically significant.

RESULTS
Sixty-one consecutive patients were included in the current study and were followed for 30 d. Mean age was 62 years in both patient groups, with a 2:1 male to female ratio. Table 2 summarizes the clinical data of the patients. According to the TNM classification system of the Union for International Cancer Control, 26 patients were stage II, and 35 cases were stage III. D2 lymphadenectomy was routinely performed in all patients. The number of lymph nodes retrieved, duration of surgery, amount of blood loss and type of surgery are shown in Table 3.

Compared to the conventional group, the ERAS group showed faster recovery with a shorter postoperative hospital stay (7.7 ± 1.1 d and 6.8 ± 1.1 d, respectively). Earlier postoperative food intake was observed in the ERAS group (2.9 ± 0.7 d) compared with the conventional group (3.5 ± 0.8 d). There was also a significant difference in defecation time between the ERAS (3.1 ± 0.7 d) and conventional (3.6 ± 0.8 d) groups. Time to ambulation (2.6 ± 0.9 d for the ERAS group and 3.1 ± 1.0 d for the conventional group) was also significantly different (Table 4).

There were two cases of ileus complications, one in each group. They were managed by fasting, nasogastric decompression and other measures. In the ERAS group, one patient developed a wound infection. The incidence of complications between the ERAS group and the conventional group was not significantly different ($P = 1.0$). Table 5 details these complications. There were no readmissions during the 30-d follow-up period. In addition, no mortality was reported.

DISCUSSION
This study set out to explore the safety and outcomes of ERAS in patients diagnosed with advanced gastric cancer. Our findings showed that the ERAS program was feasible and safe compared to conventional postoperative care. Earlier studies by Kehlet and colleagues confirmed that ERAS in colon cancer was beneficial and included reduced hospital stay, avoided or minimized short-term complications and patients had a speedier recovery and returned to their normal

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patients are scarce. Our study demonstrated that ERAS outweighed conventional care in terms of safety, hospital stay, defecation time, ambulation time and postoperative recovery. These results are consistent with those reported by Feng et al[13]. ERAS, unlike conventional care, does not require long postoperative fasting periods. Based on the concept that eating too early after surgery may cause intestinal obstruction and anastomotic disruption, surgeons routinely restrict oral intake in patients receiving conventional care. A recent prospective study confirmed that early oral food intake after laparoscopic gastric surgery is safe and might be associated with enhanced recovery with shorter hospital stay[11]. In the same context, patients with gastric cancer planning to receive conventional care have been advised to fast for 12 to 24 h before gastrectomy. Conversely, gastric cancer patients receiving fast track rehabilitation are required to fast for only 2 h before the operation. Therefore, in this study, patients were allowed carbohydrate-rich drinks up to 2 h before surgery. Some recent reports have indicated that a nasogastric tube is not necessary as it may instigate pulmonary complications[18-20]. Furthermore, ERAS advocates restriction of fluid therapy during the perioperative period. Recently published articles have shown that the infusion of extra fluid needed to sustain intraoperative infusion in conventional perioperative care augments the threat of pulmonary interstitial edema and postoperative hypoxia; but it can also raise the threat of cardiopulmonary complications. In addition, the infusion of extra fluid exacerbates gastrointestinal edema and as a consequence can lead to delayed recovery of gastrointestinal function. In the present study, this was the reason that the quantity of fluid infused in the ERAS group was restricted.[21,22]

The results of this study confirm that ERAS accelerates postoperative recovery compared with conventional care. In the ERAS group, average hospital stay was 6.8 ± 1.1 d after laparoscopic gastric resection and was 7.7 ± 1.1 d in the conventional group. Because drainage tubes increase the risk of complications including accumulation of intragastric fluid, surgeons routinely restrict oral intake in patients undergoing conventional care.[23]
abdominal fluid, infection and fistula, surgical drainage was not used in the ERAS group, and this facilitated earlier ambulation in this group compared with the conventional group (2.6 ± 0.9 d and 3.1 ± 1.0 d, respectively). In addition, our results also showed that defecation time was less in the ERAS group (3.1 ± 0.7 d, P < 0.002) than in the conventional group (3.6 ± 0.8 d).

Three patients developed postoperative complications, one in the ERAS group and two in the conventional group, the difference was not significant. Moreover, there were no readmissions or mortality reported during the follow-up period.

Importantly, if a patient is randomized to the ERAS program, clinicians may be influenced to accelerate the discharge rather than to judge the patient’s condition. Thus, in order to ensure the randomness of the study, the discharge criteria together with the clinical decisions regarding oral intake and drainage extraction should be managed by clinicians who are not involved in the study.

In conclusion, although the occurrence of postoperative complications between the two groups was not statistically significant, overall, ERAS was safe and feasible compared to conventional care in patients with advanced gastric cancer[23-27].

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