Safety and efficacy of enhanced recovery after surgery (ERAS) in patients undergoing emergency laparotomy: A single center randomized controlled trial

Brief title: Enhanced Recovery After Surgery (ERAS) in patients undergoing emergency laparotomy

Organization's Unique Protocol ID: 023-YLS-010

Study Type: Clinical trial

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Study Locations: China, Tianjin

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Tianjin Medical University Surgery Student Research Network

Research proposals

1.Affirmation of Integrity	All the researchers involved in this study solemnly declare their commitment to strict adherence to the experimental protocols and the authenticity of the data records throughout the entire phase of the study. They also promise not to have any conflict of interest.
2. Research Title	Safety and efficacy of enhanced recovery after surgery (ERAS) in patients undergoing emergency laparotomy: A single center randomized controlled trial
3. Research plan	1. August 2023-October 2023 Refine ERAS-related measures and coordinate the work of relevant sections of the agency； 2. November 2023-April 2024 In accordance with the study plan and randomization process, the study subjects were included and the study was completed 3. May 2024-June 2024 Collect experimental data and complete statistical analysis of the experiment 4. July 2024-April 2024 Completion of thesis writing and publication
4. Background	Since Kehlet first proposed enhanced recovery after surgery (ERAS) protocols in the 1990s, they have been widely adopted. Preoperative counseling, standardized anesthesia management protocols, more optimal postoperative analgesic regimens, restriction of intubation and catheterization, early postoperative mobilization, and early oral intake of food are all part of ERAS programs. These programs began in colorectal surgery and have now been expanded to other surgical specialties. Several studies have shown that patients benefit from ERAS programs, including reduced pain, faster return to bowel function, shorter hospital stays, and lower health care costs. However, we found that ERAS programs are rarely used for emergency surgery. Emergency surgery is the treatment of choice for acute abdominal conditions such as traumatic liver rupture, traumatic splenic rupture, and complete bowel obstruction. Nevertheless, we found that most clinical studies of ERAS excluded patients who underwent emergency surgery. This is because most researchers probably believe that emergency surgery does not allow enough time for ERAS-related preoperative preparation. In fact, some ERAS programs can be used for emergency surgery, such as the anesthetic modality of combined anesthesia, postoperative multimodal analgesia, earlier postoperative oral feeding and ambulation, and earlier removal of invasive catheters. However, few studies have focused on the use of ERAS in emergency surgery. The present study is a randomized controlled trial evaluating the safety and efficacy of an ERAS program in emergency abdominal surgery. We hypothesized that an ERAS program could be

	implemented into emergency surgery and reduce postoperative recovery time without increasing the complication rate and readmission rate (<30 days).
5.esearch purpose	1. Exploring the impact of accelerated rehabilitation surgery on postoperative recovery in patients undergoing open surgery for acute abdomen;. 2. Evaluating the safety of accelerated rehabilitation surgery in patients undergoing open surgery for acute abdominal conditions. 3. Evaluating the impact of accelerated rehabilitation surgery on complications in patients undergoing open surgery for acute abdominal conditions。
6.Inclusion and exclusion criteria	Inclusion criteria: 1. patients between the ages 18-70, 2. patients who completed the preoperative examination and preoperative diagnosis within 4 hours after admission for acute abdomen diseases, 3. required emergency surgery within 6 hours from surgeon encounter. Exclusion criteria 1. patients who refused to be enrolled in this study; 2. patients with any psychiatric or neurological disorders; 3. septic shock at admission; 4. duration of symptoms more than five days; 5. patients with contraindications to the placement of lumbar epidural catheters, such as coagulation disorders, severe sepsis, etc.; 6. presence of preoperative factors affecting wound healing (e.g. long-term steroid use); 7. patients with extra-abdominal injuries or terminal malignancy, or patients requiring damage control surgery; 8. patients found intraoperatively to require any procedure other than splenectomy, partial hepatectomy or liver repair, bowel resection and anastomosis, laparoscopic cholecystectomy and appendectomy, and gastrointestinal perforation repair.
7. Design proposal	This study was a continuous, two-arm, randomized, single-blind, controlled trial.
8.Sample size estimation	The primary outcome was postoperative recovery time, which required a power analysis. For this purpose, we reviewed the medical records of patients with acute abdomen who underwent emergency surgery between January 2013 and January 2023 at our hospital. The mean postoperative recovery time for these patients was 13.7 ± 2.1 days. Two days was determined to be a clinically significant difference. The power of the test was set at 90% and the significance level was set at 5%. Based on these facts, the required sample size was calculated as 72 cases per group. To increase the power of the

	study, the recruitment process was extended until there were a total of 80 patients in each group.
9.Methods of randomized and hidden grouping	Using SAS Statistical Package version 9.3, independent investigators created random numbers in a 1:1 ratio with a block size of 4. Patients were stratified according to the type of surgery. A study coordinator not associated with patient enrollment, information collection, perioperative treatment, or postoperative follow-up will enclose the randomization results in sequentially numbered opaque envelopes. Prior stratified randomization was performed according to four types of surgery: hemorrhagic trauma (traumatic liver or spleen rupture), gastrointestinal reconstruction (complete gastrointestinal obstruction), inflammatory disease (acute cholecystitis and appendicitis), and perforated disease. After the surgeon decided to proceed with the operation, the study coordinator opened the envelopes and assigned the groups. In this way, all patients enrolled in the study were randomly assigned to receive either the ERAS program (ERAS group) or usual care (usual group). In the event of a serious adverse event or any unanticipated deterioration in a patient's clinical status, group assignment could be unblinded to ensure patient safety. The case report form was used to record these events. Unblinded patients were included in the intention-to-treat population but were not included in the per-protocol analysis.
10.Blind	single-blind
11.Outcomes	Primary outcome: postoperative recovery time. Secondary outcomes: (1) postoperative recovery rate; (2) postoperative complication rate (evaluated by Clavien-Dindo classification); (3) time to first postoperative bowel movement; (4) time to tolerate a semi-liquid diet; (5) time to tolerate a soft food diet; (6) re-admission rate (within 30 days); (7) maximal pain score determined by a visual analog scale (VAS)13; (8) patient satisfaction, evaluated with the Inpatient Satisfaction Scale developed by Peking Union Medical College Hospital.
12.Definition of participant validity determination	In the event of a serious adverse event or any unforeseen deterioration in the patient's clinical status, group allocation could be unblinded and the trial withdrawn to ensure patient safety. A case report form was used to record these events. Unblinded patients were included in the intention-to-treat population but were not included in the per-protocol analysis.
13.Definition of adverse events and adverse reactions,	1. Adverse events: adverse medical events that occurred during the course of the study, but not necessarily related to ERAS-related measures. 2. Identification method: the occurrence of postoperative

identification methods and management systems	complications was evaluated according to the Clavien-Dindo classification. 3. Management system: In the event of a serious adverse reaction or any unforeseen deterioration of the patient's clinical status, group allocation could be unblinded and the trial withdrawn to ensure patient safety. Case report forms were used to record these events. Unblinded patients were included in the intention-to-treat population but were not included in the per-protocol analysis.
14. Recruitment of participants	The recruitment site was the institution where this study was conducted, and at the time of admission, investigators screened potential patients for acute abdominal diseases. These acute abdominal conditions included: hemorrhagic trauma (traumatic liver or spleen rupture), gastrointestinal obstruction (complete obstruction), and inflammatory perforating disease. After screening was completed, patients who met the inclusion and exclusion criteria were informed about the experiment and signed an informed consent form.
15.Collection of general information on participants	After obtaining informed consent from the patients, baseline information (demographics, surgical data, type of surgery, comorbidities, history of previous abdominal surgery) was collected. The investigators who undertook the preoperative selection, information collection, and evaluation were professional and qualified prior to the trial.
16.Baseline indicators and observational projects	Age, gender, BIM, history of previous abdominal surgery, comorbidities, ASA classification, duration of surgery, type of surgery, intraoperative blood loss
17.Standard Operating Procedures	Preoperative care: A number of preoperative protocols were similar in both groups, including: (1) surgical risk assessment; (2) preoperative placement of a nasogastric tube (NG); (3) preoperative administration of crystalloid fluids to replenish blood volume; (4) empiric antibiotics and acid-reducing therapy administered intravenously; and (5) intravenous analgesia. In the ERAS group, an epidural catheter was placed in the lumbar 3-4 space before surgery to facilitate intraoperative epidural anesthesia and postoperative analgesia. At the same time, ultrasound-guided internal jugular vein (IJV) cannulation was performed to monitor central venous pressure (CVP). CVP-guided infusion, i.e., goal-directed fluid therapy, was maintained at a CVP of 8-10 cm of saline. Depending on the urinary output, blood pressure, heart rate, and clinical signs of dehydration, fluids were administered according to an institutional care plan in the routine care group. Dexamethasone 4 mg IV was given shortly before induction of anesthesia.

	Intraoperative care: All patients underwent emergency open surgery. Appropriate surgical incisions were selected based on adequate provision of good surgical vision and surgical space. If intra-abdominal fluid was found, it was aspirated and sent for bacterial culture. The final decision on the surgical approach is based on the surgeon's opinion and intraoperative findings. If anastomosis was deemed unsafe, an ileostomy without anastomosis was performed. Table 1 shows the changes in the anesthesia regimen in the ERAS group. The anesthesiologist decided the anesthesia for the conventional group. In the ERAS group, an experienced surgeon set up an abdominal drain as needed during the procedure. In the conventional care group, an abdominal drain was routinely placed. Postoperative care: The postoperative drinking and eating schedules for both groups can be seen in Table 1.Patients in the ERAS group were asked to start simple bed activities, such as moving both lower limbs, on the day of surgery (POD-0), provided that the epidural catheter was secure. At POD-1, patients were asked to sit for at least 2 hours and then get out of bed after the epidural catheter was removed at POD-2. In the conventional group, patients were encouraged to be active at POD-2, starting with simple bed activities and gradually transitioning to normal walking without any specific requirements.
18.Methods of statistical analysis	SPSS (version 19.0) and GraphPad Prism (version 8.0) software were used for statistical analysis. Independent samples t-test (Student's t-test) was used to compare continuous data with normal distribution. Independent samples Mann-Whitney U test compared continuous data with non-normal distribution. Comparisons between groups of categorical variables were made using the Chi-square test, Fisher's exact test, $\chi 2$ test, or continuity-corrected $\chi 2$ test. Continuous variables were expressed as mean and standard deviation (Mean SD). Logit tests stratified by randomization parameters were used to compare primary and secondary outcomes across groups. For comparisons of postoperative recovery time, the stratified Cochran-Mantel-Haenszel test was utilized without adjustment for multiple comparisons. $P < 0.050$
19. Data management system	Data collection and recording was carried out by a regular independent investigator who was not involved in the entirety of this study