Randomised Controlled Trial

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Effectiveness of ERAS program on postoperative recovery after gastric cancer surgery: a randomized clinical trial

Ho-Jin Lee, MD, PhD[a], Jeesun Kim, MD[b], Soo-Hyuk Yoon, MD[a], Seong-Ho Kong, MD, PhD[b], Won Ho Kim, MD, PhD[a], Do Joong Park, MD, PhD[b,*], Hyuk-Joon Lee, MD, PhD[b], Han-Kwang Yang, MD, PhD[b]

Background: Previous studies have reported the effectiveness of the "enhanced recovery after surgery" program in patients who underwent gastric cancer surgery, mostly based on the 2014 gastrectomy guidelines. Therefore, based on subsequent advancements in perioperative management, this randomized, controlled, open-label, single-center study aimed to assess the impact of a recent evidence-based multimodal enhanced recovery after surgery program on the quality of early recovery after gastric cancer surgery.

Materials and methods: This study included adult patients scheduled to undergo elective laparoscopic or robotic distal gastrectomy for gastric cancer. Patients were randomly assigned to the enhanced recovery after surgery or conventional group. The primary outcome was the total Quality of Recovery-15 score assessed 24, 48, and 72 h postoperatively. Differences between both groups were evaluated using a linear mixed-effects model. We hypothesized that an increase of at least 8 points in the Korean version of Quality of Recovery-15 scores would indicate a clinically significant improvement, consistent with the minimal clinically important difference (≥8) for Quality of Recovery-15. Secondary outcomes included pain scores at rest and during coughing, cumulative fentanyl consumption through intravenous patient-controlled analgesia, postoperative nausea/vomiting incidence, and gastrointestinal dysfunction as measured using the I-FEED score – all assessed 24, 48, and 72 h postoperatively.

Results: For the 92 patients examined (enhanced recovery after surgery, n = 45; conventional, n = 47), the estimated difference in the postoperative Quality of Recovery-15 total scores between the two groups during the first days was significantly larger than the minimal clinically important difference of Quality of Recovery-15 (mean difference: 16.0, 95% confidence interval: 8.9–23.0, $P < 0.001$). Furthermore, excluding the incidence of postoperative nausea/vomiting, the enhanced recovery after surgery group demonstrated significant improvements in other secondary outcomes.

Conclusions: Our evidence-based multimodal enhanced recovery after surgery program significantly improved the quality of early postoperative recovery after minimally invasive distal gastrectomy.

Keywords: enhanced recovery after surgery, gastrectomy, pain, perioperative care, perioperative medicine, postoperative, stomach neoplasms

HIGHLIGHTS

- In South Korea, where gastric cancer is highly prevalent, many aspects recommended by the Enhanced Recovery After Surgery (ERAS) guidelines are yet to be fully implemented.
- We aimed to develop and evaluate an evidence-based, multimodal ERAS program specifically tailored for minimally invasive gastric cancer surgery, which is the standard treatment in Eastern Asia.
- Our ERAS program significantly improved the quality of early postoperative recovery after minimally invasive distal gastrectomy in patients with gastric cancer.
- These improvements are likely attributable to the use of multimodal opioid-sparing analgesia and a shortened perioperative fasting period, both of which contribute to reduced postoperative pain and accelerated gastrointestinal recovery.

Introduction

Gastric cancer remains a significant global health concern, ranking as the fifth most common cancer and the fourth leading

[a] Department of Anesthesiology and Pain Medicine, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Republic of Korea and [b] Department of Surgery and Cancer Research Institute, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Republic of Korea

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*Corresponding author. Address: Department of Surgery and Cancer Research Institute, Seoul National University Hospital, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 03080, Republic of Korea. Tel.: +82 2 2072 2318. Fax: +82 2 766 3975. E-mail: djparkmd@snu.ac.kr (D.J. Park).

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cause of cancer-related deaths in 2020[1]. Surgical resection is a critical component of gastric cancer treatment, as it is necessary for complete tumor removal and enhancement of survival rates[2]. However, gastric cancer surgery frequently involves significant complications and extended recovery periods, which can adversely affect patients' quality of life[3].

Enhanced recovery after surgery (ERAS) is an evidence-based, multidisciplinary, and multimodal approach to improve postoperative recovery[4]. ERAS was initially designed for colorectal surgery; however, it has become the standard for perioperative management across various types of surgical procedures[4]. Conversely, despite its broad application, robust evidence supporting the effectiveness of ERAS in patients who have undergone gastric cancer surgery is lacking. This may be owing to the later adoption of ERAS in Eastern Asia[5], where gastric cancer is more prevalent than that in Western countries. Furthermore, many elements of the ERAS guidelines for gastric cancer surgery have been adapted from those established for pancreaticoduodenectomy[6]. In addition, in South Korea, where gastric cancer is highly prevalent, many aspects recommended by the ERAS guidelines are yet to be fully implemented[7]. Notably, several challenges in South Korea's healthcare, such as limited manpower, insufficient policy support, poor interdepartmental collaboration, and adherence to traditional practices, have hindered ERAS implementation[8].

Therefore, in response to these challenges, we aimed to develop and evaluate an evidence-based, multimodal ERAS program specifically tailored for minimally invasive gastric cancer surgery, which is the standard treatment in Eastern Asia[9]. In this study, we shifted our focus from traditional outcomes such as length of hospital stay and postoperative complications to the quality of recovery, which we established as our primary endpoint[10]. We hypothesized that our ERAS program would significantly improve the quality of short-term recovery after minimally invasive gastric cancer surgery.

Methods

Study design and participants

This prospective randomized controlled trial was approved by the Institutional Review Board (IRB) of Seoul National University Hospital and registered with ClinicalTrials.gov (NCT05649319 on 14 December 2022). The study design and reporting of its findings followed the Consolidated Standards of Reporting Trials guidelines[11]. All participants provided written informed consent before enrollment.

Eligible participants included individuals aged 19–80 years who were scheduled for elective minimally invasive distal gastrectomy, had an American Society of Anesthesiologists (ASA) physical status of I or II, had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1, and provided informed consent. When IRB approval was initially obtained, our study was designed to include patients undergoing laparoscopic distal gastrectomy. However, given that approximately 40% of these procedures are now being performed using robotic techniques at our center, we decided to include patients undergoing robotic distal gastrectomy (IRB approval date: 13 February 2023). The exclusion criteria were chronic pain lasting over 3 months that could confound pain assessments; requiring resection of organs other than the stomach during surgery, except for cholecystectomy; history of upper abdominal surgery, except for cholecystectomy; hypersensitivity to fentanyl, ropivacaine, acetaminophen, or nonsteroidal anti-inflammatory drugs (NSAIDs), and deemed unsuitable for the clinical trial by the investigators or study coordinator.

Baseline characteristics recorded at the outpatient clinic at the time of the decision to proceed with surgery included age, sex, height, weight, body mass index, ASA physical status, TNM classification for gastric cancer, ECOG performance status, scores of the Korean version of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30), and the Hospital Anxiety and Depression Scale questionnaire. Additional variables, such as the Apfel score and the Korean version of Quality of Recovery-15 (QoR-15K)[10], were assessed preoperatively after admission for surgery.

Randomization and blinding

Patient enrollment was conducted at the surgical outpatient clinic at the time of the decision to proceed with surgery. After enrollment, patients were randomly allocated to the ERAS or conventional group using block randomization (block size: 6) in a 1:1 ratio using R software (version 3.5.1; R Foundation for Statistical Computing, Vienna, Austria). A research nurse who was blinded to the study assignments managed the randomization process. However, upon patient enrollment, the results of the randomization were disclosed to the researchers. Therefore, blinding the researchers was not feasible, given the substantial differences in perioperative management between the two groups.

Perioperative management

The vital differences in perioperative management between the two groups are summarized in Table 1, and further details are provided in Supplemental Digital Content (available at: http://links.lww.com/IJSO/A21).

Outcome measures

The primary outcome was the total QoR-15K score[10], which was assessed 24, 48, and 72 h postoperatively. Secondary outcomes included pain scores at rest and during coughing, measured using an 11-point Numeric Rating Scale (NRS) 2, 24, 48, and 72 h postoperatively. Additional secondary outcomes were total fentanyl consumption (μg) through intravenous patient-controlled analgesia (IV-PCA), incidence of postoperative nausea/vomiting (PONV) across four periods: 0–2 h, 2–24 h, 24–48 h, and 48–72 h postoperatively, and gastrointestinal dysfunction assessed using the I-FEED score 24, 48, and 72 h postoperatively[12]. We extracted data on fentanyl administration dose through IV-PCA from an electronic PCA device (Accumate® 1200, Woo Young Meditech, Seoul, South Korea).

In addition to the primary and secondary outcomes, we assessed the overall recovery time (h), presence of postoperative shoulder pain, cumulative total of postoperative fentanyl equivalent dose (μg) including rescue analgesics, and opioid-related complications other than PONV (such as hypotension, sedation, and respiratory depression). We conducted blood tests on postoperative days (PODs) 2 and 4 to measure serum white blood cell counts and high-sensitivity C-reactive protein levels. The overall recovery time was defined based on our previous study as the duration from the completion of surgery to the first point at which all of the following

Table 1

Comparison of perioperative management between the ERAS and conventional groups

	ERAS group	Conventional group
Pre-admission education on preoperative optimization	Yes	No
Preoperative phase		
Preoperative fasting	Meal: 8 h Water: 2 h	Meal and water: 8 h
Preoperative carbohydrate loading	Yes	No
Preemptive analgesia using oral non-opioid analgesics	Yes	No
Prophylactic antibiotics	Yes	Yes
Intraoperative phase		
Postoperative nausea/vomiting prophylaxis	Ramosetron + dexamethasone	Ramosetron
Ultrasound-guided transversus abdominis plane block	Yes	No
Acetaminophen administration	Yes	No
Active warming	Yes[a]	Yes
Maintenance of deep block through train-of-four monitoring	Yes	Yes
Appropriate anesthesia depth monitoring	Yes	Yes
Reversal of neuromuscular blockade	Sugammadex	Sugammadex
Postoperative phase		
Ward ambulation	POD 1 morning[b]	POD 1 morning
Thromboprophylaxis	Yes	Yes
Removal of a nasogastric tube	Immediately after surgery	POD 1 morning
Removal of a urinary catheter	POD 1 morning	POD 2 morning
Removal of an abdominal drainage	POD 3	POD 3
Intravenous patient-controlled analgesia	Yes	Yes
Regular use of non-opioid analgesics[c]	Yes	No
Resumption of water intake	POD 1 morning	6 PM on POD 2
Initiation of a soft-fluid diet	POD 2 morning	POD 3 morning
Initiation of a soft-blended diet	POD 4 morning	POD 5 morning
Scheduled discharge time	POD 5 morning	POD 6 morning

ERAS, enhanced recovery after surgery; POD, postoperative day.

[a]Preoperative warming using a warming blanket initiated upon entry into the operating room.

[b]Allow sitting on the edge of the bed, starting from the day of surgery.

[c]Administer intravenous acetaminophen every 8 h from the end of surgery until the next morning, and the morning after surgery, switch to oral acetaminophen and zaltoprofen every 8 h.

four criteria were met[13]: (1) tolerance of soft blended diet for 24 h, (2) safe ambulation until 600 m without assistance, (3) adequate pain control (NRS ≤ 3) with oral non-opioid analgesics, and (4) no abnormal physical findings or laboratory tests. The total dose of rescue analgesics was converted to an equivalent intravenous fentanyl dose based on previous studies[14,15]. We also collected data on the duration until the first postoperative gas out (h), length of postoperative hospital stay, incidence of postoperative complications, readmissions within 30 days postoperatively, emergency room visits within 30 days postoperatively, and quality of life 3 months postoperatively as measured using the EORTC QLQ-C30 questionnaire. Two research nurses who were not involved in the study performed all outcome assessments.

Statistical analysis

The required sample size for our study was predetermined using PASS 2022 version 22.0.2 (NCSS, Kaysville, UT, USA). The standard deviation of the postoperative QoR-15K score was assumed to be 15 points. We hypothesized that an increase of at least 8 points in the QoR-15K scores measured 24, 48, and 72 h postoperatively would indicate a clinically significant improvement, aligning with the minimal clinically important difference (MCID) for QoR-15[16]. Therefore, based on our prior findings, we set the correlation coefficient at 0.66[17]. Assuming compound symmetry for the correlation across time points and setting the statistical power at 80% and type I error at 0.05, we calculated that 44 participants per group would be necessary. Thus, to account for an anticipated dropout rate of 10%, we planned to recruit 49 participants per group, totaling 98 participants for the study. This setup enabled the comparison of postoperative QoR-15 scores between the groups using a linear mixed-effects model.

The analysis was conducted according to the modified intention-to-treat (mITT) principle, where the mITT population included all participants who were randomized and underwent elective laparoscopic or robotic gastrectomy, regardless of their adherence to the protocol and for whom the primary outcome assessment was completed. We evaluated the normality of the distribution of continuous variables using the Shapiro–Wilk test. These variables are presented as means with standard deviations or medians with interquartile ranges, depending on their distribution. Comparisons between groups were made using the independent *t*-test for normally distributed data or the Mann–Whitney U test for non-normally distributed data. Categorical data are described using frequencies or percentages and were analyzed using the chi-square test or Fisher's exact test based on the expected counts. Effect sizes and 95% confidence intervals (CIs) were computed.

We used a linear mixed-effects model for QoR-15K total scores measured repeatedly over the first 3 PODs. In our planned analysis, if the model revealed no significant interaction between time and treatment group, we planned to calculate adjusted mean differences in QoR-15K total scores between the groups without the interaction term. Conversely, if a significant interaction was observed, we planned to

perform post hoc pairwise multiple comparisons using the least squares mean approach. We also planned to adjust for multiple comparisons using Bonferroni correction to determine adjusted mean differences at each specific time point. This analysis was also conducted in the per-protocol (PP) group, excluding patients who underwent procedures other than distal gastrectomy and those who had significant deviations from the perioperative protocol.

All statistical analyses were performed using R software (version 4.3.2; R Foundation for Statistical Computing). The hypothesis tests were two-sided, and statistical significance was set at $P < 0.05$.

Results

Notably, 98 of the 140 patients assessed for eligibility met the inclusion criteria and were subsequently enrolled and randomly allocated to the ERAS or conventional groups between February 2023 and May 2024 (Fig. 1). Following recruitment, four patients from the ERAS group and two from the conventional group were excluded for the following reasons: cancellation of surgery (n = 3), decline to participate (n = 2), and open and closure owing to peritoneal seeding (n = 1). Consequently, 92 patients were included in the final analysis. Among them, one from each group underwent total gastrectomy instead of the scheduled distal gastrectomy. These participants were included in the mITT analysis; however, they were excluded from the PP analysis. Table 2 shows the baseline patient characteristics, and there were no significant differences in the characteristics between the two groups.

Figure 2 presents a comparison of QoR-15K scores between the two groups. In the linear mixed-effects model, the estimated difference in the postoperative QoR-15K total scores between the two groups was significantly larger than the MCID of QoR-15 (mean difference: 16.0, 95% CI: 8.9–23.0, $P < 0.001$). Post hoc analysis was not conducted because the group–time interaction was not significant ($P = 0.284$). This significant difference remained consistent in the PP analysis (mean difference: 16.4, 95% CI: 9.4–23.4, $P < 0.001$).

Table 3 presents a comparison of secondary outcomes between the two groups. Throughout all four measurement intervals, the ERAS group reported significantly lower pain scores at rest and during coughing than the conventional group. Additionally, the ERAS group demonstrated significantly reduced cumulative fentanyl consumption through IV-PCA across all three measurement periods. PONV occurrence rates

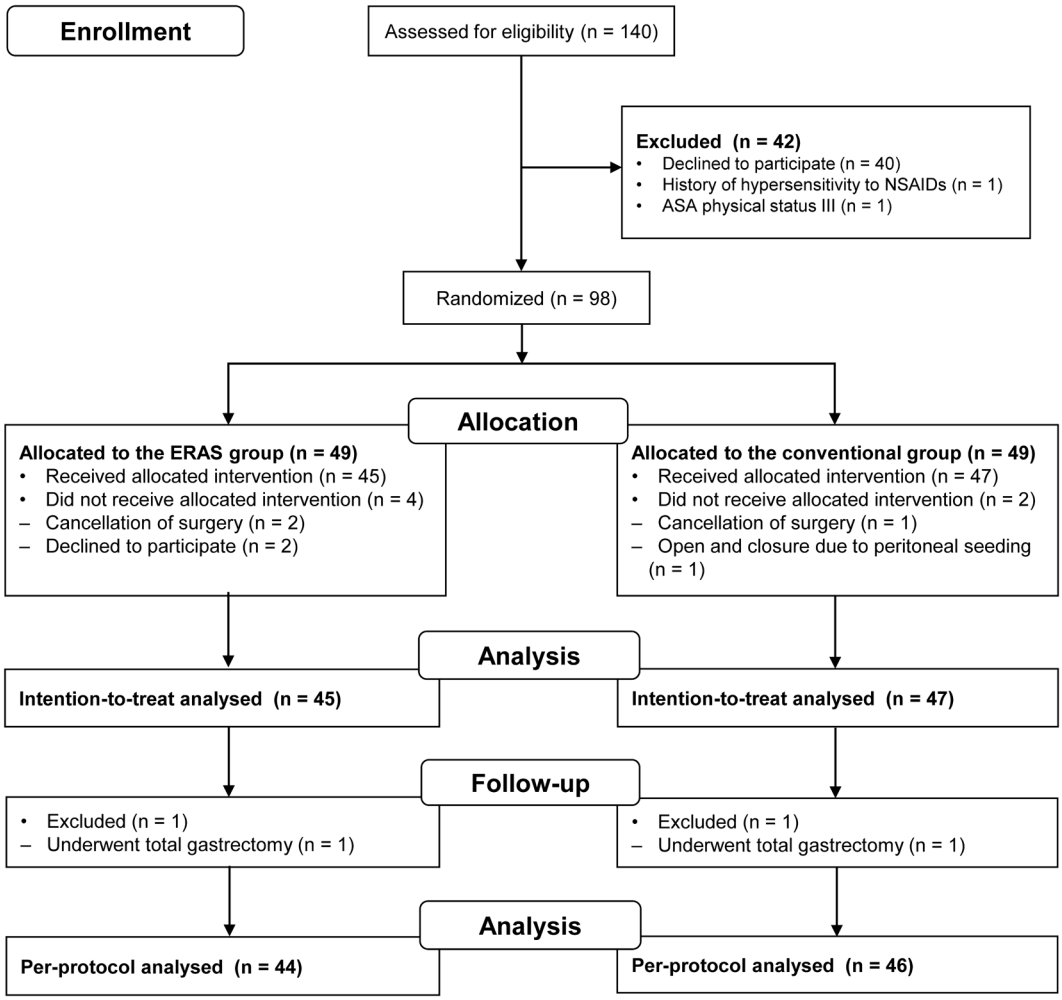

Figure 1. Flow chart of the study.

Table 2

Baseline characteristics

	ERAS group (n = 45)	Conventional group (n = 47)
Female patients	23 (51.1)	21 (44.7)
Age, years	60.2 ± 10.8	59.3 ± 10.2
Height, cm	163.7 [157.2–170.6]	161.2 [154.5–164.4]
Weight, kg	65.2 ± 11.9	63.8 ± 10.4
Body mass index, kg/m^2	24.2 ± 2.9	24.4 ± 3.2
ASA physical status, I/II	16 (35.6)/29 (64.4)	15 (31.9)/32 (68.1)
ECOG performance status, 0/1	45 (100)/0	47 (100)/0
Apfel score, 1/2/3/4	9 (20.0)/13 (28.9)/20 (44.4)/3 (6.7)	12 (25.5)/16 (34.0)/16 (34.0)/3 (6.4)
Smoking, none/ex-smoker/smoker	32 (71.1)/9 (20.0)/4 (8.9)	30 (63.8)/10 (21.3)/7 (14.9)
Preoperative QoR-15K (0–150)	150 [148–150]	150 [146.5–150]
HADS-A	0 [0–1]	0 [0–1]
HADS-D	0 [0–1]	0 [0–1]
Preoperative EORTC QLQ-C30 (0–100)	99.0 [94.8–100.0]	97.9 [95.8–99.0]
Preoperative endoscopic clipping	28 (62.2)	30 (63.8)
Surgeon, A/B/C/D	7 (15.6)/21 (46.7)/4 (8.9)/13 (28.9)	3 (6.4)/27 (57.4)/5 (10.6)/12 (25.5)
Type of approach, robotic/laparoscopic	17 (37.8)/28 (62.2)	17 (36.2)/30 (63.8)
Extent of resection		
Distal gastrectomy	34 (75.6)	37 (78.7)
Pylorus preserving gastrectomy	10 (22.2)	9 (19.1)
Total gastrectomy	1 (2.2)	1 (2.1)
Simultaneous cholecystectomy	2 (4.4)	1 (2.1)
Clinical TNM stage, I/IIa/IIb/III	41 (91.1)/1 (2.2)/2 (4.4)/1 (2.2)	38 (80.9)/2 (4.3)/4 (8.5)/3 (6.4)
Lymph node dissection, D1 +/D2	35 (77.8)/10 (22.2)	35 (74.5)/12 (25.5)
Operation time, min	180 [150–220]	175 [155–215]
Intraoperative remifentanil use, μg	1000 [820–1200]	1000 [700–1350]
Intraoperative crystalloid administration, mL	600 [600–950]	700 [500–900]
Estimated blood loss, mL	80 [50–150]	90 [50–115]

Values are presented as the mean ± standard deviation or median [interquartile range] or number (%).

ASA, American Society of Anesthesiologists; ECOG, Eastern Cooperative Oncology Group; QoR-15K, Korean version of Quality of Recovery-15; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; ERAS, enhanced recovery after surgery; HADS, Hospital Anxiety and Depression Scale.

did not differ significantly between the two groups, and the ERAS group exhibited consistently lower I-FEED scores at all three measurement points.

Supplemental Digital Content, Table S1 (available at: http://links.lww.com/IJSO/A21) presents a comparison of outcomes other than primary and secondary outcomes. The ERAS group showed better outcomes for the overall recovery time (mean difference: –24 h, 95% CI: –25 to –24 h, $P < 0.001$), cumulative fentanyl equivalent dose during the first 72 h after surgery (mean difference: –500 μg, 95% CI: –750 to –275 μg, $P < 0.001$), and time to passage of the first flatus (mean difference: –21.2 h, 95% CI: –29.6 to –13.9 h, $P < 0.001$). Additionally, the length of postoperative hospital stay was shorter in the ERAS group (mean difference: –1 day, 95% CI: –1 to –1 day, $P < 0.001$), with all patients discharged home. However, there were no significant differences in the other outcomes between the two groups.

Discussion

Our study revealed that the ERAS program significantly improved early recovery, as measured using the QoR-15K score, after minimally invasive gastric cancer surgery. The ERAS program also improved postoperative pain control, reduced postoperative opioid consumption, and enhanced the recovery of gastrointestinal function. Furthermore, it significantly decreased the length of hospital stay without any associated adverse outcomes.

Most studies on ERAS for gastric cancer surgery have relied on guidelines based on outdated evidence from the early 2000s,[6,13,18-20] necessitating a revised protocol informed by advancements in surgical techniques and perioperative care.

A critical distinction between our protocol and previous studies lies in our approach to pain management.[13,18-20] Notably, most previous studies have predominantly used thoracic epidural analgesia (TEA) as the primary analgesic method. However, with the advent of minimally invasive surgery as the standard approach for gastric cancer, there has been a shift toward less invasive analgesic techniques, as seen in updated ERAS guidelines for colorectal surgery[21,22]. Therefore, in response to this trend, we opted to use the subcostal transversus abdominis plane block instead of TEA in our ERAS protocol[23]. We also selected selective cyclooxygenase-2 inhibitors over non-selective NSAIDs to mitigate the risk of anastomotic leakage, a choice informed by our retrospective studies[24,25], and similar findings in gastrectomy[26]. Preemptive analgesia with oral non-opioid analgesics was also included, supported by robust evidence[27]. However, it was not part of earlier ERAS guidelines[6].

Our protocol differs from the ERAS guidelines in other key areas. The guidelines recommend initiating oral intake on POD 1; however, the supporting evidence is limited[28], particularly in East Asian countries[7,29]. Moreover, a prospective study indicated that early oral feeding from POD 1 did not shorten hospital stay and was associated with an increased risk of postoperative complications[29]. Therefore, we established our postoperative diet

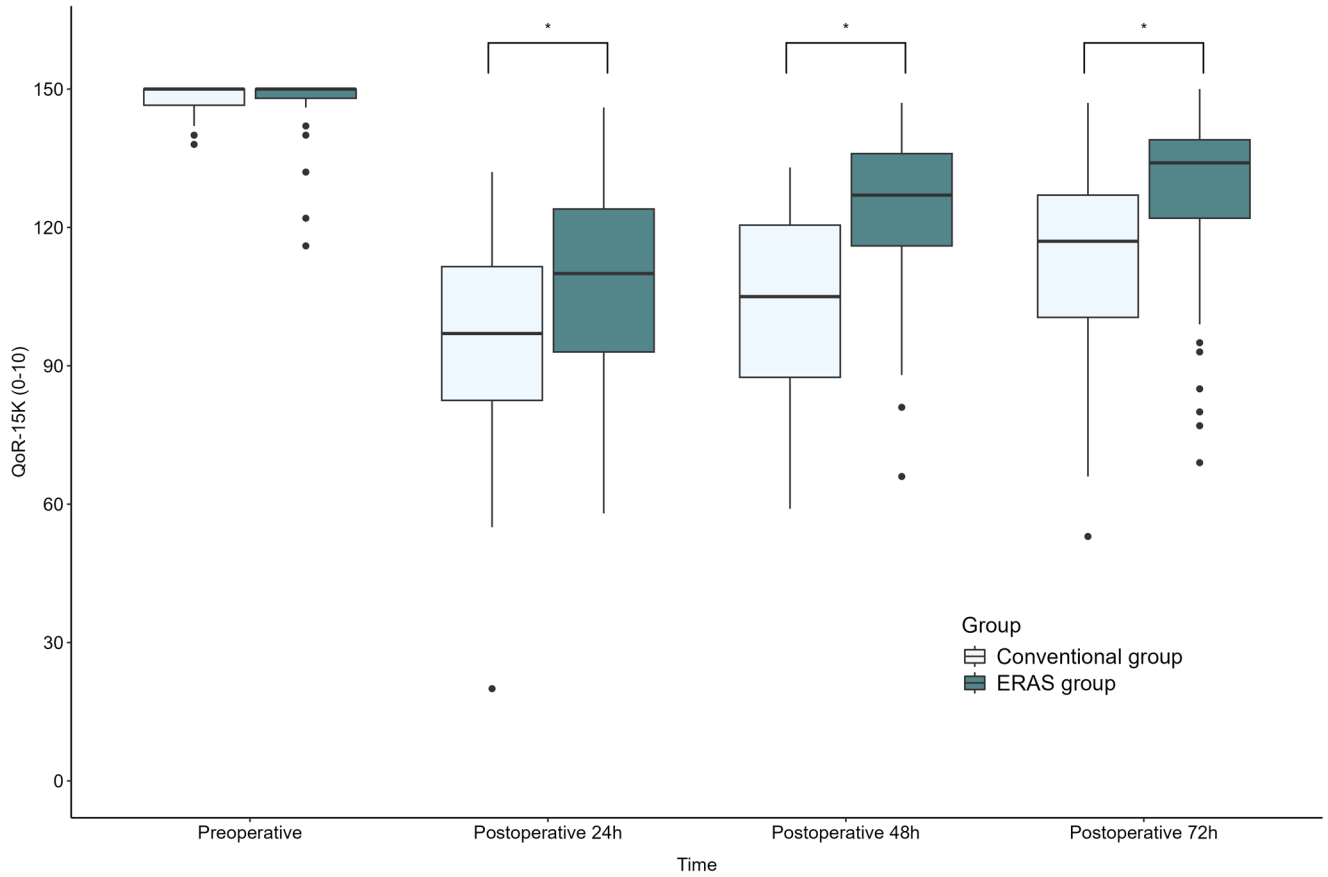

Figure 2. Comparison of QoR-15K scores between the ERAS and conventional groups. Data are shown as the median and interquartile range. QoR-15K, Korean version of Quality of Recovery-15; ERAS, enhanced recovery after surgery.

resumption timeline, which aligned with the most recent guidelines of the Japanese Gastric Cancer Association[30]. We also chose to continue the routine use of abdominal drains with removal on POD 3, until more definitive evidence is provided to support selective drainage[7,28,31].

A significant feature of our study was the focus on the quality of recovery as the primary outcome, assessed using QoR-15, a validated patient-reported outcome measure (PROM). Hospital stay length and complication rates have been emphasized in most previous studies; however, these metrics were less relevant in our context due to low complication rates at our institution and Korea's unique healthcare practices, including low patient costs and lenient attitudes toward long-term hospitalization. QoR-15, recommended by the American Society for Enhanced Recovery and the Perioperative Quality Initiative, enables comprehensive evaluation of recovery and has been shown to be a valid, reliable, and responsive metric in patients undergoing surgery[32,33]. A recent prospective, non-randomized study on ERAS for gastric cancer surgery similarly reported improved early postoperative recovery, as measured using QoR-40, until approximately POD 6, with no significant differences observed by POD 30[34], consistent with our findings. The emerging use of PROMs, such as QoR-15, may offer a more patient-centered approach to assessing ERAS effectiveness and gain increasing importance in future evaluations.

This study has some limitations. First, this single-center study has potential limitations in terms of generalizability. Perioperative practices and surgical experience can vary across institutions, potentially influencing outcomes[35]. However, our institution's high volume (over 700 annual gastric cancer surgeries) enhances the reliability of our findings, particularly in similar settings. Second, despite blinding the assessor, the open-label design may have influenced the survey responses of the participants, who were informed about the potential benefits of the ERAS program during the consent process. Third, our study population included patients in relatively good physical conditions, which may have limited the ability to observe significant intermediate-term effects of the ERAS program. Patients with poorer preoperative physical function may derive greater benefits from ERAS programs owing to their increased risk of postoperative complications. Moreover, previous studies have indicated lower compliance with ERAS protocols in this high-risk group, highlighting the challenges of implementation in such populations[36,37]. Finally, this study focused exclusively on patients undergoing laparoscopic or robotic surgery, most of whom were diagnosed with early-stage gastric cancer. While early-stage cases dominate in Korea due to the national cancer screening program[38], this may not reflect the situation in other countries. Further research is needed to validate our findings in a more diverse population, including high-risk patients and those with advanced gastric cancer, to enhance the broader applicability of our protocol.

Table 3

Comparison of secondary outcomes between the ERAS and conventional groups

	ERAS group (n = 45)	Conventional group (n = 47)	Median or risk difference (95% CI)	*P* value
Pain score, at rest (NRS, 0–10)				
2 h postoperatively	4 [3–5]	5 [3.5–7]	−1 (−2 to −1)	0.001
24 h postoperatively	2 [1–3]	3 [2–5]	−1 (−2 to −1)	<0.001
48 h postoperatively	1 [0–2]	3 [2–4]	−2 (−2 to −1)	<0.001
72 h postoperatively	1 [0–1.5]	2 [1–3]	−1 (−2 to −1)	<0.001
Pain score, during coughing (NRS, 0–10)				
2 h postoperatively	5 [3–6]	7 [5–8]	−2 (−3 to −1)	<0.001
24 h postoperatively	4 [3–5]	7 [5.5–8]	−2 (−3 to −2)	<0.001
48 h postoperatively	3 [2–4]	5 [4–7]	−3 (−3 to −2)	<0.001
72 h postoperatively	3 [2–3.5]	5 [3–6]	−2 (−3 to −2)	<0.001
Cumulative fentanyl consumption via IV-PCA, μg				
24 h postoperatively	440 [280–680]	700 [450–920]	−240 (−380 to −100)	<0.001
48 h postoperatively	700 [460–940]	1000 [710–1460]	−340 (−520 to −160)	<0.001
72 h postoperatively	780 [540–1080]	1260 [810–1770]	−460 (−680 to −240)	<0.001
Postoperative nausea and vomiting				
0–24 h postoperatively	11 (24.4)	15 (31.9)	−0.7 (−0.26 to 0.11)	0.424
24–48 h postoperatively	5 (11.1)	8 (17.0)	−0.06 (−0.20 to 0.08)	0.412
48–72 h postoperatively	2 (4.4)	6 (12.8)	−0.08 (−0.20 to 0.03)	0.148
I-FEED score				
24 h postoperatively	1 [1–1.5]	3 [3–4]	−2 (−2 to −2)	<0.001
48 h postoperatively	2 [1–2]	3 [3–3]	−1 (−2 to −1)	<0.001
72 h postoperatively	1 [1–1]	3 [2–3]	−1 (−2 to −1)	<0.001

Values are expressed as median [interquartile range] or number of patients (%).
IV-PCA, intravenous patient-controlled analgesia; NRS, Numeric Rating Scale; ERAS, enhanced recovery after surgery.

In conclusion, our study demonstrated that the ERAS program significantly enhanced the quality of early recovery after minimally invasive gastric cancer surgery. These improvements are likely attributable to the use of multimodal opioid-sparing analgesia and a shortened perioperative fasting period, both of which contribute to reduced postoperative pain and accelerated gastrointestinal recovery. However, further research, including studies on high-risk patients and multicenter trials, is necessary to extend the applicability of our protocol and confirm its benefits across broader patient populations.

Ethical approval

The study protocol was approved by the Seoul National University Hospital Institutional Review Board (IRB No. H-2207-206-1346).

Consent

All participants provided written informed consent before enrollment.

Sources of funding

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Author contributions

D.J.P. had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. H.J.L. and D.J.P.: concept and design; H.J.L., J.K.,. S.H.K., W.H.K., D.J.P., H.J.L., and H.K.Y.: acquisition, analysis, or interpretation of data; H.J.L. and D.J.P.: drafting of the manuscript; S.H.K., W.H.K., H.J.L., and H.K.Y.: critical revision of the manuscript for important intellectual content; H.J.L. and S.H.Y.: statistical analyses; H.J.L. and D.J.P.: administrative, technical, or material support; D.J.P.: supervision.

Conflicts of interest disclosure

None.

Research registration unique identifying number (UIN)

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Guarantor

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Provenance and peer review

Not commissioned, externally peer-reviewed.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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References

[1] Morgan E, Arnold M, Camargo MC, *et al*. The current and future incidence and mortality of gastric cancer in 185 countries, 2020–40: a population-based modelling study. EClinicalMedicine 2022;47:101404.
[2] Li GZ, Doherty GM, Wang J. Surgical management of gastric cancer: a review. JAMA Surg 2022;157:446–54.
[3] Karanicolas PJ, Graham D, Gönen M, *et al*. Quality of life after gastrectomy for adenocarcinoma: a prospective cohort study. Ann Surg 2013;257:1039–46.
[4] Ljungqvist O, Scott M, Fearon KC. Enhanced recovery after surgery. JAMA Surg 2017;152:292–98.
[5] How KY, Tan JJE, Roxas MFT. ERAS® Society and Asia. In: Ljungqvist O, Francis N, Urman R, eds. Enhanced Recovery after Surgery: A Complete Guide to Optimizing Outcomes. Springer International Publishing; 2020:617–22.
[6] Mortensen K, Nilsson M, Slim K, *et al*. Consensus guidelines for enhanced recovery after gastrectomy: Enhanced Recovery after Surgery (ERAS®) Society recommendations. Br J Surg 2014;101:1209–29.
[7] Jeong O, Kim HG. Implementation of enhanced recovery after surgery (ERAS) program in perioperative management of gastric cancer surgery: a nationwide survey in Korea. J Gastric Cancer 2019;19:72–82.
[8] Yoon SH, Lee HJ. Challenging issues of implementing enhanced recovery after surgery programs in South Korea. Anesth Pain Med (Seoul) 2024;19:24–34.
[9] Caruso S, Scatizzi M. Laparoscopic gastrectomy for gastric cancer: has the time come for considered it a standard procedure? Surg Oncol 2022;40:101699.
[10] Yoon S, Joo H, Oh YM, *et al*. Validation and clinical utility of the Korean version of the Quality of Recovery-15 with enhanced recovery after surgery: a prospective observational cohort study. Br J Anaesth 2020;125:614–21.
[11] Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. Int J Surg 2011;9:672–77.
[12] Hedrick TL, McEvoy MD, Mythen MG, *et al*. American Society for Enhanced Recovery and perioperative quality initiative joint consensus statement on postoperative gastrointestinal dysfunction within an enhanced recovery pathway for elective colorectal surgery. Anesth Analg 2018;126:1896–907.
[13] Kang SH, Lee Y, Min SH, *et al*. Multimodal Enhanced Recovery After Surgery (ERAS) Program is the optimal perioperative care in patients undergoing totally laparoscopic distal gastrectomy for gastric cancer: a prospective, randomized, clinical trial. Ann Surg Oncol 2018;25:3231–38.
[14] Power I, Noble DW, Douglas E, *et al*. Comparison of I.M. ketorolac trometamol and morphine sulphate for pain relief after cholecystectomy. Br J Anaesth 1990;65:448–55.
[15] Spindler JS, Mehlisch D, Brown CR. Intramuscular ketorolac and morphine in the treatment of moderate to severe pain after major surgery. Pharmacotherapy 1990;10:51S–58S.
[16] Myles PS, Myles DB, Galagher W, *et al*. Minimal clinically important difference for three quality of recovery scales. Anesthesiology 2016;125:39–45.
[17] Yoon HK, Joo S, Yoon S, *et al*. Randomized controlled trial of the effect of general anesthetics on postoperative recovery after minimally invasive nephrectomy. Korean J Anesthesiol 2024;77:95–105.
[18] Roh CK, Son SY, Lee SY, *et al*. Clinical pathway for enhanced recovery after surgery for gastric cancer: a prospective single-center phase II clinical trial for safety and efficacy. J Surg Oncol 2020;121:662–69.
[19] Jung MR, Ryu SY, Park YK, *et al*. Compliance with an enhanced recovery after a surgery program for patients undergoing gastrectomy for gastric carcinoma: a phase 2 study. Ann Surg Oncol 2018;25:2366–73.
[20] Tian Y, Cao S, Liu X, *et al*. Randomized controlled trial comparing the short-term outcomes of enhanced recovery after surgery and conventional care in laparoscopic distal gastrectomy (GISSG1901). Ann Surg 2022;275:e15–e21.
[21] Carmichael JC, Keller DS, Baldini G, *et al*. Clinical practice guidelines for enhanced recovery after colon and rectal surgery from the American Society of Colon and Rectal Surgeons and Society of American Gastrointestinal and Endoscopic Surgeons. Dis Colon Rectum 2017;60:761–84.
[22] Gustafsson UO, Scott MJ, Hubner M, *et al*. Guidelines for perioperative care in elective colorectal surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations: 2018. World J Surg 2019;43:659–95.
[23] Yoon S, Song GY, Lee J, *et al*. Ultrasound-guided bilateral subcostal transversus abdominis plane block in gastric cancer patients undergoing laparoscopic gastrectomy: a randomised-controlled double-blinded study. Surg Endosc 2022;36:1044–52.
[24] Yoon S, Kim H, Cho HY, *et al*. Effect of postoperative non-steroidal anti-inflammatory drugs on anastomotic leakage after pancreaticoduodenectomy. Korean J Anesthesiol 2022;75:61–70.
[25] Ju JW, Lee HJ, Kim MJ, *et al*. Postoperative NSAIDs use and the risk of anastomotic leakage after restorative resection for colorectal cancer. Asian J Surg 2023;46:4749–54.
[26] Kim SJ, Jeon CH, Lee HH, *et al*. Impact of postoperative NSAIDs (IV-PCA) use on short-term outcomes after laparoscopic gastrectomy for the patients of gastric cancer. Surg Endosc 2023;37:1123–31.
[27] Xuan C, Yan W, Wang D, *et al*. Efficacy of preemptive analgesia treatments for the management of postoperative pain: a network meta-analysis. Br J Anaesth 2022;129:946–58.
[28] Yamagata Y, Yoshikawa T, Yura M, *et al*. Current status of the "enhanced recovery after surgery" program in gastric cancer surgery. Ann Gastroenterol Surg 2019;3:231–38.
[29] Shimizu N, Oki E, Tanizawa Y, *et al*. Effect of early oral feeding on length of hospital stay following gastrectomy for gastric cancer: a Japanese multicenter, randomized controlled trial. Surg Today 2018;48:865–74.
[30] Japanese Gastric Cancer Association. Japanese Gastric Cancer Treatment Guidelines 2021 (6th edition). Gastric Cancer 2023;26:1–25.
[31] Weindelmayer J, Mengardo V, Ascari F, *et al*. Prophylactic drain placement and postoperative invasive procedures after gastrectomy: the Abdominal Drain After Gastrectomy (ADIGE) randomized clinical trial. JAMA Surg 2025;160:135–43.
[32] Abola RE, Bennett-Guerrero E, Kent ML, *et al*. American Society for Enhanced Recovery and Perioperative Quality Initiative Joint Consensus Statement on patient-reported outcomes in an enhanced recovery pathway. Anesth Analg 2018;126:1874–82.
[33] Myles PS, Shulman MA, Reilly J, *et al*. Measurement of quality of recovery after surgery using the 15-item quality of recovery scale: a systematic review and meta-analysis. Br J Anaesth 2022;128:1029–39.
[34] Chen Y, Liu S, Li B, *et al*. Application of the Quality of Recovery-40 questionnaire to evaluate the effectiveness of enhanced recovery after surgery protocols in gastric cancer. Updates Surg 2024;76:1365–75.
[35] Marano L, Verre L, Carbone L, *et al*. Current trends in volume and surgical outcomes in gastric cancer. J Clin Med 2023;12:2708.
[36] Park SH, Kang SH, Lee SJ, *et al*. Actual compliance rate of enhanced recovery after surgery protocol in laparoscopic distal gastrectomy. J Minim Invasive Surg 2021;24:184–90.
[37] Braga M, Pecorelli N, Scatizzi M, *et al*. Enhanced recovery program in high-risk patients undergoing colorectal surgery: results from the PeriOperative Italian Society Registry. World J Surg 2017;41:860–67.
[38] Information Committee of the Korean Gastric Cancer Association. Korean Gastric Cancer Association-led nationwide survey on surgically treated gastric cancers in 2019. J Gastric Cancer 2021;21:221–35.