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SURGERY

# Effect of Enhanced Recovery After Surgery on Laparoscopic Appendectomy Outcomes in Patients with Complicated Appendicitis: a Randomized Controlled Trial

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## Abstract

**Background** The implementation of enhanced recovery after surgery (ERAS) pathway has resulted in shorter length of stay (LOS), fewer complications, and lowering of medical costs. We aimed to investigate if ERAS protocol implementation in patients with complicated appendicitis reduces the LOS after laparoscopic appendectomy.

**Methods** In this randomized controlled trial, 38 patients were randomly assigned to laparoscopic appendectomy with ERAS protocol (LE) or with conventional care (LC). The primary outcome was the hospital LOS. The secondary outcomes included time to resume diet, postoperative complications, readmissions, and reoperation rates.

**Results** From April 2019 to December 2019, 19 patients in the LE group and 19 in the LC were included. There were no significant differences in preoperative data. Regarding the primary outcome of the study, the ERAS protocol did not significantly reduce the postoperative LOS in comparison with conventional care (63.8 ± 62.10 h vs. 95.3 ± 135.78 h, $p$=0.366). There was a significant reduction in time to resume diet (367.3 vs. 696.3 min, $p$=0.003). We did not find differences in terms of postoperative complications, pain control, readmission, and reoperation rates.

**Conclusions** Laparoscopic appendectomy with ERAS protocol was not superior to laparoscopic appendectomy with conventional care for the treatment of complicated appendicitis in terms of hospital LOS. However, postoperative morbidity, readmission, and reoperation rates were similar in both groups, making ERAS implementation a safe and feasible alternative to conventional care.

**Keywords** Acute appendicitis · Complicated appendicitis · Enhanced recovery after surgery · Laparoscopic appendectomy

## Introduction

Acute appendicitis is a common gastrointestinal disease affecting 5.7–57/per 100,000 individuals each year, with a cumulative life time incidence of 9% [1, 2]. With the evolution of minimally invasive techniques, up to 67% of cases of complicated appendicitis are performed laparoscopically, as reported recently in the USA [2]. However, while mortality is rare in acute appendicitis, complications and morbidity may arise after surgery and contribute not only to a prolonged length of stay (LOS) but also to an increased rate of readmissions and costs [3].

Following of enhanced recovery after surgery (ERAS) guidelines has resulted in a shorter LOS, fewer complications, fewer readmissions, and reduction in total medical cost, mostly in elective surgeries [4, 5]. Perioperative care in the acute care setting, for example, in patients with acute appendicitis still continues to use conventional principles of care. The implementation of ERAS protocols in an emergency setting remains challenging, just as recently stated in some gastrointestinal emergencies [4, 6, 7]. A recent meta-analysis suggested that ERAS protocols are associated with good outcomes in the acute care setting as demonstrated by reduced postoperative morbidity, accelerated recovery of bowel function, and shorter LOS without increasing need for readmission or reoperation [5].

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Observational studies have demonstrated the safety of discharging adults and children after laparoscopic appendectomy (LA) within the same day without hospitalization, with some studies applying some elements of ERAS or fast-track pathways to LA [7–14]. Also, a recent randomized controlled trial (that employed ERAS pathway) [7] and a meta-analysis [14] supported same-day discharge after laparoscopic appendectomy in patients with uncomplicated appendicitis.

For complicated acute appendicitis, the current evidence is very scarce [15, 16]. In a retrospective study, a fast-track pathway implementation for perforated appendicitis produced shorter LOS and comparable postoperative morbidity and readmissions [16]. However, there is no prospective randomized controlled trial evaluating ERAS in complicated acute appendicitis that has been reported yet. The aim of this trial was to investigate if ERAS protocol implementation in patients with complicated appendicitis decreases the LOS after laparoscopic appendectomy, in comparison with conventional care, without increasing postoperative morbidity.

## Subjects and Methods

### Study Design

We conducted a prospective, single-center, randomized, open-label, superiority trial. The study was performed at the Hospital General Dr. Manuel Gea González from April 1, 2019, to December 31, 2019. This study was approved by the institutional research and ethical review board of our hospital (Registration Number: 04-18-2019). The study was conducted according to the CONSORT statement and in accordance with the Declaration of Helsinki. The study was designed to compare ERAS and conventional care for complicated appendicitis.

### Eligibility Criteria for Participants

Patients were assessed for eligibility in the surgical acute care department. Inclusion criteria were patients of both sexes, aged 18–70 years, with an American Society of Anesthesiologist (ASA) grade of I or II, Charlson Comorbidity Index [17] of less than 1, and those who accepted and signed the informed consent form. Patients with signs of localized and generalized peritonitis and suspected complicated appendicitis were eligible for inclusion. The diagnosis of appendicitis was based on clinical, laboratory, and imaging criteria. Radiological examination by ultrasound or CT scan had to show free intraperitoneal air, free fluid, or an abscess or phlegmon in right iliac fossa. Complicated appendicitis was defined as macroscopic necrosis or perforation of the appendix with local or generalized peritonitis, as found during diagnostic laparoscopy [18, 19]. Exclusion criteria were patients taking oral anticoagulants, pregnancy, patients with findings of uncomplicated acute appendicitis in diagnostic laparoscopy (patients with non-gangrenous, non-perforated appendix, and without generalized peritonitis), patients with other concomitant pathology that required additional surgical procedures, and patients who required conversion to laparotomy.

### Randomization and Masking

Patients who fulfilled the inclusion criteria were randomly assigned (1:1) to undergo either laparoscopic appendectomy with ERAS protocol (LE) or laparoscopic appendectomy with conventional care (LC). Randomization into LE and LC was performed by computer-generated numbers using EpiData software version 2.0 (Odense, Denmark). As the trial was open label, treatment allocation was unmasked to patients, surgeons, and researchers at any timepoint.

### Intervention

The intervention consisted in implementing a modified ERAS protocol to patients with complicated appendicitis who underwent laparoscopic appendectomy. The protocol for ERAS implementation in laparoscopic appendectomy was previously described in patients with acute non-complicated appendicitis by our group [7]. We adapted that protocol to patients with complicated appendicitis (see Table 1).

### Surgical Technique in Both Groups

After informed consent was obtained, diagnostic laparoscopy was done to confirm the diagnosis of complicated appendicitis. Laparoscopic appendectomy was performed with the same surgical technique in both groups. A three port technique was employed with two 12-mm ports and one 5-mm port. The appendix and the appendicular artery were ligated with non-absorbable monofilament suture. Advanced energy device was used at discretion of the surgeon. The appendix was always retrieved within a bag. Fluid and purulent collections or abscesses were drained and aspirated, without peritoneal lavage. All procedures were performed by an attending surgeon or by a surgical resident with direct supervision of an attending surgeon.

### Outcomes

The primary outcome of the trial was the total LOS. The secondary outcomes were time to resume diet, severity of postoperative pain, postoperative LOS, 30-day postoperative complications, 30-day readmission, and 30-day reoperation rate.

**Table 1** ERAS protocol and conventional care protocol [5, 7]

| Characteristic | ERAS protocol | Conventional care |
|---|---|---|
| Preoperative care | Patients and their caregivers were informed about the protocol<br>Preop crystalloid isotonic solution (calculated according their requirements)<br>Antibiotics (ceftriaxone 1 gr IV and metronidazole 500 mg IV)<br>Standard gastric prophylaxis (omeprazole 40 mg IV)<br>Multimodal opioid-sparing analgesia (e.g., ketorolac 30 mg IV with acetaminophen 1 g IV)<br>Micturate before entering the operating room<br>Avoid bladder catheter | Standard care with IV fluids (liberal protocol)<br>Antibiotics (ceftriaxone 1 g IV q12 h and metronidazole 500 mg IV q8 h)<br>Opioid analgesics if needed (tramadol 50 mg IV)<br>Bladder catheter if needed. Antiemetics only if patients presented nausea or vomiting |
| Intraoperative care | Balanced general anesthesia<br>Strict control of fluid therapy<br>Prevention of hypothermia, analgesia, and hemodynamic changes was implemented to reduce the metabolic stress response<br>Multimodal pain control<br>Infiltration of all port sites before incision with 0.5% bupivacaine<br>Anti-emesis prophylaxis was achieved with dexamethasone (4 mg IV) and ondansetron (8 mg IV)<br>No nasogastric tubes or drains were inserted | No infiltration of the port sites was performed<br>Nasogastric tubes if needed (vomiting)<br>Drains at discretion of attending surgeon |
| Postoperative care | Admitted to the recovery room<br>Recordings of their vital signs and pain using the Visual Analogue Scale (VAS) every hour were obtained<br>Pain scores with VAS were classified as mild, moderate, or severe (0–2, 3–7, and 8–10, respectively)<br>Opioid-sparing multimodal analgesia was administered (ketorolac 30 mg IV with acetaminophen 1 g IV)<br>Multimodal antiemetic regimen (ondansetron 4 mg PO, or dexamethasone, metoclopramide)<br>Antibiotics were continued for 3 doses. Early mobilization was promoted (within 2–3 h of surgery)<br>Oral feeding with clear liquids was resumed when the patients were fully awakened | Admitted to the recovery room. Vitals and pain were recorded. Pain was controlled with opioid analgesia if it was severe (VAS=8–10)<br>Patients started oral feeding once bowel function was completely restored, defined by the presence of normal peristalsis, passage of flatus or depositions |
| Discharge criteria | Patients were discharged once they had fulfilled the following criteria:<br>Ability to take oral feeding without waiting to flatus or bowel movement, full consciousness recovered, able to ambulate alone, pain adequately controlled with oral analgesics (VAS < 2), hemodynamic stability, capable of micturition, and absence of nausea and vomiting. The decision to discharge was made by an attending surgeon<br>Patients received the following instructions for home: avoid heavy weight lifting and care for the wound daily<br>Prescriptions at home: acetaminophen 500 mg PO TID. Tramadol PRN. Oral antibiotics as recommended by infectologists | Patients were discharged home once a full normal diet was tolerated, ambulation was achieved, and pain was adequately controlled with oral analgesics (VAS < 2). Prescriptions at home: acetaminophen 500 mg PO TID. Tramadol 50 mg PO TID. Oral antibiotics as recommended by infectologists |

## Data Collection

We registered demographic and preoperative data. Variables analyzed in the study were age, sex, body mass index in kg/m$^2$ (BMI), ASA score, total leukocyte count, presenting to the emergency department with intestinal obstruction/ileus, C-reactive protein level (mg/dL), and operative time (min). Data concerning primary and secondary endpoints were collected. Hospital length of stay was reported in hours (h).

## Follow-Up

All patients were followed-up with subsequent clinical appointments at 7 and 30 days after discharge to the hospital. Postoperative complications, readmissions, and reoperations were registered if they presented during the 30-day follow-up period after discharge.

## Statistical Analysis

We based the sample size calculation on the total LOS of patients undergoing laparoscopic appendectomy for complicated appendicitis. Data available from a previous study reported a mean LOS for patients with complicated appendicitis of 4.4 days (SD= 3.2 days) [20]. To reduce the mean LOS from 4.4 days to 1.3 days, with an alpha error= 0.05 and 1-beta error= 0.80, the independent *t* test required a sample size of 17 patients per group (LE and LC groups) for this study.

The data were reported as mean values with variability expressed as standard deviation (SD), as well as total number

of patients (*n*) and percentages (%). The Pearson Chi-square test or Fisher's exact test was used for categorical variables, and Student's *t* test or Mann-Whitney *U* two-sample tests were used for continuous variables depending on the distribution. A two-sided *p* value < 0.05 was considered statistically significant. SPSS version 18.0 (SPSS Inc. Chicago, IL, USA) was used to analyze the data.

## Results

### Patients

From April 2019 to December 2019, a total of 62 patients with complicated appendicitis were assessed for eligibility. The main reason for exclusion from the study was the presence of non-complicated appendicitis during diagnostic laparoscopy. A total of 38 patients were randomly assigned to undergo laparoscopic appendectomy with ERAS protocol (*n*=19) or with conventional care (*n*= 19). There was no loss to follow-up during the study period. The study CONSORT flow chart diagram of patients included in this trial is shown in Fig. 1.

The baseline demographic and preoperative characteristics of patients included in this trial are shown in Table 2. The baseline characteristics (sex, age, BMI, ASA score) between the two treatment groups did not differ significantly. The total leukocyte count, C-reactive protein value, and the presence of ileus at admission were also similar in both groups.

### Primary Outcome

Regarding the primary outcome of the trial, the mean total LOS was 63.8 h (mean= 2.66 days; SD: 62.10 h) in the ERAS protocol group, which was similar to the control group receiving conventional care (mean of 95.4 h [mean= 3.97 days], SD: 135.78 h; *p*=0.366) (Table 3).

### Secondary Outcomes

Regarding the secondary outcomes of the study, patients in the ERAS group resumed diet faster than patients in the conventional group (367.3 vs. 696.3 min, *p*= 0.004).

Patients in both groups experimented moderate-to-severe pain at 12 h with the same frequency (LE 63.2 vs. LC 84.2%, *p*=0.140). The postoperative LOS was also similar between both groups (LE 54.6 versus LC 83.5 h, *p*=0.415).

There were no statistically significant differences between the two groups on the rate of postoperative complications, readmissions, or reoperations (Table 3). No complications were directly attributed to the intervention (ERAS protocol implementation).

## Discussion

We found in this randomized controlled trial that in patients with complicated appendicitis, a modified ERAS protocol implementation was not associated with a decrease in the total LOS in comparison with conventional care after laparoscopic appendectomy. Nevertheless, resume of diet was faster in the ERAS group, and postoperative morbidity, pain control, readmission, and reoperation rates were similar between both groups, making ERAS implementation a safe and feasible alternative to conventional care.

Surgical removal of the appendix is still considered to be the standard treatment of acute appendicitis, being laparoscopic surgery the preferred approach. The reported benefits of LA in meta-analyses are reduced frequency of surgical site infections, shorter LOS, less postoperative pain, earlier return to work, faster resume of diet, improved aesthetics and body satisfaction, and fewer incisional hernias [1, 21]. LA also appears to have significant benefits in complicated appendicitis with improved morbidity in comparison to open appendectomy [2]. Besides the advancement of minimally invasive surgical techniques, not many evidence-based interventions that aimed to improve recovery after appendectomy had been reported. And as reported by Hamill et al. [22], the results are still inconclusive, and high-quality trials are needed.

In the case of elective and recently emergency surgery, further benefits have been described when laparoscopic surgery is performed within an ERAS protocol. The ERAS concept, conceptualized in 1997 by Kehlet, is a multimodal, evidence-based, multidisciplinary approach to the care of the surgical patient [23]. The elements of the ERAS protocol are based on the diminution of surgical stress by lowering the neurohormonal response to the surgery and retaining anabolic homeostasis, resulting in less organ dysfunction and fewer complication rates [24, 25]. A recently published meta-analysis by Hajibandeh et al. [5] evaluated ERAS protocols in emergency abdominal surgery. They included patients with intestinal resection, segmental or total colectomy, operations for perforated viscus, adhesiolysis, or laparotomy. They concluded that ERAS protocols in emergency abdominal settings are associated with favorable outcomes.

We previously reported the implementation of the ERAS protocol to patients with uncomplicated acute appendicitis, and we found that ERAS was associated with significantly shorter LOS, less time to resume diet, less moderate-severe postoperative pain, and all the previous benefits without increasing the rate of complications, readmissions, or reoperations [7]. In a study published by Gignoux et al. [26], they compared outcomes of complicated and uncomplicated appendectomies performed in ambulatory and conventional settings, with ambulatory procedures performed within an ERAS protocol. They found a shorter LOS and lower incidence of complications in the ERAS group. However, we

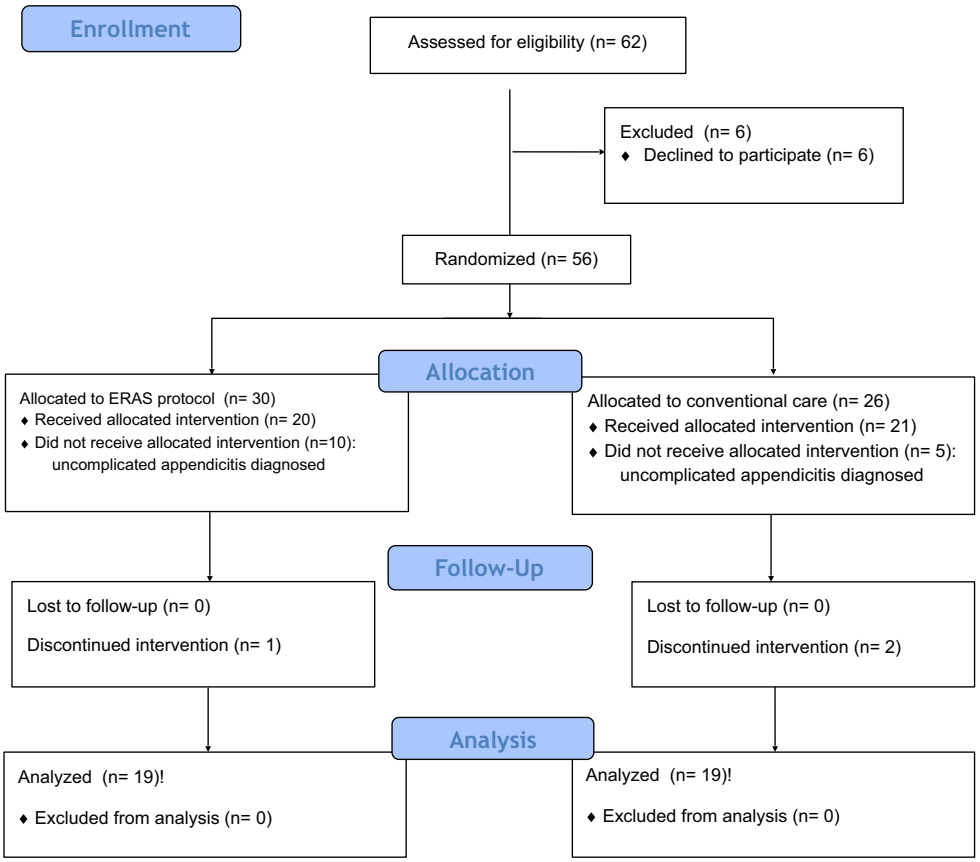


**Fig. 1** Participant CONSORT flow diagram for the study

could not replicate these previous results in patients with complicated appendicitis included in this randomized controlled trial.

The most striking result in this trial was the similar LOS between both groups, regardless of the shorter time to resume diet in patients within the ERAS protocol. We should consider that several meta-analysis have confirmed that the LOS is already shorten and reduced with LA when compared with open appendectomy [27–29]. Another relevant result was the similar rates of postoperative moderate-to-severe pain between both groups despite the multimodal pain management in the ERAS group, although our study was not powered to detect differences in pain control. We believed that the similar rates of LOS, postoperative complications, pain control,

**Table 2** Patients' baseline characteristics

| Characteristic | All patients (*n*=38) | LE (*n*= 19) | LC (*n*= 19) | *P* value (<0.05) |
|---|---|---|---|---|
| Sex, no. (%) | | | | |
| Female | 14 (36.84) | 6 (31.57) | 8 (42.10) | 0.736 |
| Male | 24 (63.15) | 13 (68.42) | 11(57.89) | |
| Age, yr. mean (SD) | 39.4 ± 14 | 36.5 ± 12.72 | 42.4 ± 14.93 | 0.202 |
| Body mass index. Mean (SD) | 26.9 ± 3.45 | 27.4 ± 4.12 | 26.4 ± 2.63 | 0.383 |
| ASA score, no. (%) | | | | |
| I | 0 | 0 | 0 | - |
| II | 38 (100) | 19 (100) | 19 (100) | |
| Total leukocyte count, $\times 10^9$/L. Mean (SD) | 14.8 ± 5.39 | 16.7 ± 5.28 | 12.9 ± 4.97 | 0.292 |
| C-reactive protein (mg/dL). Mean (SD) | 21.1 ± 8.11 | 19.9 + 8.19 | 22.0 ± 8.15 | 0.650 |
| Intestinal obstruction/ileus, no. (%) | 3 (7.9) | 2 (10.5) | 1 (5.3) | 0.547 |

*LE* laparoscopic appendectomy with ERAS, *LC* laparoscopic appendectomy with conventional care, *SD* standard deviation, *ASA* American Society of Anesthesiologist

**Table 3** Postoperative outcomes for patients undergoing LE vs. LC for uncomplicated acute appendicitis

| Variable | All patients ($n$= 38) | LE ($n$= 19) | LC ($n$= 19) | $P$ value (<0.05) |
|---|---|---|---|---|
| Operative time (min.), mean (SD) | 107.5 ± 68.94 | 97.4 ± 28.85 | 117.6 ± 93.39 | 0.377 |
| Postoperative pain (VAS), no. (%) | | | | 0.140 |
| 12 h—mild | 10 (26.3) | 7 (36.8) | 3 (15.8) | |
| 12 h—moderate–severe | 28 (73.7) | 12 (63.2) | 16 (84.2) | |
| Time to resume diet (min), mean (SD) | 531.8 ± 358.91 | 367.4 ± 230.28 | 696.3 ± 393.26 | 0.004 |
| Total length of stay (h), mean (SD) | 79.6 ± 105.36 | 63.8 ± 62.10 (2.66 days) | 95.36 ± 135.78 (3.97 days) | 0.366 |
| Postoperative length of stay (h), mean (SD) | 69.1 ± 107.30 | 54.6 ± 64.26 | 83.6 ± 138.19 | 0.415 |
| 30-day complications, no. (%) | | | | |
| Ileus | 3 (7.9) | 2 (10.5) | 1 (5.3) | 0.547 |
| Stump leak | 1 (2.6) | 0 | 1 (5.3) | 1.000 |
| Intestinal perforation | 1 (2.6) | 0 | 1 (5.3) | 1.000 |
| Deep abscess | 3 (7.9) | 3 (15.8) | 0 | 0.229 |
| Overall | 8 (21.1) | 5 (26.3) | 3 (15.8) | 0.692 |
| Reoperation, no. (%) | 4 (10.5) | 3 (15.8) | 1 (5.3) | 0.603 |
| Readmission, no. (%) | 4 (10.5) | 2 (10.5) | 2 (10.5) | 1.000 |

*LE* laparoscopic appendectomy with ERAS, *LC* laparoscopic appendectomy with conventional care, *SD* standard deviation, *VAS* Visual Analogue Scale for pain

reoperations, and readmissions found in this trial should be attributed to the fact that both groups were operated with laparoscopic surgery. Finding small differences (or exploring different primary endpoints, like readmission rate, morbidity, or pain control) among patients with ERAS protocol versus conventional care, in the context of both groups undergoing laparoscopic surgery, would need a very large sample size.

One potential advantage of implementing a modified ERAS protocol to patients with complicated acute appendicitis is the fact that enhanced recovery programs are associated with important cost savings when compared to conventional perioperative management [30, 31]. Bernard et al. [31] found that fast-track outpatient laparoscopic appendectomy saves approximately $1000 USD per patient.

As we stated in our previous publication [7], and the same issue was found by Hajibandeh et al. [5] in a meta-analysis, some of the elements of the ERAS protocol (such as nutritional support, carbohydrate loading, preoperative optimization, cease smoking, and alcohol use) are very difficult, if not impossible, to implement in the acute care setting. However, the majority of the components of ERAS protocol can be applicable in the emergency setting, as demonstrated by this trial and previous studies [5, 7]. In fact, the recently published Jerusalem guidelines of the World Society of Emergency Surgery recommended the adoption of outpatient laparoscopic appendectomy, for uncomplicated appendicitis, with a well-defined ERAS protocol [32].

Despite that this is a randomized controlled trial, a major limitation of our study was the lack of masking, with the subsequent risk of performance bias. This limitation has been reported in several published trials comparing ERAS protocol implementation vs. conventional care and also in our previous publication about ERAS in uncomplicated appendicitis [7, 33–36]. A further limitation was the fact that we did not measure compliance to ERAS pathway; however, a checklist was employed, and the researchers supervised the fulfillment of the entire protocol. Despite these limitations, this is the first trial of adult patients with complicated appendicitis that underwent laparoscopic appendectomy within the ERAS protocol. Additional larger and maybe multi-centric trials including more patients could be done, in order to corroborate or refute our findings or add further evidence to improve the management of this common surgical disease.

## Conclusions

In this randomized controlled trial, laparoscopic appendectomy with ERAS protocol was not superior to laparoscopic appendectomy with conventional care for the treatment of complicated appendicitis in terms of hospital length of stay. However, postoperative morbidity, readmission, and reoperation rates were similar between both groups, making ERAS implementation a safe and feasible alternative to conventional care.

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**Author Contribution** ANV, MTA, and ECL were involved in study conception and design. ANV did data acquisition. ECL and MTA performed statistical analyses, drafted the manuscript, contributed to study concept, critically revised the manuscript, performed overall supervision, and

contributed to the final approval of the manuscript. CVS, JHE, and MMP interpreted the data, drafted the manuscript, critically revised the manuscript, and contributed to the final approval of the manuscript.

## Declarations

**Ethics Approval and Consent to Participate** All procedures were performed in accordance with the ethical standards of the institutional research committee. The present study was approved by the institutional research and ethical board of our hospital (Registration Number: 04-18-2019).

**Informed Consent** Informed consent for participation was obtained from all patients included in the study.

**Conflict of Interest** The authors declare no competing interests.

## References


1. Gorter RR, Eker HH, Gorter-Stam MA, Abis GS, Acharya A, Ankersmit M, et al. Diagnosis and management of acute appendicitis. EAES consensus development conference 2015. Surg Endosc. 2016;30:4668–90.
2. Athanasiou C, Lockwood S, Markides GA. Systematic review and meta-analysis of laparoscopic versus open appendicectomy in adults with complicated appendicitis: an update of the literature. World J Surg. 2017;41:3083–99.
3. Bailey K, Choynowski M, Kabir SMU, Lawler J, Badrin A, Sugrue M. Meta-analysis of unplanned readmission to hospital post-appendectomy: an opportunity for a new benchmark. ANZ J Surg. 2019;89:1386–91.
4. Gustafsson UO, Scott MJ, Schwenk W, Demartines N, Roulin D, Francis N, et al. Guidelines for perioperative care in elective colonic surgery: enhanced recovery after surgery (ERAS) society recommendations. World J Surg. 2013;37:259–84.
5. Hajibandeh S, Hajibandeh S, Bill V, Satyadas T. Meta-analysis of enhanced recovery after surgery (ERAS) protocols in emergency abdominal surgery. World J Surg. 2020;44:1336–48.
6. Cash CL, Frazee RC, Abernathy SW, Childs EW, Davis ML, Hendricks JC, et al. A prospective treatment protocol for outpatient laparoscopic appendectomy for acute appendicitis. J Am Coll Surg. 2012;215:101–5.
7. Trejo-Avila ME, Romero-Loera S, Cárdenas-Lailson E, Blas-Franco M, Delano-Alonso R, Valenzuela-Salazar C, et al. Enhanced recovery after surgery protocol allows ambulatory laparoscopic appendectomy in uncomplicated acute appendicitis: a prospective, randomized trial. Surg Endosc. 2019;33:429–36.
8. Scott A, Shekherdimian S, Rouch JD, Sacks GD, Dawes AJ, Lui WY, et al. Same-day discharge in laparoscopic acute non-perforated appendectomy. J Am Coll Surg. 2017;224:43–8.
9. Cross W, Chandru Kowdley G. Laparoscopic appendectomy for acute appendicitis: a safe same-day surgery procedure? Am Surg. 2013;79:802–5.
10. Akkoyun I. Outpatient laparoscopic appendectomy in children: a single center experience with 92 cases. Surg Laparosc Endosc Percutan Tech. 2013;23:49–50.
11. Alkhoury F, Burnweit C, Malvezzi L, Knight C, Diana J, Pasaron R, et al. A prospective study of safety and satisfaction with same-day discharge after laparoscopic appendectomy for acute appendicitis. J Pediatr Surg. 2012;47:313–6.
12. Jain A, Mercado PD, Grafton KP, Dorazio RA. Outpatient laparoscopic appendectomy. Surg Endosc. 1995;9:424–5.
13. Grewal H, Sweat J, Vazquez D. Laparoscopic appendectomy in children can be done as a fast-track or same-day surgery. JSLS. 2004;8:151–4.
14. Trejo-Avila M, Cárdenas-Lailson E, Valenzuela-Salazar C, Herrera-Esquivel J, Moreno-Portillo M. Ambulatory versus conventional laparoscopic appendectomy: a systematic review and meta-analysis. Int J Color Dis. 2019;34:1359–68.
15. Lasso-Betancor CE, Ruiz-Hierro C, Vargas-Cruz V, Orti-Rodriguez RJ, Vazquez-Rueda F, Paredes-Esteban RM. Implementation of "fast-track" treatment in paediatric complicated appendicitis. Cir Pediatr. 2013;26:63–8.
16. Frazee R, Abernathy S, Davis M, Isbell T, Regner J, Smith R. Fast track pathway for perforated appendicitis. Am J Surg. 2017;213:739–41.
17. Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. J Clin Epidemiol. 1994;47:1245–51.
18. Bolmers MDM, de Jonge J, van Rossem CC, van Geloven AAW, Bemelman WA, Snapshot Appendicitis Collaborative Study group. Discrepancies between intraoperative and histological evaluation of the appendix in acute appendicitis. J Gastrointest Surg. 2019.
19. Van Rossem CC, Bolmers M, Schreinemacher MHF, Van Geloven AAW, Bemelman WA. Prospective nationwide outcome audit of surgery for suspected acute appendicitis. Br J Surg. 2016;103:144–51.
20. Dhupar R, Evankovich J, Ochoa LG, Hughes SJ. Outcomes of operative management of appendicitis. Surg Infect. 2012;13:141–6.
21. Sauerland S, Jaschinski T, Neugebauer EA. Laparoscopic versus open surgery for suspected appendicitis. Cochrane Database Syst Rev. 2010;10:CD001546.
22. Hamill JK, Rahiri JL, Gunaratna G, Hill AG. Interventions to optimize recovery after laparoscopic appendectomy: a scoping review. Surg Endosc. 2016;31:2357–65.
23. Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. Br J Anaesth. 1997;78:606–17.
24. Garulli G, Lucchi A, Berti P, Gabbianelli C, Siani LM. "Ultra" E.R.A.S. in laparoscopic colectomy for cancer: discharge after the first flatus? A prospective, randomized trial. Surg Endosc. 2016;31:1806–13.
25. Kehlet H. Surgical stress and postoperative outcome from here to where? Reg Anesth Pain Med. 2006;31:47–52.
26. Gignoux B, Blanchet MC, Lanz T, Vulliez A, Saffarini M, Bothorel H, et al. Should ambulatory appendectomy become the standard treatment for acute appendicitis? World J Emerg Surg. 2018;13:28.
27. Markides G, Subar D, Riyad K. Laparoscopic versus open appendectomy in adults with complicated appendicitis: systematic review and meta-analysis. World J Surg. 2010;34:2026–40.
28. Wei B, Qi CL, Chen TF, Zheng ZH, Huang JL, Hu BG, et al. Laparoscopic versus open appendectomy for acute appendicitis: a metaanalysis. Surg Endosc. 2011;25:1199–208.
29. Yu MC, Feng YJ, Wang W, Fan W, Cheng HT, Xu J. Is laparoscopic appendectomy feasible for complicated appendicitis? A systematic review and meta-analysis. Int J Surg. 2017;40:187–97.
30. Joliat GR, Hübner M, Roulin D, Demartines N. Cost analysis of enhanced recovery programs in colorectal, pancreatic, and hepatic surgery: a systematic review. World J Surg. 2020;44:647–55.
31. Bernard ET, Davenport DL, Collins CM, Benton BA, Bernard AC. Time is money: quantifying savings in outpatient appendectomy. Trauma Surg Acute Care Open. 2018;3:e000222.
32. Di Saverio S, Podda M, De Simone B, Ceresoli M, Augustin G, Gori A, et al. Diagnosis and treatment of acute appendicitis: 2020 update of the WSES Jerusalem guidelines. World J Emerg Surg. 2020;15:27.
33. Mohsina S, Shanmugam D, Sureshkumar S, Kundra P, Mahalakshmy T, Kate V. Adapted ERAS pathway vs. standard care in patients with perforated duodenal ulcer: a randomized controlled trial. J Gastrointest Surg. 2018;22:107–16.

34. Lemanu DP, Singh PP, Berridge K, Burr M, Birch C, Babor R, et al. Randomized clinical trial of enhanced recovery versus standard care after laparoscopic sleeve gastrectomy. Br J Surg. 2013;100: 482–9.
35. Spanjersberg WR, Reurings J, Keus F, van Laarhoven CJ. Fast track surgery versus conventional recovery strategies for colorectal surgery. Cochrane Database Syst Rev. 2011;2:CD007635.
36. Ljungqvist O, Scott M, Fearon KC. Enhanced recovery after surgery: a review. JAMA Surg. 2017;152:292–8.