## Contents

**EDITORIAL**  
117 Classification and guidelines of hemorrhoidal disease: Present and future  
*Rubbini M, Ascanelli S*

122 Liver preservation prior to transplantation: Past, present, and future  
*Chedid MF, Pinto MA, Juchem JFG, Grezzana-Filho TJM, Kruel CRP*

**REVIEW**  
126 Liver graft preservation methods during cold ischemia phase and normothermic machine perfusion  
*Tchilikidi KY*

143 Management of pancreatic head adenocarcinoma: From where to where?  
*Dolay K, Malya FU, Akbulut S*

**MINIREVIEWS**  
155 Conduit necrosis following esophagectomy: An up-to-date literature review  
*Athanasiou A, Hennessy M, Spartalis E, Tan BHL, Griffiths EA*

**ORIGINAL ARTICLE**  
Prospective Study  
169 Learning curve of enhanced recovery after surgery program in open colorectal surgery  
*Lohsiriwat V*

**SYSTEMATIC REVIEW**  
179 Single incision laparoscopic fundoplication: A systematic review of the literature  
*Perivoliotis K, Sarakatsianou C, Tepetes K, Baloyiannis I*

**CASE REPORT**  
191 Laparoscopic celiac plexus ganglioneuroma resection: A video case report  
*Hemmati P, Ghanem O, Bingener J*
ABOUT COVER

Editorial Board of *World Journal of Gastrointestinal Surgery*, Robert AFM Chamuleau, MD, PhD, Professor, Department of Hepatology, Academic Medical Center, University of Amsterdam, Amsterdam BK 1105, Netherlands

AIMS AND SCOPE

*World Journal of Gastrointestinal Surgery* (World J Gastrointest Surg, WJGS, online ISSN 1948-9366, DOI: 10.4240) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

The *WJGS* covers topics concerning micro-invasive surgery; laparoscopy; hepatic, biliary, pancreatic and splenic surgery; surgical nutrition; portal hypertension, as well as associated subjects. The current columns of *WJGS* include editorial, frontier, diagnostic advances, therapeutics advances, field of vision, mini-reviews, review, original articles, case report, etc.

We encourage authors to submit their manuscripts to *WJGS*. We will give priority to manuscripts that are supported by major national and international foundations and those that are of great basic and clinical significance.

INDEXING/ABSTRACTING

The *WJGS* is now abstracted and indexed in PubMed, PubMed Central, Emerging Sources Citation Index (Web of Science), China National Knowledge Infrastructure (CNKI), China Science and Technology Journal Database (CSTJ), and Superstar Journals Database.

RESPONSIBLE EDITORS FOR THIS ISSUE

Responsible Electronic Editor: Yan-Liang Zhang  Proofing Editorial Office Director: Jin-Lei Wang

NAME OF JOURNAL

*World Journal of Gastrointestinal Surgery*

ISSN

ISSN 1948-9366 (online)

LAUNCH DATE

November 30, 2009

FREQUENCY

Monthly

EDITORS-IN-CHIEF

Varut Lohsiriwat, Shu-You Peng

EDITORIAL BOARD MEMBERS

https://www.wjgnet.com/1948-9366/editorialboard.htm

EDITORIAL OFFICE

Jin-Lei Wang, Director

PUBLICATION DATE

March 27, 2019

COPYRIGHT

© 2019 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS

https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION MISCONDUCT

https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE

https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS

https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION

https://www.f6publishing.com
Prospective Study

Learning curve of enhanced recovery after surgery program in open colorectal surgery

Varut Lohsiriwat

ORCID number: Varut Lohsiriwat (0000-0002-2252-9509).

Author contributions: Lohsiriwat V solely contributed to this study and wrote the manuscript.

Institutional review board statement: The study was approved by the institutional ethics committee (Si 498/2017).

Informed consent statement: All the participants provided written consent to participate in the study. The identity of the subjects was omitted and anonymized.

Conflict-of-interest statement: The author declared that I had no conflict of interest.

CONSORT 2010 statement: This study report was in compliance with the CONSORT 2010 statement.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

Manuscript source: Invited manuscript

Varut Lohsiriwat, Division of Colon and Rectal Surgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand

Corresponding author: Varut Lohsiriwat, MD, PhD, Associate Professor of Surgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand. bolloon@hotmail.com

Telephone: +66-2-4198005
Fax: +66-2-4121370

Abstract

BACKGROUND
Enhanced recovery after surgery (ERAS) reduces hospitalization and complication following colorectal surgery. Whether the experience of multidisciplinary ERAS team affects patients’ outcomes is unknown.

AIM
To evaluate and establish a learning curve of ERAS program for open colorectal surgery.

METHODS
This was a review of prospectively collected database of 380 “unselected” patients undergoing elective “open” colectomy and/or proctectomy under ERAS protocol from 2011 (commencing ERAS application) to 2017 in a university hospital. Patients were divided into 5 chronological groups (76 cases per quintile). Surgical outcomes and ERAS compliance among quintiles were compared. Learning curves were calculated based on criteria of optimal recovery: defined as absence of major postoperative complications, discharge by postoperative day 5, and no 30-d readmission.

RESULTS
Hospitalization more than 5 d occurred in 22.6% (n = 86), major complication was present in 2.9% (n = 11) and 30-d readmission rate was 2.4% (n = 9) accounting for unsuccessful recovery of 25% (n = 95). Conversely, the overall rate of optimal recovery was 75%. The optimal recovery significantly increased from 57.9% in 1st quintile to 72.4%-85.5% in the following quintiles (P < 0.001). Average compliance with ERAS protocol gradually increased over the time - from 68.6% in 1st quintile to 75.5% in 5th quintile (P < 0.001). The application of preoperative counseling, nutrition support, goal-directed fluid therapy, O-ring wound protector and scheduled mobilization significantly increased over the study period.
CONCLUSION

A number of 76 colorectal operations are required for a multidisciplinary team to achieve a significantly higher rate of optimal recovery and high compliance with ERAS program for open colorectal surgery.

Key words: Enhanced recovery after surgery; ERAS; Colon; Rectum; Surgery; Learning curve; Outcome; Compliance

©The Author(s) 2019. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Whether the learning curve of surgeon and multidisciplinary team affects enhanced recovery after surgery (ERAS) outcomes is unknown. This study showed that a number of 76 cases are required for an ERAS team to achieve a high compliance (>70%) with ERAS program and a significantly higher rate of optimal recovery following open colorectal surgery. The application of preoperative counseling, nutrition support, goal-directed fluid therapy, O-ring wound protector and scheduled mobilization significantly increased over the study period.

INTRODUCTION

Enhanced recovery after surgery (ERAS) has been shown to reduce morbidities and length of hospital stay following elective and emergency colorectal surgery[1,2]. This multimodal program introduces a number of preoperative, intraoperative and postoperative measures aiming to minimize surgical stress responses and facilitate patient’s recovery[3]. There have been several reports showing that improved adherence to the ERAS program is significantly associated with improved clinical outcomes after colorectal operations[4,5]. However, the effective implementation of ERAS requires close collaboration of multidisciplinary ERAS team comprising surgeons, anesthesiologists, nurses, nutritionists and physiotherapists. The initial stage of ERAS application into surgical practice could be a crucial phase of this patient-centered perioperative pathway because the workflow of health care personals needs to be adopted and the guideline has to assimilate into a daily practice. A prospective study of early implementation of ERAS program in laparoscopic colorectal surgery has demonstrated that at least 30 patients and a period of 6 mo are required to achieve an ERAS compliance of 80% or more[6].

Despite increasing uptake of laparoscopic colorectal surgery worldwide, open surgery still remained the most common approach for colorectal resections[7,8]. When comparing laparoscopy and open surgery within an ERAS program for colorectal surgery, the latter had a higher rate of complication and was more difficulty to implement an ERAS program[9]. There are several studies on the impact of ERAS compliance on surgical outcomes[10,11,12], but little attention is drawn to the analysis of the early stage of ERAS implementation into colorectal operation especially in an open surgery - as a learning curve of a multidisciplinary ERAS team.

The primary objective of the study was to evaluate and establish the learning curve for the implementation of an ERAS program in “open” colorectal operations using defined criteria of optimal recovery (no major postoperative complication, i.e., Clavien-Dindo grade ≥ III, discharge by postoperative day 5, and no 30-d readmission)[13].

MATERIALS AND METHODS

Patients

A prospectively collected database has been maintained since the beginning of ERAS program in 2011 for elective colorectal surgery in our Colorectal Unit (Faculty of Medicine Siriraj Hospital, Mahidol University - the largest tertiary referral hospital in
Thailand). All unselected patients undergoing open colectomy and/or proctectomy with this ERAS program from January 2011 to October 2017 were reviewed. Patients undergoing laparoscopic colorectal surgery were excluded because this study focused on the analysis of learning curve for ERAS program - not the that for laparoscopic surgery which may be influenced by surgeon’s experience and operative complexity. Moreover, laparoscopy might be a key factor offering independent advantages beyond an ERAS program\cite{9,10}. Patients undergoing non-resection surgery (e.g., loop colostomy and colonic bypass procedures) and those with clinical peritonitis or acute colonic obstruction were also excluded. The study was approved by the institutional ethics committee (Si 498/2017) and written informed consent was obtained from each patient.

**The development and implementation of our ERAS protocol**

The application of ERAS strategies into elective colorectal surgery in our unit was initiated by a board-certified colorectal surgeon (the author) who learnt the concept of this perioperative care pathway while studying a PhD degree in Gastrointestinal Surgery in the United Kingdom. In late 2010, a multidisciplinary ERAS team was formed by a colorectal surgeon, two anesthesiologists, a nutritionist, ostomy nurses, nursing staffs and surgical residents. At that time, our ERAS protocol for open colorectal operations had 17 core elements (Table 1) which were adopted from the consensus review of ERAS society for elective colorectal surgery\cite{13}. In early 2011, the protocol was routinely applied into a daily surgical practice with a regular audition. We set a targeted discharge by postoperative day 5 because in the literature review an ERAS protocol reduced the length of hospital stay by 2-3 d\cite{1} and hospital stay after open colorectal operations under a conventional pathway in our unit was about 7-8 d\cite{14,15}. Patients would be discharged from the hospital if they met all criteria: no fever, satisfactory gastrointestinal recovery, adequate pain control with oral analgesics, and a good level of ambulation. All of the patients were scheduled for follow-up at 7-10 d and 30 d after an operation. Notably, all of the studied patients were operated on and treated by single surgeon (the author) and his multidisciplinary team. Since an ERAS program is a dynamic multimodal care pathway, some elements were added into the program later. These interventions were the administration of synthetic albumin in patients with persistent oliguria after the adequate infusion of crystalloid solution (from June 2015) and the routine postoperative administration of prokinetic agent (from April 2016).

**Data collection**

Data including patient characteristics, operative details, and postoperative outcomes were prospectively collected. Patient characteristics included age, gender, body mass index, American Society of Anesthesiologists (ASA) classification, and ColoRectal Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity (CR-POSSUM) score\cite{16}. Operative details included type of operation, operative time, and estimated blood loss. Postoperative outcomes included postoperative complications (graded I-V according to the Clavien-Dindo classification system)\cite{17}, time to tolerate solid food, time to first bowel movement, length of postoperative stay, death and readmission within 30 d after the operation. Overall compliance with ERAS protocol of each patient was determined based on our initial ERAS protocol (17 core elements).

**Outcome measures**

Patients were divided into 5 chronological groups (1st–5th quintile). Surgical outcomes and compliance with ERAS protocol between groups were compared. Learning curves were calculated based on the criteria of optimal recovery (defined as no major postoperative complication, i.e., Clavien-Dindo grade ≥ III, discharge by postoperative day 5, and no 30-d readmission)\cite{12}.

**Statistical analysis**

All statistical analyzes were performed using the PASW Statistics software (SPSS version 18.0 for Windows, Illinois, United States). Continuous variables were expressed as mean ± SD or median (interquartile range; IQR) and were compared among groups using one-way analysis of variance (ANOVA) or the Kruskal-Wallis test. Categorical data were expressed as number (percentage) and were compared using the Pearson Chi-square test or Fisher exact probability test. A P-value of <0.05 was considered statistically significant.

**RESULTS**
### Table 1 Enhanced recovery after surgery protocol for open colorectal surgery

| Preadmission | 1 Cessation of smoking and intake of alcohol; 2 Nutrition assessment and nutrition support as needed; 3 Medical optimization of chronic disease |
| Preoperative | 4 Structured preoperative counseling to patients and their relatives; 5 No mechanical bowel preparation; 6 Administration of appropriate prophylactic antibiotics; 7 Prophylaxis of postoperative nausea and vomiting |
| Intraoperative | 8 Use of epidural anesthesia; 9 Use ofatraumatic O-ring wound retractor/protector; 10 Avoid hypothermia; 11 Maintaining fluid balance and vasopressors to support blood pressure control; 12 No intraabdominal or pelvic drain |
| Postoperative | 13 Early intake of oral fluids and semi-solid foods (day of surgery); 14 Early ambulation (postoperative day 1); 15 Multimodal approach to opioid-sparing pain control; 16 Removal of urinary catheter by postoperative day 3; 17 Discontinuous intravenous fluid infusion by postoperative day 3 |

During the study period of 82 mo, 489 colorectal resections were performed by the author and his multidisciplinary team under an ERAS protocol. Of these, 57 operations were for acute colonic obstruction or peritonitis, and 52 operations were laparoscopic surgery. Therefore, there were 380 patients undergoing elective “open” colectomy and/or proctectomy. These patients were divided into 5 chronological groups (76 cases per quintile). Of 380 cases, 75 patients (20%) had ASA classification ≥ 3 and a median CR-POSSUM predicting mortality of 1.8 (IQR 1.00-2.58). Colorectal cancer was the most indication for surgery (n = 347, 91%). Some 165 patients (43%) underwent proctectomy and 82 patients (22%) had temporary or permanent stoma formation. Patients’ characteristic and operative details were comparable among quintiles (Table 2).

Prolonged hospitalization > 5 d occurred in 22.6% (n = 86), major postoperative complication was present in 2.9% (n = 11) and the rate of 30-d readmission was 2.4% (n = 9) - accounting for unsuccessful recovery of 25% (n = 95). Accordingly, the overall rate of optimal recovery in this ERAS program was 75%. The rate of optimal recovery significantly increased from 57.9% in 1st quintile to 72.4%-85.5% in the following quintiles (P < 0.001) (Figure 1). The average compliance with ERAS protocol gradually increased over the time - from 68.6% in the first quintile to 75.5% in the last quintile (P < 0.001) (Table 3). Regarding each individual element of our ERAS protocol, the compliance of 5 out of 17 ERAS elements have increased over the study period. These elements were preoperative detailed counseling, perioperative nutrition support, intraoperative goal-directed fluid therapy, intraoperative use of atraumatic O-ring wound protector and postoperative scheduled mobilization (Figure 2).

## DISCUSSION

An ERAS program is an integrated, evidence-based approach that fundamentally changes in perioperative care and surgical practice, and can therefore take time to achieve favorable outcomes. The introduction of ERAS in daily practice could be a learning-by-doing process relying on experiencing as a way for a multidisciplinary ERAS team to acquire skill and familiarize each ERAS element in order to get better surgical outcomes. The learning curve of ERAS implementation is somewhat different from that of a surgical intervention because an ERAS implementation requires both technical maneuvers and non-technical skills such as communication, collaboration and commitment from both patients and all members of multidisciplinary ERAS team.

The first step in determining the learning curve of ERAS program in colorectal surgery is the selection of an appropriate outcome measure. In this regard, we use a composite endpoint of three relevant clinical outcomes (no major postoperative complication, discharge by postoperative day 5, and no 30-d readmission) to determine an optimal recovery. These surgical outcomes have commonly been used as a proxy in the measurement of successful ERAS implementation in the literature. Based on our prospectively collected database of colorectal surgery in a university hospital, this study demonstrated that a number of 76 colorectal operations are required for a multidisciplinary team to achieve a high rate of ERAS compliance and a high rate of optimal recovery following an open colorectal resection. It is worth noting that the 3rd quintile had the highest rate of 30-d readmission although it did not reach a statistical significance. There are several possible explanations on these findings such as the 3rd quintile had the highest percentage of patients with ASA classification ≥ 3. High ASA classification has been shown to be an independent
It would appear that the implementation of ERAS program in open colorectal surgery may have a longer learning curve (i.e., more patients and a longer period of time) to achieve an optimal recovery than that in laparoscopic surgery. Pedziwiatr et al[12] showed that at least 30 patients over a period of 6 mo were required before their multidisciplinary team can effectively integrate an ERAS protocol into laparoscopic colorectal surgery. In this European study, there was a significant increase in some ERAS elements implemented over the study period such as no drains, use of epidural analgesia, early feeding and early ambulation. In the Alberta Heath Services Canada, Gramlich et al[9] reported that the active phase of ERAS implementation took 9-12 mo and recommended to use data on a baseline cohort of 50 patients in pre- and post-implementation period to define compliance with ERAS program. A possible explanation for a longer learning curve of successful ERAS implementation in open colorectal surgery is the fact that open surgery is associated with higher systemic stress response and more surgical trauma than laparoscopic surgery[10,11,12]. Therefore, patients undergoing open surgery could have a higher rate of postoperative complication and are more difficulty to follow an ERAS protocol[13,14,15], especially for postoperative compliance with an ERAS protocol[16]. Although it may take more times to achieve a successful ERAS program in open colorectal surgery, a recent report from 15 academic hospitals in Canada has suggested that ERAS has more positive effect in patients undergoing open surgery than those with laparoscopic approach[17].

The introduction of the ERAS program required a closed collaboration and communication among surgical team members and other health care professionals as well as the continuous monitoring of its outcomes. Since not all elements could be introduced immediately, the ERAS compliance was lower than 70% in the early period of ERAS implementation in our institute. However, the rate of ERAS compliance significantly increased after our multidisciplinary ERAS team experienced the application of this program in 76 patients. A high ERAS compliance was then maintained thereafter at approximately 75%. Increasing ERAS compliance has been shown to be associated with a successful improved outcome including fewer complications, shorter hospital stay[18-20] and better oncological outcomes[21,22]. Two large European studies have suggested a cut-off point at 70% compliance with ERAS protocol to be correlated with a significant improvement in short-term and long-term outcomes following colorectal surgery[23,24]. It is arguable that full implementation of ERAS program may be not required to achieve better clinical outcomes.

Some components of our ERAS protocol encountered difficulties in their initial implementation, partly, due to the habit of conventional care and the lack of knowledge or instruments. Thanks to the cooperation of our multidisciplinary ERAS team and the support of hospital authorities, many components of our ERAS protocol increasingly implemented over the study period including preoperative detailed counseling, perioperative nutrition support, intraoperative goal-directed fluid

---

**Table 2 Patients’ characteristics and operative details**

| Predictor                          | Overall *(n = 380)* | 1st quintile *(n = 76)* | 2nd quintile *(n = 76)* | 3rd quintile *(n = 76)* | 4th quintile *(n = 76)* | 5th quintile *(n = 76)* | P value  |
|-----------------------------------|---------------------|------------------------|------------------------|------------------------|------------------------|------------------------|---------|
| Age (yr)                          | 62.8 ± 12.7         | 60.9 ± 14.8            | 62.2 ± 12.2            | 63.7 ± 12.4            | 61.6 ± 12.9            | 62.4 ± 11.5            | 0.227   |
| Male                              | 206 (54)            | 43 (57)                | 40 (53)                | 41 (54)                | 44 (51)                | 38 (50)                | 0.877   |
| BMI (kg/m²)                       | 23.0 ± 4.1          | 23.7 ± 4.5             | 23.0 ± 3.8             | 23.2 ± 3.8             | 22.3 ± 4.2             | 23.1 ± 3.9             | 0.371   |
| ASA classification ≥ 3            | 75 (20)             | 9 (12)                 | 19 (25)                | 20 (26)                | 13 (17)                | 14 (18)                | 0.146   |
| CR-POSSUM                         | 1.80                | 1.77                   | 1.88                   | 1.75                   | 1.80                   | 1.90                   | 0.675   |
| Predicting mortality              | (1.00-2.58)         | (0.96-2.58)            | (0.98-3.18)            | (0.95-2.58)            | (1.30-3.28)            | (1.30-2.50)            |         |
| Hematocrit (%)                    | 36.8 ± 5.4          | 36.6 ± 5.5             | 36.1 ± 5.1             | 37.3 ± 5.5             | 37.4 ± 5.6             | 36.5 ± 5.3             | 0.548   |
| Cancer surgery                    | 347 (91)            | 70 (92)                | 68 (90)                | 69 (91)                | 71 (93)                | 69 (91)                | 0.930   |
| Rectal surgery                    | 165 (43)            | 34 (45)                | 30 (40)                | 39 (38)                | 40 (53)                | 32 (42)                | 0.397   |
| Stoma formation                   | 82 (22)             | 19 (25)                | 20 (26)                | 13 (17)                | 20 (26)                | 10 (15)                | 0.157   |
| Multi-organ Resection¹            | 36 (10)             | 9 (12)                 | 10 (13)                | 5 (7)                  | 9 (12)                 | 3 (4)                  | 0.227   |
| Blood loss (mL)                   | 150 (73-300)        | 200 (100-425)          | 200 (100-400)          | 150 (90-300)           | 150 (55-385)           | 140 (55-200)           | 0.067   |

Data are presented as mean ± SD, median (IQR) or number (percentage).

¹Multi-organ resection excluded the resection of appendix, gallbladder, ovaries and fallopian tubes, small bowel, and part of urinary bladder (partial cystectomy). ASA: American Society of Anesthesiologists; BMI: Body mass index; CR-POSSUM: ColoRectal Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity.
therapy, intraoperative use of atraumatic O-ring wound protector and postoperative scheduled mobilization. A recent multi-center observational study in Ontario suggested that postoperative ERAS interventions had the greatest impact on optimal recovery after colorectal surgery\(^{12}\).

This study has three major strengths. First, the data was extracted from a prospectively collected database of unselected patients undergoing open colectomy and/or proctectomy with an ERAS protocol. All patients were operated on and taken care of by the same surgeon and his multidisciplinary team thus minimizing bias. Second, to determine an optimal recovery, this study used a composite endpoint of three clinical outcomes (no major postoperative complication, discharge by postoperative day 5, and no 30-d readmission) which have commonly been used as a proxy in the measurement of successful ERAS implementation\(^{6,11,12}\). Third, this study provided detailed data on compliance with ERAS protocol and its individual elements.

The limitations of this study include the fact that it included only open colorectal operation. Whether the learning curve in this study is applicable to laparoscopic colorectal surgery or other intra-abdominal operations needs to be determined. Second, this study used only common clinical outcomes (i.e., major complication, hospital stay and readmission) as representatives for optimal recovery\(^{6,11,12}\). It did not assess any patient-reported outcomes such as time to return to normal activities and quality of life – which could be other important outcome measures for optimal recovery in the future study. Last, we acknowledged that there are several methods to quantify learning curve such as a simple linear regression and various curve fitting methods, a cumulative sum analysis and a chronological division of consecutive cases (data splitting method)\(^{26}\) – each has its pros and cons. We used the latter design because it was evident that data splitting method can be used to identify a change over time even in case of case-mix complexity\(^{27}\). As a result, it was the most common method used to measure the learning curve effect in health technology\(^{27}\). However, the cut-off point of consecutive cases is arbitrary and information derived from the underlying learning curve may be limited.

This study showed that a number of 76 colorectal operations are required for a multidisciplinary team to achieve a significantly higher rate of optimal recovery and compliance with an ERAS protocol for open colorectal operation. These findings could call surgical communities to find the best ways to shorten the learning curve of ERAS program – especially in open laparotomy. It may include a structured program of education, training, cooperation and experience sharing between surgeons and nurses.
non-surgical health care personals as an integrated ERAS team, or between a well-established ERAS center and a newly-implied ERAS hospital. The regular audition of relevant outcomes and closed collaboration between many different stakeholders, including patients and their family, are also required to achieve the best care and optimal recovery of surgical patients.
Optimal recovery was defined as no major postoperative complication, discharge by postoperative day 5, and no 30-d readmission. Clavien-Dindo grade ≥ III (the most severe complication was registered for patients with more than one complication); the 2nd quintile had a higher rate of composite unfavorable outcomes than 1st and 5th quintile; 1st quintile had a higher number of patients discharged after postoperative day 5 than the others; 1st quintile had a longer length of postoperative stay than 5th quintile; 1st quintile had a shorter period of time to resume normal diet than 5th quintile; $P < 0.05$. Data are presented as mean ± standard deviation, median (IQR) or number (percentage).

| Table 3 Surgical outcomes | Overall | 1st quintile | 2nd quintile | 3rd quintile | 4th quintile | 5th quintile | $P$ value |
|---------------------------|---------|-------------|-------------|-------------|-------------|-------------|-----------|
| Time to resume normal diet (d) | 2 (1.3) | 2 (1.3) | 1 (0.2)$^a$ | 2 (0.8) | 2 (1.3) | 2 (1.2) | $< 0.001^a$ |
| Time to first bowel movement (d) | 3 (2.3) | 3 (2.3) | 3 (2.3) | 3 (2.3) | 2 (2.4) | 3 (2.3) | 0.848 |
| Overall complication | 83 (21.8) | 18 (23.7) | 20 (26.3) | 16 (21.1) | 18 (23.7) | 11 (14.5) | 0.457 |
| Major complication$^b$ | 11 (2.9) | 1 (1.3) | 3 (3.9) | 2 (2.6) | 3 (3.9) | 2 (2.6) | 0.860 |
| Hospital stay (d) | 4 (4-5) | 5 (4-7)$^d$ | 4 (4-5) | 4 (4-5) | 5 (4-5.8) | 4 (3.5) | $< 0.001^d$ |
| Hospital stay >5 d | 86 (22.6) | 31 (40.8)$^d$ | 12 (15.8) | 15 (18.4) | 19 (25.0) | 10 (13.2) | $< 0.001^d$ |
| 30-d readmission | 9 (2.4) | 1 (1.3) | 0 | 5 (6.6) | 2 (2.6) | 1 (1.3) | 0.077 |
| 30-d mortality | 1 (0.3) | 0 | 1 (1.3) | 0 | 0 | 0 | 0.405 |
| ERAS compliance % | 73.5 ± 11.8 | 68.6 ± 16$^d$ | 75.4 ± 11.1 | 73.7 ± 9.9 | 74.3 ± 10.2 | 75.3 ± 9.5 | $< 0.001^a$ |
| Optimal recovery$^c$ | 288 (75.0) | 44 (57.9)$^d$ | 64 (84.2) | 57 (75.0) | 55 (72.4) | 65 (85.5) | $< 0.001^a$ |

$^a$P < 0.05. 2nd quintile had a shorter period of time to resume normal diet than 1st and 4th quintile; 1st quintile had a longer length of postoperative stay than 5th quintile; 1st quintile had a higher number of patients discharged after postoperative day 5 than the others; 1st quintile had a lower compliance rate of ERAS protocol than 2nd, 4th and 5th quintile; 1st quintile had a higher rate of composite unfavorable outcomes than 2nd, 4th and 5th quintile.

$^b$Clavien-Dindo grade ≥ III (the most severe complication was registered for patients with more than one complication);

$^c$Optimal recovery was defined as no major postoperative complication, discharge by postoperative day 5, and no 30-d readmission.

ERAS: Enhanced recovery after surgery.

**ARTICLE HIGHLIGHTS**

**Research background**
Enhanced recovery after surgery (ERAS) reduces hospitalization and complication following colorectal surgery. Whether the experience of multidisciplinary ERAS team affects patients' outcomes is unknown especially for open colorectal surgery – which is known to be associated with higher rates of complication and more difficulty to implement an ERAS program than laparoscopic surgery.

**Research motivation**
The initial stage of ERAS application into surgical practice, i.e., learning curve, could be a crucial phase of this patient-centered perioperative pathway because the workflow of health care personals needs to be adopted and the guideline has to assimilate into a daily practice.

**Research objectives**
This study aimed to evaluate and establish a learning curve of ERAS program for open colorectal surgery.

**Research methods**
This was a review of prospectively collected database of 380 “unselected” patients undergoing elective “open” colectomy and/or proctectomy under ERAS protocol from 2011 (commencing ERAS application) to 2017 in a university hospital. Patients were divided into 5 chronological groups (76 cases per quintile). Surgical outcomes and ERAS compliance among quintiles were compared. Learning curves were calculated based on criteria of optimal recovery: defined as absence of major postoperative complications, discharge by postoperative day 5, and no 30-d readmission.

**Research results**
Hospitalization more than 5 d occurred in 22.6% ($n = 86$), major complication was present in 2.9% ($n = 11$) and 30-d readmission rate was 2.4% ($n = 9$) accounting for unsuccessful recovery of 25% ($n = 95$). Conversely, the overall rate of optimal recovery was 75%. The optimal recovery significantly increased from 57.9% in 1st quintile to 72.4%-85.5% in the following quintiles ($P < 0.001$). Average compliance with ERAS protocol gradually increased over the time: from 68.6% in 1st quintile to 72.4%-85.5% in the following quintiles ($P < 0.001$). The application of preoperative counseling, nutrition support, goal-directed fluid therapy, O-ring wound protector and scheduled mobilization significantly increased over the study period.

**Research conclusions**
A number of 76 colorectal operations are required for a multidisciplinary team to achieve a significantly higher rate of optimal recovery and high compliance with ERAS program for open colorectal surgery.

**Research perspectives**
These findings could call surgical communities to find the best ways to shorten the learning curve of ERAS program – especially in open laparotomy. The barriers to the conduct, application and maintenance of ERAS program for colorectal surgery should be identified and solved systematically in order to achieve the best care and optimal recovery of surgical patients.

ACKNOWLEDGEMENTS

The author would like to thank Mr. Suthipol Udompunthurak from Clinical Epidemiology Unit, for his Research and Development, Faculty of Medicine Siriraj Hospital, for his kind assistance with statistical analysis.

REFERENCES

1. Zhuang CL, Ye XZ, Zhang XD, Chen BC, Yu Z. Enhanced recovery after surgery programs versus traditional care for colorectal surgery: a meta-analysis of randomized controlled trials. *Dis Colon Rectum* 2013; 56: 667-678 [PMID: 23575408 DOI: 10.1097/DCR.0b013e3182812842]

2. Lohsiriwat V. Enhanced recovery after surgery vs conventional care in emergency colorectal surgery. *World J Gastroenterol* 2014; 20: 13950-13955 [PMID: 25203052 DOI: 10.3748/wjg.v20.i38.13950]

3. Ljungqvist O, Scott M, Fearon KC. Enhanced Recovery After Surgery: A Review. *JAMA Surg* 2017; 152: 292-298 [PMID: 28977502 DOI: 10.1001/jamasurg.2016.4972]

4. Gustafsson UO, Hausedl J, Thorell A, Ljungqvist O, Soo M, Nygren J; Enhanced Recovery After Surgery Study Group. Adherence to the enhanced recovery after surgery protocol and outcomes after colorectal cancer surgery. *Arch Surg* 2011; 146: 571-577 [PMID: 21242424 DOI: 10.1001/archsurg.2010.309]

5. ERAS Compliance Group. The Impact of Enhanced Recovery Protocol Compliance on Elective Colorectal Cancer Resection: Results From an International Registry. *Ann Surg* 2015; 261: 1153-1159 [PMID: 25671587 DOI: 10.1097/SLA.0000000000001029]

6. Pędziszew M, Kisialański M, Wierdzak M, Stanek M, Niatkiewicz M, Matlok M, Major P, Malczak P, Budziński A. Early implementation of Enhanced Recovery After Surgery (ERAS®) protocol - Compliance improves outcomes: A prospective cohort study. *Int J Surg* 2015; 21: 75-81 [PMID: 26231994 DOI: 10.1016/j.ijsu.2015.06.087]

7. Dobbins TA, Young JM, Solomon MJ. Uptake and outcomes of laparoscopically assisted resection for colon and rectal cancer in Australia: a population-based study. *Dis Colon Rectum* 2014; 57: 415-422 [PMID: 24680296 DOI: 10.1001/jama.2014.26059]

8. Lee MG, Chiu CC, Wang CC, Chang CN, Lee SH, Lee M, Hsu TC, Lee CC. Trends and Outcomes of Surgical Treatment for Colorectal Cancer between 2004 and 2012: an Analysis using National Inpatient Database. *Sci Rep* 2017; 7: 2006 [PMID: 28515452 DOI: 10.1038/s41598-017-02224-y]

9. Spanjersberg WR, van Sanbeek JD, Bremers A, Rosman C, van Laarhoven CJ. Systematic review and meta-analysis for laparoscopic versus open colon surgery with or without an ERAS programme. *Surg Endosc* 2015; 29: 3443-3453 [PMID: 25801106 DOI: 10.1007/s00464-015-4148-3]

10. Braga M, Borghi F, Scatizzi M, Missana G, Guicciardi MA, Bon A, Sica F, Maspero M, Pecorelli N; PeriOperative Italian Society. Impact of laparoscopy on adherence to an enhanced recovery pathway and readiness for discharge in elective colorectal surgery: Results from the PeriOperative Italian Society registry. *Surg Endosc* 2017; 31: 4393-4399 [PMID: 28209772 DOI: 10.1007/s00464-017-5486-0]

11. Pecorelli N, Hershorn O, Baldini G, Fiore JF, Stein BL, Liberman AS, Chiaravalli P, Carli F, Feldman LS. Development of a dedicated risk-adjustment scoring system for colorectal surgery (colorectal POSSUM). *Dig Surg* 2008; 25: 191-197 [PMID: 18577863 DOI: 10.1159/000140688]

12. Tekkis PP, Pyytyreth DR, Kocher HM, Senapati A, Poloniecki JD, Stamatakis JD, Windsor AC. Compliance improves outcomes: A prospective cohort study. *Ann Surg* 2011; 261: 1153-1159 [PMID: 25671587 DOI: 10.1097/SLA.0000000000001029]

13. Lohsiriwat V, Ljungqvist O, Von Meyenfeldt M, Revhaug A, Dejong CH, Lassen K, Nygren J, Hausel J, Fearon KC. Enhanced Recovery After Surgery: A Review. *World J Gastroenterol* 2014; 20: 13950-13955 [PMID: 25203052 DOI: 10.3748/wjg.v20.i38.13950]

14. Aarts MA, Rotteveel OD, Pearsall EA, Victor JC, Okraaene A, McKenzie M, McCluskey SA, Cunn LG, McLeod RS; iERAS group. Postoperative ERAS Interventions Have the Greatest Impact on Optimal Recovery: Experience With Implementation of ERAS Across Multiple Hospitals. *Ann Surg* 2018; 267: 992-997 [PMID: 29303803 DOI: 10.1097/SLA.0000000000002632]

15. Fearon KC, Ljungqvist O, Von Meyenfeldt M, Revhaug A, Dejong CH, Lassen K, Nygren J, Hausel J, Soop M, Andersen J, Kehlet H. Enhanced recovery after surgery: a consensus review of clinical care for patients undergoing colorectal resection. *Clin Nutr* 2005; 24: 466-477 [PMID: 15896435 DOI: 10.1016/j.clnu.2005.02.002]

16. Lohsiriwat V, Lohsiriwat D, Chinswangwatanakul V, Akaraviputh T, Lert-Akyamanee N. Outcome of sphincter-saving operation for rectal cancer without protective stoma and its survival and short-term outcomes between laparoscopically-assisted vs. transverse-incision open right hemicolectomy for right-sided colon cancer: a retrospective study. *World J Oncol Colorect* 2007; 5: 49 [PMID: 17498289 DOI: 10.1186/1477-7819-5-49]

17. Lohsiriwat V, Lohsiriwat D, Boomnuch W, Chinswangwatanakul V, Akaraviputh T, Riansuwann W, Lert-Akyamanee N. Outcomes of sphincter-saving operation for rectal cancer without protective stoma and pelvic drain, and risk factors for anastomotic leakage. *Dig Surg* 2008; 25: 191-197 [PMID: 18577863 DOI: 10.1159/000140685]

18. Tekkis PP, Pyytyreth DR, Kocher HM, Senapati A, Poloniecki JD, Stamatakis JD, Windsor AC. Development of a dedicated risk-adjustment scoring system for colorectal surgery (colorectal POSSUM). *Br J Surg* 2004; 91: 1174-1182 [PMID: 15449270 DOI: 10.1002/bjs.4430]

19. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 636 patients and results of a survey. *Ann Surg* 2004; 240: 205-213 [PMID: 15273542 DOI: 10.1097/01.sla.0000138308.54934.ae]

20. Tran A, Mai T, El-Haddad J, Lampron J, Yelle JD, Pagliarello G, Matar M. Preinjury ASA score as an independent predictor of readmission after major traumatic injury. *Trauma Surg Acute Care Open* 2017; 2: e000128 [PMID: 29766118 DOI: 10.1136/trauma-2017-000128]

21. Tevis SE, Weber SM, Kent KC, Kennedy GD. Nomogram to Predict Postoperative Readmission in Patients Who Undergo General Surgery. *JAMA Surg* 2015; 150: 505-510 [PMID: 25902340 DOI: 10.1001/jamasurg.2014.4043]

22. Gramlich LM, Sheppard CE, Wasylik T, Gilmour LE, Ljungqvist O, Basualdo-Hammond C, Nelson G.
Implementation of Enhanced Recovery After Surgery: a strategy to transform surgical care across a health system. *Implement Sci* 2017; 12: 67 [PMID: 28526041 DOI: 10.1186/s13012-017-0597-5]

21 Delgado S, Lacy AM, Filella X, Castells A, Garcia-Valdecasas JC, Pique JM, Mombián D, Visa J. Acute phase response in laparoscopic and open colectomy in colon cancer: randomized study. *Dis Colon Rectum* 2001; 44: 638-646 [PMID: 11357021 DOI: 10.1007/BF02234558]

22 Veenhof AA, Vlug MS, van der Pas MH, Sietes C, van der Peet DL, de Lange-de Klerk ES, Bonjer HJ, Bemelman WA, Cuesta MA. Surgical stress response and postoperative immune function after laparoscopy or open surgery with fast track or standard perioperative care: a randomized trial. *Ann Surg* 2012; 255: 216-221 [PMID: 22241289 DOI: 10.1097/SLA.0b013e31825336c2]

23 Zhuang CL, Huang DD, Zhou CJ, Zheng BS, Chen BC, Shen X, Yu Z. Laparoscopic versus open colorectal surgery within enhanced recovery after surgery programs: a systematic review and meta-analysis of randomized controlled trials. *Surg Endosc* 2015; 29: 2091-2100 [PMID: 25414064 DOI: 10.1007/s00464-014-3922-y]

24 Gustafsson UO, Oppelstrup H, Thorell A, Nygren J, Ljungqvist O. Adherence to the ERAS protocol is Associated with 5-Year Survival After Colorectal Cancer Surgery: A Retrospective Cohort Study. *World J Surg* 2016; 40: 1741-1747 [PMID: 26913728 DOI: 10.1007/s00268-016-3460-y]

25 Pisarska M, Pędziwiatr M, Malczak P, Major P, Ochenduszko S, Zub-Pokowiecka A, Kulaświk J, Budzyński A. Do we really need the full compliance with ERAS protocol in laparoscopic colorectal surgery? A prospective cohort study. *Int J Surg* 2016; 36: 377-382 [PMID: 27876677 DOI: 10.1016/j.ijsu.2016.11.088]

26 Khan N, Abboudi H, Khan MS, Dasgupta P, Ahmed K. Measuring the surgical ‘learning curve’: methods, variables and competency. *BJU Int* 2014; 113: 504-508 [PMID: 23819461 DOI: 10.1111/bju.12197]

27 Ramsay CR, Grant AM, Wallace SA, Garthwaite PH, Monk AF, Russell IT. Statistical assessment of the learning curves of health technologies. *Health Technol Assess* 2001; 5: 1-79 [PMID: 11319991]

Lohsiriwat V. Learning curve of ERAS in colorectal surgery
