

Enhanced recovery after pancreatic surgery: A prospective randomized controlled clinical trial

Muhammer Ergenc MD¹  | Sakir Karpuz MD¹  | Merve Ergenc MD²  |
Cumhur Yegen MD¹ 

¹Department of General Surgery, School of Medicine, Marmara University, Istanbul, Turkey

²Department of Anesthesiology and Reanimation, School of Medicine, Marmara University, Istanbul, Turkey

Correspondence

Muhammer Ergenc, Department of General Surgery, Marmara University Istanbul Pendik Training and Research Hospital, Fevzi Cakmak Mah. Muhsin Yazicioglu Cad. No:10, Pendik, Istanbul 34899 Turkey.

Email: muhammerergenc@gmail.com

Abstract

Background and Objectives: The enhanced recovery after surgery (ERAS) protocol is a perioperative care bundle designed to achieve early healing after surgical procedures. This study aims to investigate the effect of the ERAS protocol on postoperative complications, length of hospital stay (LOS), and readmission rates in pancreatic surgery patients.

Methods: The study was designed as a prospective and randomized controlled study between January 2016 and November 2018 on pancreatic surgery patients. A total of 38 patients were analyzed, 18 of whom were in the ERAS group and 20 in the control group. Patient demographics, intraoperative variables, and postoperative outcomes were recorded.

Results: The groups were similar regarding age, sex, surgery type, American Society of Anesthesiologists scores, and laboratory results. There was no significant difference in the intraoperative variables. Early oral feeding was preferred, mostly in the ERAS group compared to the control group. Perioperative complication rates, including delayed gastric emptying and pancreatic fistula, LOS, and readmission rates, were similar between the two groups.

Conclusions: The ERAS protocol provided a minimal decrease in the total complication rates and had no effect on severe complications. Therefore, the ERAS protocol seems feasible and can be applied safely in pancreatic surgery patients.

KEYWORDS

enhanced recovery after surgery, ERAS, pancreas cancer, pancreaticoduodenectomy, pancreatectomy

1 | INTRODUCTION

Pancreatic surgery has traditionally been considered a high-risk abdominal surgery associated with high morbidity and mortality rates. Advances in diagnostic and surgical techniques in recent decades and improved management of intensive care units have led to better outcomes after pancreatic resection.¹ However, while the mortality rates are low, morbidity remains high at a rate of 40%–60%.^{2–4} The postoperative length of hospital stay (LOS) after pancreaticoduodenectomy (PD) ranges from

14 to 20 days in various studies.^{4–6} Postoperative complications are the main reasons for prolonged LOS. Therefore, surgeons are seeking to develop perioperative strategies that enhance patient recovery, which will lead to a shorter LOS.⁷

The enhanced recovery after surgery (ERAS) protocol is a perioperative care bundle designed to achieve early healing after surgical procedures by maintaining intravenous hydration restrictions, postoperative early oral feeding, providing more effective analgesia, early drain withdrawal, and early patient mobilization.⁸ The purpose of an

ERAS program is to accelerate postoperative recovery and shorten the postoperative LOS without an increase in morbidity or readmissions.¹ However, there are only a limited number of studies on applying the ERAS protocol after PD.^{9,10} Therefore, more prospective randomized studies are needed for the protocol to be routinely applied.

This study aims to investigate the effect of the ERAS protocol on postoperative complications, length of hospital stay, and readmission rates in patients undergoing pancreatic surgery.

2 | MATERIALS AND METHODS

2.1 | Patients

Patients who underwent elective pancreatic cancer surgery with laparotomy at the Marmara University General Surgery Clinic between January 2016 and November 2018 were invited to participate in the

study. Patients with the following criteria were excluded from the study: (1) Emergent surgery requirements, (2) had laparoscopic surgery, (3) an American Society of Anesthesiologists (ASA) score of 4, (4) cannot be mobilized, (5) severe malnutrition, (6) need for intensive care in the postoperative period, and (7) refused to participate.

The study was designed as prospective and randomized. The Research Ethics Committee approved the study (Marmara University Faculty of Medicine Clinical Research Ethics Committee Date/Number: 09.2014.0012) All patients provided written informed consent before their participation. The group of patients included in the study was determined according to the order of patient admission with a randomly generated scheme from the website <https://www.randomizer.org/>.

The ERAS protocol for pancreatic surgery included the following basic elements: preoperative counseling, no mechanical bowel preparation, postoperative multimodal analgesia, postoperative restricted intravenous fluid treatment, early oral feeding-mobilization, and early withdrawal of the nasogastric tube, urinary catheter, and intraabdominal drains (Table 1). All surgical

	ERAS group	Control group
Day before surgery	Special informed consent	Traditional informed consent
	No mechanical bowel preparation	Liquid food intake
	Clear liquids until 4 h before surgery	Overnight fasting
POD 0	Antimicrobial prophylaxis	Antimicrobial prophylaxis
	Epidural PCA	IV PCA
	Central line	Central line
	Nasogastric tube	Nasogastric tube
	Urinary catheter	Urinary catheter
	2 intra-abdominal drains	2 intra-abdominal drains
	Heater blanket	Heater blanket
POD 1	Removal of NGT	Removal of NGT if output ≤ 300 mL
	Mobilization out of bed	Mobilization according to patient's ability
	Removal of urinary catheter	Continue urinary catheter
	Oral sips of water	Fasting until flatus
	Restricted IV fluid	Nonrestrictive IV fluid
POD 2	Mobilization	Mobilization according to patient's ability
	Oral liquids	Removal of urinary catheter
POD 3	Drain removal (if output < 100 ml and drain amylase less than three-fold serum)	Drain fluid amylase
	Oral semisolid diet	
POD 4	Normal diet	Oral liquids
	Continue mobilization	Untargeted mobilization

TABLE 1 Protocol between ERAS and control group perioperative items

Abbreviations: ERAS, enhanced recovery after surgery; IV, intravenous; NGT, nasogastric tube; PCA, patient-controlled analgesia; POD, postoperative day.

procedures were performed by the same experienced pancreatic surgeons. Pylorus-preserving PD and also vascular resection was not performed in any patients. While pancreaticojejunostomy (duct-to-mucosa) and hepaticojejunostomy reconstructions were performed retrocolic, gastrojejunostomy was performed as an antecolic 40–50 cm distal to the hepaticojejunostomy. Two abdominal drains were routinely placed. Drain removal criteria were determined as drain outputs of less than 50 ml/day and drain amylase level not suggestive of postoperative pancreatic fistula (POPF) (less than three times the upper limit of normal serum amylase) as per the International Study Group of Pancreatic Surgery (ISGPS) guidelines.¹¹ All complications were defined according to the ISGPS criteria, including pancreatic fistula, delayed gastric emptying (DGE), and post pancreatectomy hemorrhage.^{11–13} Patients were discharged when they were fully mobile, oral intake was adequate, and there was no evidence of local or systemic complications. Mortality was defined as any death that occurred within 30 days after surgery or during the hospital stay. Readmission was defined as admission to the hospital within 1 month of discharge. All surgical procedures were performed by the same experienced pancreatic surgeons.

Data regarding demographics, body mass indexes, smoking history, drugs used, ASA scores, and neoadjuvant treatment status of the patients included in the study, as well as the routine preoperative laboratory examination results (hemogram, biochemistry, and tumor markers), were recorded. The volume of fluid given during the operation, the volume of bleeding and transfusion, and the volume of intravenous fluid given daily in the postoperative period were recorded. Analgesic use and visual analog scale (VAS) scores, nausea-vomiting symptoms, bowel movements, flatus, and defecation were monitored daily during hospitalization. The days of first mobilization, oral feeding, and withdrawal of nasogastric and Foley catheter drains were noted. Complications developed during hospitalization, discharge dates, readmission status, and duration were also recorded.

The primary outcome of this study was to determine whether there was a difference between the two groups in terms of postoperative complications, length of hospital stay, and incidence of readmission rates.

2.2 | Statistical analysis

We performed statistical analyses using the Statistical Package for Social Sciences for Windows version 23 (SPSS Inc). Categorical variables were expressed as percentages. Continuous variables were expressed as the mean \pm standard deviation if they showed a normal distribution, while those that did not show a normal distribution were expressed as the median-limit value. Nonparametric *T*-tests, analysis of variance, and Spearman correlation tests were used for continuous variables, and the χ^2 test was used to compare categorical variables. *p* values less than 0.05 were considered statistically significant.

3 | RESULTS

A total of 80 consecutive patients who underwent elective pancreatic cancer surgery with laparotomy at the Marmara University General Surgery Clinic between January 2016 and November 2018 were assessed for eligibility for this study. Eighteen patients were excluded from the study as follows: eight patients with limited mobilization, five patients who needed intensive care, four patients with severe malnutrition, and one patient with emergent surgery. The number of patients who refused to participate was 12. A total of 50 patients underwent randomization; 25 of whom were in the ERAS group and 25 in the control group (Figure 1). In the ERAS group, seven patients were excluded (five for not undergoing PD and two for withdrawal of informed consent after allocation). In the control group, five patients were excluded (four for not undergoing PD and one for withdrawal of informed consent after allocation). Data analysis was performed on 18 patients in the ERAS group and 20 patients in the control group.

The demographics and preoperative variables are shown in Table 2. The ERAS and control groups were similar regarding age, sex, ASA scores, body mass indexes (BMI), previous abdominal surgery, comorbidities, and preoperative routine laboratory results. Also, one patient from each group had neoadjuvant therapy before the surgery.

The intraoperative variables of the patients are summarized in Table 3. The median duration of operation was 248 (180–330) min for the ERAS group and 240 (120–360) min for the control group. The median blood loss during the operation was 300 ml (100–550) in the ERAS group and 500 ml (200–750) in the control group. There was also no difference in the type of surgery, intraoperative fluid replacement, or transfusion volumes between the ERAS and control groups.

The postoperative outcomes and clinicopathologic factors of the patients are presented in Table 4. There was no significant difference between the ERAS and control groups regarding daily intravenous fluid replacement, nasogastric tube withdrawal day, postoperative VAS values, or the median time to flatus and defecation. Epidural analgesia was applied to all patients in the ERAS group but not in the control group. Additionally, all patients received opioid-sparing multimodal analgesia including paracetamol and nonsteroidal anti-inflammatory drugs. When postoperative Days 1 and 2 were considered early oral feeding, it was preferred in 94% ($n = 17$) of the ERAS group and 55% ($n = 11$) of the control group ($p = 0.009$). The number of patients with urinary catheter withdrawal on postoperative Day 1 was 15 (83%) in the ERAS group and 3 (15%) in the control group ($p = 0.000$). Also, ERAS and control groups were similar in terms of pathological diagnosis. The interval between the surgery and adjuvant chemotherapy was not different between the two groups. Although it is not statistically significant, the median time to adjuvant treatment after surgery was 37 days in the ERAS group while 45 days in the control group.

Perioperative complication rates, including pancreatic fistula, delayed gastric emptying, and postpancreatectomy hemorrhage, were similar between the ERAS and control groups. In the ERAS

- ERAS: Enhanced Recovery After Surgery

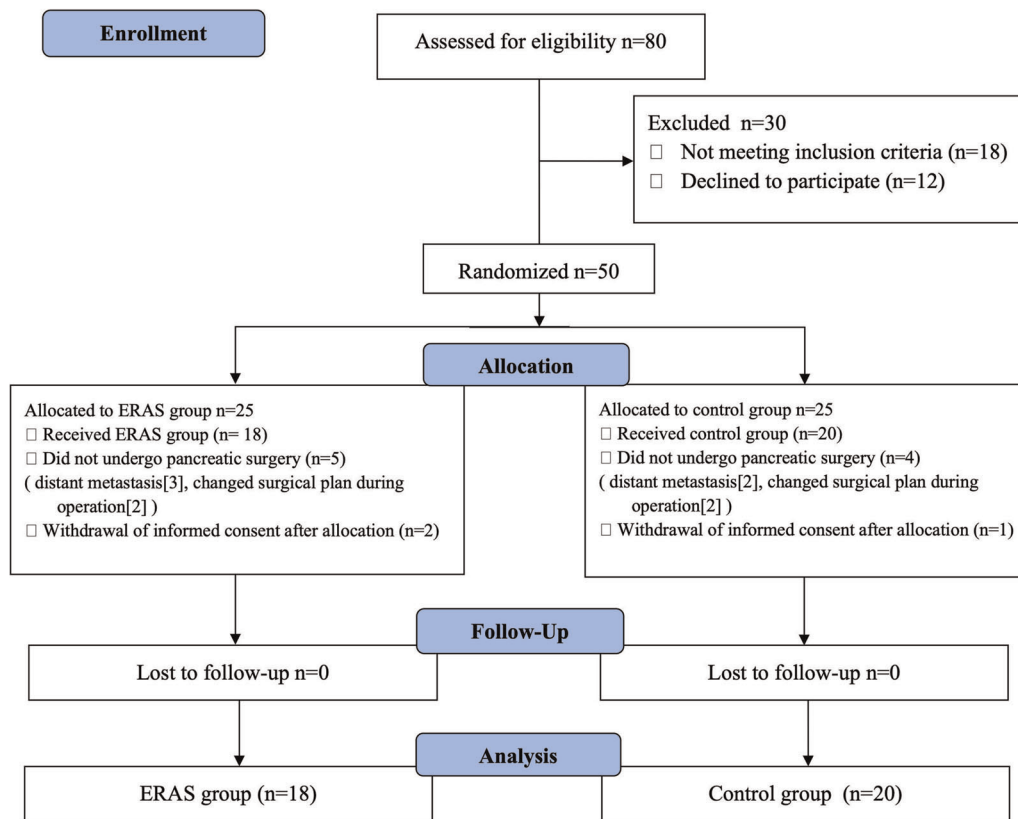


FIGURE 1 Flow chart according to CONSORT

TABLE 2 Demographics and preoperative variables

	ERAS group (18)	Control group (20)	p value
Age	51 (36–76)	64 (28–85)	0.16
Gender			
Male	9 (50%)	13 (65%)	0.35
Female	9 (50%)	7 (35%)	
ASA score 1	1 (5.6%)	1 (5%)	0.61
ASA score 2	16 (88.8%)	16 (80%)	
ASA score 3	1 (5.6%)	3 (15%)	
Previous surgery	1 (5.6%)	–	0.47
Cardiovascular disease	6 (33%)	10 (50%)	0.29
Diabetes	6 (33%)	9 (45%)	0.46
BMI kg/m ²	28 (21–35)	26 (20–36)	0.33
Preoperative blood glucose mg/dL	112 (87–183)	123 (82–249)	0.87
Preoperative albumin g/dL	3.8 (2–4.6)	4 (3–4.6)	0.36
Preoperative hemoglobin g/dL	12.5 (9.6–17.2)	13.4 (8.9–16.8)	0.17
Preoperative biliary drainage	10 (55%)	10 (50%)	0.73

Abbreviations: ASA, American Society of Anesthesiology; BMI, Body mass index; ERAS, enhanced recovery after surgery.

TABLE 3 Intraoperative variables

	ERAS group (18)	Control group (20)	p value
Operative procedure			
Whipple	16 (88%)	15 (75%)	0.4
Distal pancreatectomy	1 (6%)	2 (10%)	
Subtotal pancreatectomy	1 (6%)	2 (10%)	
Total pancreatectomy	0	1 (5%)	
Vascular resection	0	0	-
Duration of surgery (min)	248 (180-330)	240 (120-360)	0.6
Intraoperative IV fluid (ml)	2000 (750-3000)	2350 (1300-3500)	0.31
Operative blood loss (ml)	300 (100-550)	500 (200-750)	0.5
Intraoperative transfusion	5 (28%)	4 (20%)	0.7

Abbreviations: ERAS, enhanced recovery after surgery; IV, intravenous.

TABLE 4 Postoperative outcomes and clinicopathologic factors

	ERAS group (18)	Control group (20)	p value
Daily iv fluid replacement (ml)	1850 (1233-2400)	2585 (1740-3865)	0.6
Epidural analgesia	18 (100%)	-	
Day of NGT removal	PO 1: 16 (88%)	PO1: 16 (80%)	0.66
Day of urinary catheter removal	PO 1: 15 (83%)	PO 1: 3 (15%)	0.000
Early oral feeding	17 (94%)	11 (55%)	0.009
VAS score	3 (2-6)	4 (2-8)	0.13
Postop flatus	3 (2-6)	3 (2-5)	0.83
Postop defecation	4 (3-9)	5 (3-7)	0.43
LOS	7 (5-28)	8 (5-15)	0.78
Readmission	5 (28%)	7 (35%)	0.63
Pathology			0.62
Ductal adenocarcinoma	9 (50%)	11 (55%)	
Duodenal adenocarcinoma	4 (22%)	2 (10%)	
Cholangiocarcinoma	1 (6%)	1 (5%)	
Neuroendocrine tumor	2 (10%)	2 (10%)	
IPMN	1 (6%)	3 (15%)	
Others	1 (6%)	1 (5%)	
Time to adjuvant treatment (days-median)	37 (31-83)	45 (41-110)	0.18

Abbreviations: ERAS, enhanced recovery after surgery; IPMN, intraductal papillary mucinous neoplasm; LOS, length of hospital stay; NGT, nasogastric tube; VAS, visual analog scale.

TABLE 5 Postoperative complications

	ERAS group (18)	Control group (20)	p value
POPF (A-B-C)	8-0-0	11-1-0	0.33
DGE (A-B-C)	2-0-0	2-1-0	1.00
Wound infection	4	3	0.68
Pulmonary infection	2	3	1.00
PPH (A-B-C)	1-1-0	3-1-0	0.66
Intra-abdominal infection	1	1	1.00
Mortality	1	0	0.47

Abbreviations: DGE, delayed gastric emptying; ERAS, enhanced recovery after surgery; PPH, post pancreatectomy hemorrhage; POPF, postoperative pancreatic fistula.

group, one patient died on POD28 due to septic shock that developed after pancreatic leakage. Additionally, there was no statistically significant difference between the two groups in terms of wound-related infections, pulmonary infections, and intraabdominal infections. Overall, the length of hospital stay, perioperative complication rates, and readmission rates, which are the primary outcomes of the study, were similar between the two groups (Table 5).

4 | DISCUSSION

The ERAS protocol is a multimodal, multidisciplinary, and evidence-based approach in which surgeons, nurses, anesthesiologists, and other specialties work together to reduce surgical stress and enhance recovery in the postoperative period. ERAS programs can also be referred to as “fast-track surgery,” “fast-track pathway,” and “clinical pathway.”¹⁴ This method was first applied in colorectal

surgery, and the contribution of the recommendations at each step to perioperative care was analyzed.¹⁵ By the time, it has started to be used in different surgical fields, such as orthopedics, urology, and gynecological surgery. The data of these disciplines have shown that standardized ERAS methods reduce postoperative complications, accelerate postoperative recovery, reduce hospital costs, and prevent the waste of medical resources.¹⁶

Pancreatic surgery is considered one of the most complicated abdominal surgeries with high mortality and morbidity rates, although the mortality has been reduced to 2% in advanced centers with the help of surgical developments. Few systematic reviews and meta-analyses suggest that the implementation of an ERAS program in pancreatic resections is feasible and safe. In the review by Kagedan et al.,¹⁰ 10 studies were analyzed and the ERAS protocols in pancreatic surgery resulted in equivalent or better outcomes in terms of LOS, morbidity, mortality, and hospital readmission rates without evidence of harm. Additionally, Coolsen et al.¹ reported a systematic review and meta-analysis that revealed the implementation of an ERAS program in pancreatic resections may contribute to a shorter hospital stay and does not seem to compromise outcome measures, such as delayed gastric emptying, pancreatic fistula, mortality, and readmission.

Our ERAS program, which is based on the ERAS Society,¹⁷ included the following basic elements: no bowel preparation, clear liquid intake until 2 h before surgery, restrictive intravenous fluid treatment, postoperative multimodal analgesia, early oral feeding and mobilization, and early removal of drainage tubes. The short preoperative fasting period in ERAS patients can result in less insulin resistance in the postoperative period. Analgesic treatment can also lower the stress caused by pain. Additionally, early food intake and mobilization accelerate the recovery of the gastrointestinal tract.⁷

ERAS programs aim to speed up patient recovery by reducing complications. Among these, rehabilitation of gastrointestinal function is the most important after abdominal surgery. Early oral feeding is the most compatible method for digestive system physiology. It is also known to have positive effects on the immunological and inflammatory systems. Early nutrition provides early initiation of bowel movements, protects the mucosal barrier, shortens the time of gas-stool output, and reduces possible complications.¹⁸

In a meta-analysis including 3694 patients, it was reported that the delayed gastric emptying rate, infectious complications, and length of hospital stay were lower in the ERAS group. There was no difference between the groups in terms of pancreatic fistula, severe postoperative complications, mortality, or the need for readmission or reoperation.¹⁹

Age, nutritional status, and comorbidities are important factors that affect the postoperative complication rate and recovery process.²⁰ In the present study, compliance with ERAS protocols was achieved to a great extent. There was no difference between the groups in terms of age, sex, ASA score, previous surgery, comorbidities, BMI, biliary drainage, or routine blood tests. However, the morbidity of the ERAS group was lower than that of the control group. Therefore, this

situation can be interpreted as due to the positive effect of the ERAS protocols on the postoperative recovery process.

Although some authors have suggested not using any intraperitoneal drainage in low-risk fistula patients, most groups use drainage while recommending early withdrawal.⁷ While a study showed that intraperitoneal drains could be safely removed on the third postoperative day after standard pancreatic resection,²¹ another study indicated that a drain should be removed on postoperative Day 5 regardless of the amylase level in the drainage fluid.²² In the present study, drain removal criteria were determined as drain output less than 50 ml/day and drain amylase level less than three times the upper limit of normal serum amylase. Although the goal was to withdraw drains earlier in the ERAS group as a target, drains had to be removed for a similar time in the control group. Therefore, no significant difference was observed between the two groups.

The decrease in the length of hospital stay is one of the most important indicators of the implementation of the ERAS program. In the present study, we determined a period in favor of the ERAS group, although it was not statistically significant. There was no difference in terms of readmission rates, which can be interpreted as the implementation of the ERAS program not causing any additional morbidity. Although some studies showed that ERAS in cancer surgeries can improve the on-time initiation and completion of adjuvant chemotherapy after surgery, no significant reduction in the interval between the surgery and chemotherapy was observed in the ERAS group patients compared with the control group in the presented study.^{23,24}

In addition, there was relatively less delayed gastric emptying in the ERAS group, and this finding was similar to the results of other studies.^{25,26} As a complication that prolongs the length of hospital stay and thus increases medical costs, the reduction of DGE is important as the desired result in centers where pancreatic surgery is performed. Although the rate of the pancreatic fistula was similarly low, this is not enough to explain the positive effect of the ERAS protocols because of the presence of many factors affecting this development.

Our study has certain limitations. It is a single-center and low-volume study. Larger multicenter randomized studies will be required to further evaluate and compare the ERAS protocol in pancreatic surgery patients.

5 | CONCLUSIONS

In conclusion, this study shows that the ERAS protocol provides a minimal decrease in the total complication rate and has no effect on severe complications such as abdominal infection, hospitalization time, delayed gastric emptying, and overall mortality. The ERAS protocol seems safe and feasible. Therefore, this protocol could be applied safely in pancreatic surgery patients without compromising patient safety or increasing postoperative complications.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in (repository name, e.g., "figshare") at reference number (reference number).

ORCID

Muhammer Ergenc  <http://orcid.org/0000-0002-9233-0570>

Sakir Karpuz  <http://orcid.org/0000-0001-9245-1404>

Merve Ergenc  <http://orcid.org/0000-0001-6272-7174>

Cumhur Yegen  <http://orcid.org/0000-0002-9231-0940>

REFERENCES

- Coolsen M, Van Dam R, Van Der Wilt A, Slim K, Lassen K, Dejong C. Systematic review and meta-analysis of enhanced recovery after pancreatic surgery with particular emphasis on pancreaticoduodenectomies. *World J Surg.* 2013;37(8):1909-1918.
- DeOliveira ML, Winter JM, Schafer M, et al. Assessment of complications after pancreatic surgery: a novel grading system applied to 633 patients undergoing pancreaticoduodenectomy. *Ann Surg.* 2006;244(6):931-937.
- de Wilde RF, Besselink MG, van der Tweel I, et al. Impact of nationwide centralization of pancreaticoduodenectomy on hospital mortality. *Br J Surg.* 2012;99(3):404-410.
- Gouma DJ, van Geenen RC, van Gulik TM, et al. Rates of complications and death after pancreaticoduodenectomy: risk factors and the impact of hospital volume. *Ann Surg.* 2000;232(6):786-795.
- Richter A, Niedergethmann M, Sturm JW, Lorenz D, Post S, Trede M. Long-term results of partial pancreaticoduodenectomy for ductal adenocarcinoma of the pancreatic head: 25-year experience. *World J Surg.* 2003;27(3):324-329.
- Williams GA, Liu J, Chapman WC, et al. Composite length of stay, an outcome measure of postoperative and readmission length of stays in pancreatoduodenectomy. *J Gastrointest Surg.* 2019;24:1-8.
- Dai J, Jiang Y, Fu D. Reducing postoperative complications and improving clinical outcome: enhanced recovery after surgery in pancreaticoduodenectomy: a retrospective cohort study. *Int J Surgery.* 2017;39:176-181.
- Mahendran R, Tewari M, Dixit VK, Shukla HS. Enhanced recovery after surgery protocol enhances early postoperative recovery after pancreaticoduodenectomy. *Hepatobiliary Pancreat Dis Int.* 2019; 18(2):188-193.
- Xiong J, Szatmary P, Huang W, et al. Enhanced recovery after surgery program in patients undergoing pancreaticoduodenectomy: a PRISMA-compliant systematic review and meta-analysis. *Medicine.* 2016;95:18.
- Kagedan DJ, Ahmed M, Devitt KS, Wei AC. Enhanced recovery after pancreatic surgery: a systematic review of the evidence. *HPB.* 2015; 17(1):11-16.
- Bassi C, Marchegiani G, Dervenis C, et al. The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 years After. *Surgery.* 2017;161(3): 584-591.
- Wente MN, Bassi C, Dervenis C, et al. Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). *Surgery.* 2007;142(5):761-768.
- Wente MN, Veit JA, Bassi C, et al. Postpancreatectomy hemorrhage (PPH)—an international study group of pancreatic surgery (ISGPS) definition. *Surgery.* 2007;142(1):20-25.
- Lobo DN, Bostock KA, Neal KR, Perkins AC, Rowlands BJ, Allison SP. Effect of salt and water balance on recovery of gastrointestinal function after elective colonic resection: a randomised controlled trial. *Lancet.* 2002;359(9320):1812-1818.
- Lassen K, Soop M, Nygren J, et al. Consensus review of optimal perioperative care in colorectal surgery: enhanced recovery after surgery (ERAS) group recommendations. *Arch Surg.* 2009;144(10):961-969.
- Barbieri A, Vanhaecht K, Van Herck P, et al. Effects of clinical pathways in the joint replacement: a meta-analysis. *BMC Med.* 2009;7(1):1-11.
- Lassen K, Coolsen MM, Slim K, et al. Guidelines for perioperative care for pancreaticoduodenectomy: Enhanced Recovery After Surgery (ERAS[®]) Society recommendations. *World J Surg.* 2013;37(2):240-258.
- Gianotti L, Nespoli L, Torselli L, Panelli M, Nespoli A. Safety, feasibility, and tolerance of early oral feeding after colorectal resection outside an enhanced recovery after surgery (ERAS) program. *Int J Colorectal Dis.* 2011;26(6):747-753.
- Ji H-B, Zhu W-T, Wei Q, Wang X-X, Wang H-B, Chen Q-P. Impact of enhanced recovery after surgery programs on pancreatic surgery: a meta-analysis. *World J Gastroenterol.* 2018;24(15):1666-1678.
- Kobayashi S, Segami K, Hoshino H, et al. Risk factors for failure of early recovery from pancreatoduodenectomy despite the use of enhanced recovery after surgery protocols and a physical aging score to predict postoperative risks. *J Hepato-Biliary Pancreat Sci.* 2018;25(4):231-239.
- Bassi C, Molinari E, Malleo G, et al. Early versus late drain removal after standard pancreatic resections: results of a prospective randomized trial. *Ann Surg.* 2010;252(2):207-214.
- Kobayashi S, Ooshima R, Koizumi S, et al. Perioperative care with fast-track management in patients undergoing pancreaticoduodenectomy. *World J Surg.* 2014;38(9):2430-2437.
- St-Amour P, St-Amour P, Joliat G-R, et al. Impact of ERAS compliance on the delay between surgery and adjuvant chemotherapy in hepatobiliary and pancreatic malignancies. *Langenbecks Arch Surg.* 2020;405(7):959-966.
- Pang Q, Duan L, Jiang Y, Liu H. Oncologic and long-term outcomes of enhanced recovery after surgery in cancer surgeries: a systematic review. *World J Surg Oncol.* 2021;19(1):1-10.
- Balzano G, Zerbi A, Braga M, Rocchetti S, Beneduce A, Di Carlo V. Fast-track recovery programme after pancreatico-duodenectomy reduces delayed gastric emptying. *Br J Surg.* 2008;95(11): 1387-1393.
- Zouros E, Liakakos T, Machairas A, Patapis P, Agalinos C, Dervenis C. Improvement of gastric emptying by enhanced recovery after pancreaticoduodenectomy. *Hepatobiliary Pancreat Dis Int.* 2016;15(2):198-208.

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