



An Institutional Experience of Introducing an Enhanced Recovery After Surgery (ERAS) Program for Pancreaticoduodenectomy

Toru Aoyama^{1,2}, Keisuke Kazama¹, Masaaki Murakawa¹, Koichiro Yamaoku¹, Yosuke Atsumi¹, Manabu Shiozawa¹, Satoshi Kobayashi³, Makoto Ueno³, Manabu Morimoto³, Hideki Taniguchi⁴, Norio Yukawa², Takashi Oshima², Takaki Yoshikawa², Yasushi Rino², Munetaka Masuda², Soichiro Morinaga¹

¹*Department of Gastrointestinal Surgery, Kanagawa Cancer Center, Yokohama, Japan*

²*Department of Surgery, Yokohama City University, Yokohama, Japan*

³*Department of Hepatobiliary Pancreatic Oncology, Kanagawa Cancer Center, Yokohama, Japan*

⁴*Department of Anesthesiology, Kanagawa Cancer Center, Yokohama, Japan*

This study assessed whether our enhanced recovery after surgery (ERAS) program for pancreaticoduodenectomy (PD) is safe and feasible. The subjects included 109 consecutive patients who underwent PD between 2012 and 2014 at the Department of Gastrointestinal Surgery, Kanagawa Cancer Center. They received perioperative care according to the ERAS program. All data were retrieved retrospectively. Outcome measures included postoperative mortality, morbidity, hospitalization, and 30-day readmission rate. Our ERAS program included 12 elements (4 preoperative, 3 intraoperative, and 5 postoperative elements). Of the 109 patients studied, the overall incidence of morbidity was 51.4%, the incidence of mortality was 1.8%, and the incidence of readmission was 1.8%. The median postoperative hospital stay (23 days) was significantly shorter than the pre-ERAS value (29 days). Though 4 preoperative and 2 intraoperative elements were feasible, only 1 among 5 postoperative elements was applicable. Our ERAS program for PD has succeeded in shortening the postoperative

Corresponding author: Toru Aoyama, MD, PhD, Department of Gastrointestinal Surgery, Kanagawa Cancer Center, 2-3-2 Nakao, Asahi-ku, Yokohama 241-8515, Japan.

Tel.: +81 45 520 2222; Fax: +81 45 520 2226; E-mail: t-aoyama@lilac.plala.or.jp

hospital stay without increasing the risk of morbidity or mortality. The cutoff values of postoperative ERAS elements, however, were not feasible and should be reconsidered.

Key words: Pancreatic cancer – ERAS – PD

Pancreaticoduodenectomy (PD) remains the mainstay of surgical treatment for hepatobiliary and pancreatic malignancy and offers the only chance of long-term survival.^{1,2} However, the morbidity after PD has been reported to range from 30% to 65%, and the complications are sometimes fatal.^{3–8} Moreover, previous studies have demonstrated that the development of postoperative complications increases the risk of both disease recurrence and overall survival.^{9,10} Therefore, it is important to determine the most appropriate perioperative care.

Enhanced recovery after surgery (ERAS), fast-track, or clinical pathway programs are multimodal strategies that aim to attenuate the loss of or to improve the restoration of functional capacity after surgery.^{11,12} ERAS programs have many elements, including preoperative education, preoperative carbohydrate loading, omission of bowel preparation, epidural analgesia without opioids, early postoperative enteral feeding, and early mobilization of patients.¹³ ERAS is considered to reduce the rate of morbidity and shorten the length of hospital stay.^{12–14} Several studies have reported that ERAS programs are feasible and useful in gastric cancer surgery and colorectal surgery.^{12,15}

Recently, an international working group within the ERAS society published a comprehensive and evidence-based framework to enhance perioperative care in patients undergoing PD.¹⁶ However, few studies have assessed the implementation of an ERAS program following PD.^{17–19} Some studies have reported the effect of ERAS on reducing the postoperative length of hospital stay and hospital costs. Other studies have demonstrated lower morbidity, mortality, and readmission rates following the implementation of fast-track programs. However, the safety and feasibility of ERAS has not been well evaluated in patients undergoing PD.

The aim of this study was to evaluate the safety and feasibility of implementing an ERAS program for patients undergoing PD in a high-volume center.

Patients and Methods

Patients and surgical procedure

The patients were selected from the medical records of 109 consecutive patients who underwent PD at

Kanagawa Cancer Center from 2012 to 2014. All operations were performed by 4 surgeons of the pancreatic unit. All pancreatic surgeries were performed in accordance with standardized procedures described elsewhere.^{6,20–22} In brief, we performed subtotal stomach-preserving PD as the standard procedure. Lymph node groups resected *en bloc* included both the anterior and posterior pancreaticoduodenal lymph nodes, nodes in the lower hepatoduodenal ligament, and nodes along the right lateral aspect of the superior mesenteric artery and vein. In our institution, we cut the pancreas using the energy device. Modified Child method of reconstruction, including an end-to-side pancreaticojejunostomy and an end-to-side hepaticojejunostomy was performed. In the end-to-side pancreaticojejunostomy, a duct-to-mucosa anastomosis with 5-French lost stent tube was performed with eight 5-0 monofilament absorbable sutures, and an approximation of the pancreas stump and jejunal wall by four 3-0 monofilament absorbable interrupted sutures was performed.²³ An end-to-side hepaticojejunostomy was performed without a stent. Anastomosis between the jejunum and the stomach with retrocolic reconstruction was made. Multiple intraperitoneal drains were placed: the first was posterior to the hepaticojejunostomy and the second was on the anterior surface of the pancreaticojejunostomy. To prevent hypothermia, a blanket-warming system and warming set for intravenous infusions were used.

ERAS program

In their Cochrane review, Spanjersberg *et al* regard ERAS protocols as programs that include 7 or more of 17 ERAS items.¹³ Our ERAS program included 12 items: parameter 1 (preoperative counseling); parameter 2 (use of oral bowel preparation); parameter 3 (preoperative fasting and preoperative treatment with carbohydrates); parameter 4 (no preanesthetic medication); parameter 5 (use of epidural analgesia); parameter 6 (use of short-acting anesthetic agent); parameter 7 (use of warm-air body heating in operating room); parameter 8 (mobilization-care pathway); parameter 9 (prevention of nausea and vomiting); parameter 10 (stimulation of gut motility).

Table 1 Time table of the enhanced recovery after surgery program

Element	No. parameter	Operative day								
		-1	0	1	2	3	4	5	6	7
Preoperative counseling	1	Preoperative counseling was held in the outpatient clinic before hospitalization and in the ward after admission.								
Bowel preparation	2	Use of oral bowel preparation (1 g magnesium oxide)								
Oral intake	3, 10, 12	Normal diet until midnight	Oral hydration solution 3 hours before surgery	Drink water (POD 2)	Solid food (POD 4)					
Premedication	4	Patients do not receive any sedation.								
Anesthesia and analgesics	5	Use of epidural analgesia								
Body heating	6, 9	Use of short-acting anesthetic agent and prevention of nausea and vomiting								
	7	Use of warm-air body heating during surgery								
Mobilization care	8	Sit out of bed (POD 1) Walk the ward (POD 2)								
Removal of catheters	11	NGT (POD 1)								
		Urinary catheter (POD 3)								
		Drain (POD 7)								

ty); parameter 11 [early removal of catheters: removal of nasogastric tube (NGT) at day 1, removal of epidural and urinary catheter at day 3, and removal of drain at day 7]; and parameter 12 (perioperative oral nutrition; start solid food at day 5). In the present study, we set the cutoff values of parameters 11 and 12 as follows: we removed the NGT at day 1, since NGTs are unnecessary in PD,^{24,25} and abundant high-level evidence of early removal in abdominal surgery,²⁶ including pancreatic ERAS,¹⁷⁻¹⁹ has been reported. The epidural analgesia catheter was removed at day 3, since its usefulness is limited to <72 hours after open abdominal surgery.²⁷ The urinary catheter was scheduled to be removed at day 3, following the epidural analgesia removal.^{18,19} Our standard removal of the abdominal drain at day 7 seems late compared with the recent trend toward early removal.⁵ Oral intake of solid food at day 5 was implemented since this is the standard in previous ERAS program for major upper gastrointestinal (GI) and hepatobiliary-pancreatic surgery, including PD.¹⁷⁻¹⁹

Preoperative care

Preoperative counseling was held in the outpatient clinic before hospitalization and in the ward after admission. Patients were allowed to eat a normal diet until dinner of the day before surgery. Magnesium oxide was administered on the day before surgery (Table 1).

Perioperative care

The patients, excluding those who had gastric obstruction with decreased output, were allowed to eat until midnight on the day before the surgery and were required to drink the contents of two 500-mL plastic bottles containing oral rehydration solution, finishing 3 hours before surgery. Anesthesia consisted of a combination of epidural analgesia and general anesthesia.

Postoperative care

On the day of surgery and for 2 to 4 days post surgery, a continuous thoracic epidural infusion of analgesics was given. On postoperative day (POD) 1, the NGT was removed if the drainage volume was <500 mL, and patients were encouraged to sit out of bed. On POD 2, oral intake was started with water, and patients were encouraged to walk the length of the

ward. On POD 3, epidural analgesia and urinary catheter were removed. On POD 5, patients started to eat soft food; they were stepped up to regular food every 2 days (3 steps). Intra-abdominal drain monitored daily drain output volumes. Assessment of amylase content was performed at POD 1, POD 3, POD 5, and POD 7. Intra-abdominal drains were removed if (1) drain volume was <100 mL per day, (2) fluid was clear in color, and (3) amylase was less than 500 IU/L. The criteria for discharge were as follows: adequate pain relief, soft diet intake, normal laboratory data, and return to preoperative mobility level.

Definition of surgical complications

Complications of grade 2 to 5, according to the Clavien-Dindo classification, occurring during hospitalization and/or within 30 days after surgery were retrospectively determined from each patient's record. Pancreatic fistula was defined according to the International Study Group on Pancreatic Fistula (ISGPF) criteria.²⁸ Delayed gastric emptying (DGE) was indicated by an NGT that remained *in situ* or was reinserted after POD 3 (ISGPS definition).²⁹ Grade 1 complications were not evaluated to exclude the possibility of a description bias in the patient's records.

Data collection and evaluations

The ERAS program evaluated in the present study was developed by a team of surgeons and anesthesiologists working in close cooperation with a data safety monitoring committee (DSMC). This study, a retrospective analysis, was performed upon the approval of the Institutional Review Board of Kanagawa Cancer Center (Study No.: 2015.KCCH epidemiologic study - 32). Before surgery, informed consent was obtained, and the clinical data was used without identifying personal information. Continuous data are expressed as medians (range). This study was in compliance with the Declaration of Helsinki.

Results

Patients

One hundred nine patients were eligible for this study and underwent PD following the introduction of an ERAS protocol. Patient background and operative data are shown in Table 2. There were 59 men and 50 women. The median age was 70 years (range, 49–86 years). The American Society of Anesthesiologists physical status classification was

Table 2 Clinicopathological features

Parameter	No. of patients	Percentage
Age, y (range) ^a	70 (49–86)	
Sex		
Male	59	54.1
Female	50	45.9
BMI, kg/m ² (range) ^a	21.5 (14.9–31.2)	
ASA-PS		
1	10	9.2
2	92	84.4
3	7	6.4
Previous smoking habit		
Yes	54	49.5
No	55	50.5
Hypertension		
Yes	44	40.4
No	65	59.6
Diabetes mellitus		
Yes	27	24.8
No	82	75.2
Chronic pulmonary obstruction		
Yes	7	6.4
No	102	93.6
Indication for surgery		
Head of pancreatic carcinoma	75	68.8
Ampullary carcinoma	13	11.9
Distal common bile duct carcinoma	16	14.7
Endocrine neoplasm	2	1.8
Other	3	2.8
Operation time, min (range) ^a	460 (300–715)	
Bleeding, mL (range) ^a	750 (90–6730)	
Transfusion		
Yes	57	52.3
No	52	47.7

ASA-PS, American Society of Anesthesiologists physical status.

^aData are shown as median (range).

2 in most patients. The median body mass index (BMI) was 21.5 (range, 14.9–31.2).

Surgical morbidity and mortality

Postoperative complications were found in 56 of the 109 patients (51.4%). Surgical mortality was observed in 2 patients (1.8%) as a result of pneumonia. The details of the complications are shown in Table 3. Pancreatic fistula was the most frequently diagnosed complication, followed by abdominal abscess, and DGE. Grade 2 complications occurred in 64.2% of the patients, grade 3 in 28.6%, grade 4 in 3.6%, and grade 5 in 3.6%.

Implementation of the ERAS protocol

Implementation of the ERAS protocol was as follows: parameter 1 (preoperative counseling), 109

Table 3 Details of complications

	Grade 2	Grade 3a/3b	Grade 4a/4b	Grade 5	Percentage
Pancreatic fistula	11	4/1	0/0	0	14.7
Abdominal abscess	5	5/3	0/1	0	12.8
Anastomotic leakage	1	2/0	0/0	0	2.8
Pneumonia	1	0/0	0/0	2	2.8
Postoperative bleeding	1	1/0	0/0	0	1.8
Wound abscess	2	0/0	0/0	0	1.8
DGE	13	0/0	0/0	0	11.9
Portal vein thrombosis	1	0/0	0/0	0	0.9
Paralytic ileus	1	0/0	0/0	0	0.9
Bile leak	2	0/0	0/0	0	1.8
Delirium	2	0/0	0/0	0	1.8
Cholangitis	1	0/0	0/0	0	0.9
Chylous ascites	2	0/0	0/0	0	1.8
Ascites	4	0/0	0/0	0	3.6
Upper GI bleeding	2	1/0	0/0	0	1.8
Urinary tract infection	1	0/0	0/0	0	0.9
Pulmonary edema	0	0/0	1/0	0	0.9

of 109 patients (100%); parameter 2 (use of oral bowel preparation), 109 of 109 patients (100%); parameter 3 (preoperative fasting and preoperative treatment with carbohydrates), 109 of 109 patients (100%); parameter 4 (no preanesthetic medication), 109 of 109 patients (100%); parameter 5 (use of epidural analgesia), 87 of 109 patients (79.8%) [87 patients (79.8%) were commenced on epidural analgesia; in 22 (20.2%) patients, an epidural catheter was not placed owing to a coagulation disorder ($n = 4$), spinal-related disease ($n = 14$), or technical problem ($n = 4$)]; parameter 6 (use of short-acting anesthetic agent), 109 of 109 patients (100%); parameter 7 (use of warm-air body heating in theatre, 109 of 109 patients (100%); parameter 8 (mobilization-care pathway), 87 of 109 patients (79.8%); parameter 9 (prevention of nausea and vomiting), 109 of 109 patients (100%); parameter 10 (stimulation of gut motility), 102 of 109 patients (93.6%); parameter 11 (early removal of catheters): (1) removal of NGT at day 1, 102 of 109 patients (93.6%), (2) removal of epidural catheter at day 3, 27 of 87 patients (31.0%), (3) removal of urinary catheter at day 3, 16 of 109 patients (14.7%), (4) removal of drain at day 7, 40 of 109 patients (36.7%); parameter 12 (perioperative oral nutrition; start solid food at day 5), 86 of 109 patients (78.9%). In the present study, preoperative elements (parameters 1–4) and intraoperative elements (parameters 5–7) seemed feasible, but parameter 5 (87 of 109 patients (79.8%). Among the 5 postoperative elements (parameters 8–12), only parameter 9 and NGT removal (in parameter 11) seem feasible, accounting

90% < performance rate; however, the rest of the parameters seem unfeasible.

Postoperative course

The median postoperative hospital stay was 23 days (range, 7–76 days). Between 2007 and 2011, there were 71 patients who received PD in our institution. In this period, the median length of hospital stay was 29 days (range, 18–86 days). The median length of hospital stay was significantly shorter in the patients who received ERAS program ($P = 0.018$). Moreover, in patients without complications, the median postoperative hospital stay was 18 days (range, 7–30 days). However, in patients with complications, the median postoperative hospital stay was 36 days (14–76 days). Two (1.8%) patients were readmitted within 30 days after surgery. The reason for readmission was abdominal abscess.

Discussion

This study evaluated the safety and feasibility of the ERAS program in patients who underwent PD. In our study, the overall incidence of morbidity was 51.4% and the incidence of mortality was 1.8%. These results obtained with our ERAS program are safe compared with morbidity and mortality rates without the ERAS program (30%–65% and 1%–5%, respectively). Our ERAS program included 12 elements. Among the 12 elements, 4 of the preoperative elements and 2 of the intraoperative elements seemed feasible. However, of the 5 postoperative elements, only 1 parameter and NGT removal seemed feasible, while the rest of the parameters seemed unfeasible. Moreover, the median postoperative hospital stay was 23 days. The median length of stay was significantly shorter than our pre-ERAS value, while the median length of stay was longer than previous ERAS reports.

In the present study, the postoperative complications were found in 56 of the 109 patients (51.4%) and surgical mortality was observed in 2 patients (1.8%). Further, pancreatic fistula was the most frequently diagnosed complication, followed by abdominal abscess and DGE. The overall incidence of postoperative complications and mortality were similar to other PD fast-track studies. For example, Robertson *et al* evaluated the safety and efficacy of implementing an ERAS program for 50 consecutive patients undergoing PD.¹⁸ They found that the postoperative complication rate was 46% (23 patients), and the mortality rate was 4% (2 patients).

DGE was the most common complication (14%). In addition, Braga *et al* assessed compliance with an ERAS protocol and its impact on short-term outcome in 115 consecutive patients undergoing PD.¹⁷ They found the overall postoperative complication rate was 60.0% (69 patients), and the mortality rate was 3.5% (4 patients). Complications of grade 2–5 according to the Clavien-Dindo classification affected 60 patients (52.2%). Moreover, Balzano *et al* compared a large group of patients treated according to a fast-track program group ($n = 252$) with a conventionally treated group after PD ($n = 252$).¹⁹ They found that the rates of pancreatic fistula and other intra-abdominal complications were similar in the 2 groups. In addition, DGE was significantly reduced in the fast-track group (13.9% versus 24.6%, respectively; $P = 0.004$). These results suggest that the ERAS program is safe and feasible without an increase in postoperative complications and mortality, and the application of the ERAS program was not associated with any harmful effect.

ERAS is a structured, multimodal, perioperative strategy aimed at reducing surgical stress and improving patient functional capacity and quality of life after surgery.³⁰ It provides the patient with preoperative education regarding their expectations in recovery, and it is also intended to give a structured timeline for health care personnel in the management of patients. Preoperative elements and intraoperative elements were met by the majority of patients in the present study. However, postoperative elements, especially early removal of catheters, were more challenging. The number of patients having their urinary catheter removed on POD 3 was lower than expected. This was mainly because the epidural catheter was removed on POD 5 in a majority of patients. Urinary catheters were often removed only after epidural analgesia had been stopped. Why was the epidural catheter removed on POD 5? One possibility is that neither a nonsteroidal antiinflammatory drug (NSAID) nor acetaminophen was routinely used in the postoperative course in this study. Baseline NSAID analgesics could be sufficient for the prevention of postoperative pain regardless of the short-term action of the epidural analgesic.³¹ Less pain facilitated early mobilization. Moreover, Lassen *et al* previously recommended the use of NSAIDs or acetaminophen oral multimodal analgesia in their guidelines for perioperative care for PD.¹⁶ A revised ERAS protocol should include the use of NSAIDs or acetaminophen and earlier epidural catheter and urinary catheter removal. Another concern was the removal of intra-abdom-

inal drains. When comparing the previous reports and our present study, the removal of intra-abdominal drains were trend to later in the present study. There is still debate on whether or not drains should be routinely placed following PD, and their use is based on low-level evidence. However, a randomized controlled trial found significantly decreased rates of pancreatic fistula, abdominal, and pulmonary complications with early drain removal (POD 3) compared with late drain removal (POD 5 and later) in patients at low risk for pancreatic fistula (amylase values of <5000 U/L on POD 3).^{32,33} A revised ERAS protocol should perhaps include earlier analysis of drain fluid amylase, with the target of achieving earlier drain removal.

The overall median length of stay was 23 days. Although the median length of stay was significantly shorter than our pre-ERAS value, the median length of stay was longer than previous ERAS reports. This discrepancy can be explained by several factors. One possible reason is the late removal of intra-abdominal drains. A randomized controlled trial found that a prolonged period of drain insertion is associated with increased hospital stay.¹⁵ A second possible reason is that physicians are reluctant to discharge PD patients too soon after surgery, since major complications can even occur with some delay after surgery. In a recent study in patients undergoing colonic surgery, only half of the patients were discharged when all discharge criteria were met, and 43% of this group was kept in hospital because of surgeons' judgment. For this reason, several authors advise to at least add data on time-to-recovery compared with length-of-stay as outcome of ERAS programs.³⁴ A third possible reason is that the medical system after discharge is different in Japan than in other countries. Almost all the patients were discharged to home in this study, while discharge with home health care or discharge to a nursing facility might be used in other studies in other countries.³⁵

There were many limitations in this study. First, this was a retrospective single-center study with a relatively small sample size. A randomized controlled trial comparing ERAS with traditional care in PD would be the strongest way to assess the true effect of ERAS. However, this brings up ethical questions, since the majority of ERAS protocol elements have been separately proven to be effective in randomized controlled trials and meta-analysis, and several ERAS protocol elements have now become standard care.³⁶ Second, our ERAS program

did not include fluid management, which is one of the key elements of an ERAS program. Third, the optimal period of starting nutrition support was unclear in the present study. Oral intake of solid food stimulates pancreatic gland secretion of pancreatic juice; pancreatic surgeons have largely been conservative in starting early enteral feeding for pancreatic surgery patients. One concern of pancreatic surgeons is how early to start patients on a solid diet without causing a severe adverse event. It seems appropriate in settling the clinical question. However, there is a lack of evidence to support the optimal period for starting solid food, and early diet has been shown to be safe following major upper GI and hepatobiliary-pancreatic surgery, including PD. Therefore, we chose this period from the previous ERAS program for PD. However, it is unclear whether this period is fast or not. Fourth, most patients had good performance status. Patients with poor performance status (e.g., Eastern cooperative oncology group performance status ≥ 3 , severe dementia, swallowing difficulty) could not be treated in our hospital because we specialize in cancer treatment. This could be selection bias.

In conclusion, this study showed the feasibility and safety of an ERAS program following PD. However, some targets, especially postoperative elements, were challenging. Further modification of the protocol and additional education of patients and health professionals may help to improve recovery, shorten hospital stay, and enhance the return of normal function.

Acknowledgments

This work was supported, in part, by the Kanagawa Prefectural Hospitals Cancer Fund, the Uehara Memorial Foundation, and Takeda Science Foundation. Toru Aoyama and Keisuke Kazama contributed equally to this article. The authors declare that they have no competing interests.

References

- Diener MK, Knaebel HP, Heukauf C, Antes G, Büchler MW, Seiler CM. A systematic review and meta-analysis of pylorus-preserving versus classical pancreaticoduodenectomy for surgical treatment of periampullary and pancreatic carcinoma. *Ann Surg* 2007;**245**(2):187–200
- Sperti C, Pasquali C, Piccoli A, Pedrazzoli S. Survival after resection for ductal adenocarcinoma of the pancreas. *Br J Surg* 1996;**83**(5):625–631
- Povoski SP, Karpeh MS Jr, Conlon KC, Blumgart LH, Brennan MF. Association of preoperative biliary drainage with postoperative outcome following pancreaticoduodenectomy. *Ann Surg* 1999;**230**(2):131–142
- Yeo CJ, Cameron JL, Lillemoe KD, Sohn TA, Campbell KA, Sauter PK *et al.* Pancreaticoduodenectomy with or without distal gastrectomy and extended retroperitoneal lymphadenectomy for periampullary adenocarcinoma, part 2: randomized controlled trial evaluating survival, morbidity, and mortality. *Ann Surg* 2002;**236**(3):355–368
- Kawai M, Tani M, Terasawa H, Ina S, Hirono S, Nishioka R *et al.* Early removal of prophylactic drains reduces the risk of intra-abdominal infections in patients with pancreatic head resection: prospective study for consecutive 104 patients. *Ann Surg* 2006;**244**(1):1–7
- Büchler MW, Friess H, Wagner M, Kulli C, Wagnener V, Z'Graggen K. Pancreatic fistula after pancreatic head resection. *Br J Surg* 2000;**87**(7):883–889
- Munoz-Bongrand N, Sauvanet A, Denys A, Sibert A, Vilgrain V, Belghiti J. Conservative management of pancreatic fistula after pancreaticoduodenectomy with pancreaticogastrostomy. *J Am Coll Surg* 2004;**199**(2):198–203
- Tran KT, Smeenk HG, van Eijck CH, Kazemier G, Hop WC, Greve JW *et al.* Pylorus preserving pancreaticoduodenectomy versus standard Whipple procedure: a prospective, randomized, multicenter analysis of 170 patients with pancreatic and periampullary tumors. *Ann Surg* 2004;**240**(5):738–745
- Lagarde SM, de Boer JD, ten Kate FJ, Busch OR, Obertop H, van Lanschoot JJ. Postoperative complications after esophagectomy for adenocarcinoma of the esophagus are related to timing of death due to recurrence. *Ann Surg* 2008;**247**(1):71–76
- Lerut T, Moons J, Coosemans W, Van Raemdonck D, De Leyn P, Decaluwé H *et al.* Postoperative complications after transthoracic esophagectomy for cancer of the esophagus and gastroesophageal junction are correlated with early cancer recurrence: role of systematic grading of complications using the modified Clavien classification. *Ann Surg* 2009;**250**(5):798–807
- Lassen K, Soop M, Nygren J, Cox PB, Hendry PO, Spies C *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
- Varadhan KK, Neal KR, Dejong CH, Fearon KC, Ljungqvist O, Lobo DN. The enhanced recovery after surgery (ERAS) pathway for patients undergoing major elective open colorectal surgery: a meta-analysis of randomized controlled trials. *Clin Nutr* 2010;**29**(5):434–440
- 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
- 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. *Clin Nutr* 2012;**31**(6):783–800

15. Yamada T, Hayashi T, Aoyama T, Shirai J, Fujikawa H, Cho H *et al.* Feasibility of enhanced recovery after surgery in gastric surgery: a retrospective study. *BMC Surg* 2014;**14**:41.
16. Lassen K, Coolsen MM, Slim K, Carli F, de Aguiar-Nascimento JE, Schäfer M *et al.* Guidelines for perioperative care for pancreaticoduodenectomy: enhanced recovery after surgery (ERAS®) society recommendations. *Clin Nutr* 2012;**31**(6):817–830
17. Braga M, Pecorelli N, Ariotti R, Capretti G, Greco M, Balzano G *et al.* Enhanced recovery after surgery pathway in patients undergoing pancreaticoduodenectomy. *World J Surg* 2014;**38**(11):2960–2966
18. Robertson N, Gallacher PJ, Peel N, Garden OJ, Duxbury M, Lassen K *et al.* Implementation of an enhanced recovery programme following pancreaticoduodenectomy. *HPB (Oxford)* 2012;**14**(10):700–708
19. Balzano G, Zerbi A, Braga M, Rocchetti S, Beneduce AA, Di Carlo V. Fast-track recovery programme after pancreaticoduodenectomy reduces delayed gastric emptying. *Br J Surg* 2008;**95**(11):1387–1393
20. Wagner M, Z'Graggen K, Vagianos CE, Redaelli CA, Holzinger F, Sadowski C *et al.* Pylorus-preserving total pancreatectomy: early and late results. *Dig Surg* 2001;**18**(3):188–195
21. Andrén-Sandberg A, Wagner M, Tihanyi T, Löfgren P, Friess H. Technical aspects of left-sided pancreatic surgery for cancer. *Dig Surg* 1999;**16**(4):305–312
22. Seiler CA, Wagner M, Sadowski C, Kulli C, Büchler MW. Randomized prospective trial of pylorus-preserving vs. classic duodenopancreatectomy (Whipple procedure): initial clinical results. *J Gastrointest Surg* 2000;**4**(5):443–452
23. Kakita A, Yoshida M, Takahashi T. History of pancreaticojejunostomy in pancreaticoduodenectomy: development of a more reliable anastomosis technique. *J Hepatobiliary Pancreat Surg* 2001;**8**(3):230–237
24. Fisher WE, Hodges SE, Cruz G, Artinyan A, Silberfein EJ, Ahern CH *et al.* Routine nasogastric suction may be unnecessary after a pancreatic resection. *HPB (Oxford)* 2011;**13**(11):792–796
25. Kunstman JW, Klemen ND, Fonseca AL, Araya DL, Salem RR. Nasogastric drainage may be unnecessary after pancreaticoduodenectomy: a comparison of routine vs selective decompression. *J Am Coll Surg* 2013;**217**(3):481–488
26. Nelson R, Edwards S, Tse B. Prophylactic nasogastric decompression after abdominal surgery. *Cochrane Database Syst Rev* 3:CD004929
27. Werawatganon T, Charuluxanun S. Patient controlled intravenous opioids analgesia versus continuous epidural analgesia for pain after intra-abdominal surgery. *Cochrane Database Syst Rev* 1:CD004088
28. Bassi C, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J *et al.* Postoperative pancreatic fistula: an international study group definition. *Surgery* 2005;**138**(1):8–13
29. Wente MN, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, Izbicki JR *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
30. Fearon KC, Ljungqvist O, Von Meyenfeldt M, Revhaug A, Dejong CH, Lassen K *et al.* Enhanced recovery after surgery: a consensus review of clinical care for patients undergoing colonic resection. *Clin Nutr* 2005;**24**(3):466–477
31. Soop M, Carlson GL, Hopkinson J, Clarke S, Thorell A, Nygren J *et al.* Randomized clinical trial of the effects of immediate enteral nutrition on metabolic responses to major colorectal surgery in an enhanced recovery protocol. *Br J Surg* 2004;**91**(9):1138–1145
32. Conlon KC, Labow D, Leung D, Smith A, Jarnagin W, Coit DG *et al.* Prospective randomized clinical trial of the value of intraperitoneal drainage after pancreatic resection. *Ann Surg* 2001;**234**(4):487–493
33. Bassi C, Molinari E, Malleo G, Crippa S, Butturini G, Salvia R *et al.* Early versus late drain removal after standard pancreatic resections: results of a prospective randomized trial. *Ann Surg* 2010;**252**(2):207–214
34. Fiore JF Jr, Faragher IG, Bialocerkowski A, Browning L, Denehy L. Time to readiness for discharge is a valid and reliable measure of short-term recovery after colorectal surgery. *World J Surg* 2013;**37**(12):2927–2934
35. Coolsen MM, Bakens M, van Dam RM, Olde Damink SW, Dejong CH. Implementing an enhanced recovery program after pancreaticoduodenectomy in elderly patients: is it feasible? *World J Surg* 2015;**39**(1):251–258
36. Coolsen MM, van Dam RM, Chigharoe A, Olde Damink SW, Dejong CH. Improving outcome after pancreaticoduodenectomy: experiences with implementing an enhanced recovery after surgery (ERAS) program. *Dig Surg* 2014;**31**(3):177–184