Enhanced Recovery Pathways in Pancreatic Surgery

Joshua G. Barton, MD

KEYWORDS

• Enhanced recovery after surgery • ERAS • Fast-track • Pancreatoduodenectomy
• Distal pancreatectomy

KEY POINTS

- Enhanced recovery after surgery (ERAS) protocols, or fast-track pathways, use evidence-based medicine to improve recovery from surgery via institutional guidelines, nursing protocols, and order templates.
- ERAS protocols address factors in preoperative, intraoperative, and postoperative settings.
- ERAS protocols in pancreatic surgery focus on early mobilization, early oral intake, neutral fluid balance, optimal analgesia, drain management, and antibiotic selection.

INTRODUCTION

Mortality following pancreatic surgery, particularly pancreatoduodenectomy (PD), has improved dramatically over the past 4 decades. Mortality in the 1970s was as high as 25% and is now commonly lower than 2% in high-volume centers.[1] Morbidity, however, often remains in excess of 40%, despite advances in surgical technique, anesthesia, preoperative imaging, and antimicrobials. In fact, the complications most particular to pancreatic surgery, postoperative pancreatic fistula (POPF) and delayed gastric emptying (DGE), have not improved.[1]

Enhanced recovery after surgery (ERAS), or fast-track protocols, were first introduced in the 1990s to help recovery following colorectal surgery.[2] The purpose of such pathways is to use evidence-based medicine in a multidisciplinary fashion to optimize recovery from surgery and potentially decrease postoperative pain, improve complications, and shorten hospital stay. Enhanced recovery protocols focus on the entire range of surgical care, including preoperative assessment, intraoperative technique, postoperative care, and outpatient follow-up. There is significant evidence

No disclosures.

Center for Pancreatic and Liver Diseases, St. Luke's Mountain States Tumor Institute, 100 E Idaho St, STE 301, Boise, ID 83712, USA
E-mail address: bartonjo@slhs.org

Surg Clin N Am 96 (2016) 1301–1312
http://dx.doi.org/10.1016/j.suc.2016.07.003 surgical.theclinics.com
0039-6109/16/

supporting the utility of enhanced recovery protocols following colorectal surgery with few dissenting studies.[3] Studies have shown earlier resolution of postoperative ileus, shorter hospital stay, and fewer complications.[4,5] ERAS protocols have since been studied in a variety of other general surgery specialties and even orthopedics with similarly promising results.[6–9]

STUDIES ON ENHANCED RECOVERY AFTER SURGERY PROTOCOLS IN PANCREATIC SURGERY

Enhanced recovery protocols following pancreatic surgery have been studied since the early 2000s.[10–20] Each study, however, used different institutional-based protocols, which makes comparisons difficult. Furthermore, not all studies share the details of the protocol used. To address the difficulty of comparing studies and implementing protocols in institutions interested in ERAS, the ERAS Society, European Society for Clinical Nutrition and Metabolism (ESPEN), and the International Association for Surgical Metabolism (IASMEN) recently published a framework to guide future ERAS programs and studies in pancreatic surgery based on best-practices and clinical evidence.[21]

None of the available studies on ERAS in pancreatic surgery contain high levels of evidence.[22] Studies covering ERAS protocols are limited to retrospective case series or comparative case-control studies using historical controls. No completely prospective, randomized studies have been published. Despite the limited strengths of studies covering ERAS protocols in pancreatic surgery, several important findings have been made. Of 8 studies assessing length of stay (LOS), 7 found that their ERAS protocols decreased LOS by 6 to 10 days with no increase in readmission rates.[10,11,13–15,17,18,20] All the studies found that their protocols were safe with none finding an increase in morbidity or mortality. Only 1 study found a reduction in morbidity from 59% to 47% and was the largest study to date.[10] Two of 4 studies assessing hospital costs found a reduction when using ERAS protocols[11,14,15,18] (**Table 1**).

Table 1
Enhanced recovery after surgery (ERAS) protocols in pancreatic surgery

Authors, Year of Publication	Length of Stay, Days		Readmissions Rate n (%)		Morbidity, n (%)	
	Control	ERAS	Control	ERAS	Control	ERAS
Porter et al,[18] 2000	15	12[a]	10 (15)	9 (11)	20 (29)	24 (30)
Vanounou et al,[11] 2007	8	8	4 (6)	13 (9)	40 (62)	77 (54)
Kennedy et al,[15] 2007	13	7[a]	3 (7)	7 (8)	19 (44)	34 (37)
Berberat et al,[16] 2007	—	10	—	9 (4)	—	105 (41)
Balzano et al,[10] 2008	15	13[a]	16 (6)	18 (7)	148 (59)	119 (47)[a]
Kennedy et al,[14] 2009	10	7[a]	10 (25)	5 (7)[a]	15 (38)	11 (16)
di Sebastiano et al,[12] 2011	—	10	—	9 (6)	—	56 (39)
Robertson et al,[19] 2012	—	10	—	2 (4)	—	23 (46)
Nikfarjam et al,[17] 2013	14	8[a]	0 (0)	3 (15)	—	—
Abu Hilal et al,[13] 2013	13	8[a]	2 (10)	1 (4)	16 (67)	8 (40)
Coolsen et al,[20] 2014	20	14[a]	14 (14)	11 (12.8)	19 (20)	29 (34)

[a] Significant difference: *P*>.05.
Data from Refs.[10–20]

There are several systematic reviews covering ERAS protocols in pancreatic surgery and 1 meta-analysis.[23–27] The meta-analysis by Coolsen and colleagues[24] included 8 studies that met final inclusion criteria with a total of 1558 patients. Despite no overwhelming evidence within the individual studies reviewed, Coolsen and colleagues[24] found a significant risk reduction in postoperative complications by 8.2% with no increase in mortality or readmission rates when the data were assessed from a meta-analysis perspective.

FACETS OF ENHANCED RECOVERY AFTER SURGERY PROTOCOLS IN PANCREATIC SURGERY

ERAS protocols cover a variety of preoperative, intraoperative, and postoperative factors that are implemented through a variety of institutional guidelines, nursing protocols, and order templates (**Box 1**). Some facets within ERAS protocols include measures commonly accepted or previously controlled by governing bodies.[28] These facets include the following:

1. Preoperative hair removal
2. Venous thromboembolism prophylaxis
3. Neutral fluid balance
4. Early mobilization
5. Normothermia

Other facets of ERAS protocols in pancreatic surgery are not commonly accepted or controlled by governing bodies. These facets are detailed in the following sections.

Perioperative Antibiotics

The Centers for Medicare and Medicaid Services and the Centers for Disease Control and Prevention implemented the Surgical Infection Prevention Project and Surgical Care Improvement Project (SCIP) to decrease the morbidity and mortality associated

Box 1
Facets of enhanced recovery after surgery (ERAS) protocols

1. Preoperative
    a. Preoperative counseling (operation expectations, smoking cessation, alcohol consumption, nutrition optimization, mobility)
    b. Biliary drainage
    c. Mechanical bowel preparation
    d. Deep venous thrombosis prophylaxis
    e. Preoperative carbohydrate loading
2. Intraoperative
    a. Perioperative antibiotics
    b. Hypothermia management
    c. Pain management
    d. Fluid management
3. Postoperative
    a. Nutrition management
    b. Nasogastric tube management
    c. Urinary catheter management
    d. Pain management
    e. Medication management (somatostatin analogues)
    f. Drain management

with surgical site infections (SSI) in 2003.[29,30] SCIP measures addressing SSIs include the following:

1. Administration of antibiotics within 1 hour of incision time
2. Selection of appropriate antibiotic therapy
3. Discontinuation of antibiotics within 24 hours of surgery end time

SCIP measures do not specifically address antibiotic selection for pancreatic operations. For patients who are not allergic to penicillin, SCIP measures recommend cefotetan, cefoxitin, ampicillin-sulbactam, ertapenem, or cefazolin/cefuroxime with metronidazole for colonic surgery.[31] SCIP antibiotic selection for colonic surgery is often used in pancreatic surgery. Interestingly, guidelines published by the American Society of Health-System Pharmacists (ASHP), the Infectious Disease Society of America, the Surgical Infection Society, and the Society for Healthcare Epidemiology of America specify antibiotic selection for pancreatoduodenectomy, and this recommendation is limited to cefazolin.[32]

Several studies have found that antibiotics recommended by SCIP and ASHP do not address SSI concerns in pancreatic surgery adequately.[33–35] This is likely due to the prevalence of *Enterococcus* and *Enterobacter* species in SSIs following pancreatic operations. As such, piperacillin-tazobactam is considered a more appropriate choice for antibiotic prophylaxis in pancreatic surgery, particularly pancreatoduodenectomy[34] in patients who have had preoperative biliary stenting.

Preoperative Biliary Drainage

Obstructive jaundice is the most common presenting symptom of peri-ampullary carcinomas. Preoperative biliary drainage (PBD) is commonly done in the setting of obstructive jaundice to alleviate symptoms and prevent complications, namely vitamin K–associated coagulopathy. Several studies have supported the role of PBD and have indicated it is associated with a decrease in morbidity and mortality.[36–38] Other studies, including 2 meta-analyses, however, failed to show positive or negative effects of PBD.[39–41] In fact, a multicenter, randomized trial comparing routine plastic endoscopic biliary stenting with surgery alone showed that routine PBD increases the rate of complications following PD.[42] A follow-up study on that trial assessing fully covered self-expanding metal stents (FCSEMS) reaffirmed that surgery alone was associated with fewer complications, but indicated that FCSEMS were superior to plastic stents with regard to stent-related complications (but not surgery-related complications).[43] The preponderance of evidence indicates that PBD should be done only when surgery cannot be scheduled within a reasonable time frame (eg, neoadjuvant therapy) or if prolonged prothrombin time indicates that there is a risk of vitamin K–deficient coagulopathy.[44]

Oral Bowel Preparation

Historically, oral bowel preparation was used in a vast majority of gastrointestinal operations, not only as means of decreasing intracolonic bacterial counts and, hence, decreasing SSIs, but also to aid in the manipulation of bowel and conducting operations in general.[45] The negative physiologic effect of bowel preparation is not insignificant.[46] Dehydration associated with oral bowel preparation can lead to adverse effects, particularly in the elderly. Multiple clinical and animal studies fail to reveal any benefit of oral bowel preparations in colon surgery.[47,48] As a result, current recommendations by the ERAS Society recommend against oral bowel preparation for colon operations.[49]

Oral bowel preparation in pancreatic surgery has not been well studied. Retrospective studies have not found a benefit with oral bowel preparation in pancreatic surgery.[50] Therefore, oral bowel preparation is not recommended in pancreatic surgery.

Intra-Abdominal Drainage

Intra-abdominal drainage following pancreatic surgery has been an intensely debated and studied topic. In 2001, a single-institution randomized trial indicated that intra-abdominal drainage failed to reduce the morbidity and mortality following PD. Additionally, this study indicated that patients with drains were more likely to develop intra-abdominal abscesses and various fistulae, including POPF.[51] Subsequent studies, including meta-analyses, supported the findings that intra-abdominal drainage following pancreatic surgery may not offer any benefit and might increase complications, particularly in patients undergoing PD.[52–54]

In 2005, the International Study Group on Pancreatic Fistula (ISGPF) proposed a unifying definition of POPF.[55] Using a modern definition of POPF, a recent multicenter, randomized trial found that the elimination of drainage in PD was associated with a fourfold increase in mortality.[56] The findings were so profound that the trial was stopped early despite the study group hypothesizing that routine intra-abdominal drainage was unnecessary. Additionally, 2 prospective randomized trials found that early drain removal was not only safe, but actually improved postoperative morbidity, even when they were removed aggressively. Accordingly, intra-abdominal drains are recommended following pancreatic surgery with early removal on postoperative day 3 when the drain amylase content is less than 3 times the normal serum amylase (ISGPF definition of POPF).[57,58]

Preoperative Fasting and Carbohydrate Loading

Current guidelines from the American Academy of Anesthesiologists recommend the cessation of liquids and solids 2 and 6 hours before the induction of anesthesia, respectively. Although the ingestion of a carbohydrate-rich liquid approximately 2 hours before the induction of anesthesia may not result in decreased postoperative morbidity, it does decrease patient discomfort, and it may improve insulin sensitivity and skeletal muscle preservation without increasing aspiration or complications. Because it may offer some benefit and does not violate the recommended fasting guidelines, the ingestion of a carbohydrate liquid 2 hours before induction of anesthesia is recommended before pancreatic surgery.[59–61]

Gastric Decompression

Gastric decompression via nasogastric (NG) intubation is likely one of the more dogmatically adhered to principles in gastrointestinal surgery with little substantive evidence supporting its usage. Although NG tubes are commonly thought to prevent pulmonary complications, decrease the length of ileus, and decrease the risk of anastomotic dehiscence and fistula, routine usage has been long shown to be unwarranted and possibly not necessary at all,[62–65] even following pancreatoduodenectomy.[66] One of the most common facets of studies assessing ERAS protocols in pancreatic surgery is either the removal of NG tubes at the end of operation[12,16,20] or on postoperative day 1,[10,14,15,19] with no increase in overall complications. Although DGE is not an insignificant complication following pancreatic surgery,[1,67] gastric decompression does not appear to be preventive, and NG tube insertion should be used if it develops. Therefore, it is recommended that NG tubes be removed ideally at the end of pancreatic operations or on postoperative day 1 with usage only for the treatment of DGE.

Postoperative Nutrition

In a manner similar to the placement of NG tubes, maintaining a nil per os (NPO) status until bowel function returns has been adhered to particularly after upper gastrointestinal surgery, including pancreatic surgery, despite a lack of supporting evidence. A multicenter, randomized controlled trial indicated that withholding oral nutrition does not offer any benefit.[68] Along those lines, feeding jejunostomy tubes are not beneficial and possibly harmful following pancreatic surgery.[69,70] The early resumption of oral intake on postoperative day 1 is a common feature of published studies assessing ERAS protocols after pancreatic surgery and has not been associated with increased morbidity.[12–16,20]

Somatostatin Analogues

The use of somatostatin analogues in the postoperative setting to decrease the incidence of POPF is not entirely agreed on. Randomized trials have shown both that it is effective[71–73] and ineffective.[74,75] A meta-analysis involving 17 trials and 2143 patients found that although somatostatin analogues appear to decrease postoperative complications and overall POPF, they do not decrease LOS, mortality, or clinically significant POPF (ISGPF Grades B and C).[76] It is theorized that the utility of somatostatin analogues may be found in using it only for high-risk glands (soft texture and/or small duct diameter), but even this usage has dissenting evidence.[75] Until further subset studies are conducted, the routine use of somatostatin analogues cannot be recommended.

Postoperative Analgesia

The management of postoperative pain can be difficult. Although patient-controlled analgesia (PCA) with intravenous opioids can control pain, midthoracic continuous epidural analgesia (CEA) appears to provide better pain relief[77] with fewer postoperative complications.[78,79] CEA catheter malfunction, however, can occur frequently and is associated with complications and increased workload.[80]

Continuous wound infusion (CWI) with local anesthetics (OnQ Pain Relief System; Halyard Health, Inc, Alpharetta, GA) in conjunction with PCA appears to be superior to PCA alone[81] and provides pain relief equal to CEA[82] following colorectal surgery. Few studies other than case series have been conducted following pancreatic surgery, but CWI with PCA appears to at least decrease opioid consumption compared with PCA alone.[83] Alternatively, transversus abdominis plane (TAP) blocks may be equivalent to CEA in relief of pain.[84] If an institution's CEA malfunction rate can be optimized, CEA should be considered. Otherwise, CWI plus PCA or TAP block can be used.

SUMMARY

ERAS protocols were designed to optimize postoperative management in several surgical specialties. An example of an ERAS protocol used at the St. Luke's Center for Pancreatic and Liver Diseases in Boise, Idaho, is provided (**Box 2**). ERAS protocols in colorectal surgery have been shown to be effective at improving several patient outcomes, including LOS and, perhaps, morbidity. Although outcomes specific to pancreatic surgery have not been completely studied, they appear to be similar to outcomes in colorectal surgery.

Box 2
St. Luke's Center for Pancreatic and Liver Diseases ERAS protocol in pancreatic surgery

Daily pathway

Preoperative evaluation
- <30-day-old imaging
- Counseling (nutrition, hand hygiene, mobility exercises)
- Informed consent

Day before operation
- Normal oral intake until 6 hours before anesthesia
- Chlorhexidine shower PM before or AM of operation

Day of operation
- Carbohydrate drink 2 hours before anesthesia
- Hair clipping in preoperative holding
- SCD placement in preoperative holding
- Heparin 5000 IU subcutaneously in preoperative holding
- Preoperative piperacillin-tazobactam within 1 hour of incision
- Removal of nasogastric tube at end of operation
- Usage of wound protector
- Closing instruments separated from main instruments
- Gloves changed for closing
- OnQ catheters + patient-controlled analgesia (PCA)[a]

POD 1
- Up and out of bed in AM and then > 4 times a day (QID)
- Clear liquids limited 60–100 mL/h
- Acetaminophen intravenously (IV) and ketorolac[b] adjunct to analgesia
- IV fluids decreased for neutral fluid balance
- Incision cleaned with chlorhexidine wipes

POD 2
- Ambulating in hallways > QID
- Unlimited full liquids if clear liquids tolerated
- IV fluids reduced to keep vein open if oral intake >500 mL on POD 1
- Remove urinary catheter
- Incision cleaned with chlorhexidine wipes

POD 3
- Continue ambulation
- Regular diet
- Discontinue IV fluids if liquids tolerated >1000 mL
- Discontinue PCA and start oral analgesics

POD 4+
- See discharge criteria

Drain management

Check daily drain amylase

Remove on POD 3 regardless of volume if
- Drain amylase <3× normal serum value
- No sinister appearance of fluid

Discharge criteria[c]

Ambulating independently

Pain controlled with oral analgesia

Bowel function resumed
- Tolerating >67% of kcal needs orally
- Capable of self-care
- Patient consenting to discharge

Abbreviations: POD, post-operative day; SCD, sequential compression device.
[a] We have abandoned epidural usage at our institution due to a high malfunction rate.
[b] If not contraindicated due to renal function or bleeding risk.
[c] Evaluate daily (especially beyond POD 5). If ambulation or self-care criteria are not met while all other criteria are met, then consider referral to rehabilitation center.

REFERENCES

1. Cameron JL, He J. Two thousand consecutive pancreaticoduodenectomies. J Am Coll Surg 2015;220(4):530–6.
2. Kehlet H. Fast-track colorectal surgery. Lancet 2008;371(9615):791–3.
3. Dy SM, Garg P, Nyberg D, et al. Critical pathway effectiveness: assessing the impact of patient, hospital care, and pathway characteristics using qualitative comparative analysis. Health Serv Res 2005;40(2):499–516.
4. Chestovich PJ, Lin AY, Yoo J. Fast-track pathways in colorectal surgery. Surg Clin North Am 2013;93(1):21–32.
5. Kehlet H, Wilmore DW. Evidence-based surgical care and the evolution of fast-track surgery. Ann Surg 2008;248(2):189–98.
6. Kehlet H. Fast-track hip and knee arthroplasty. Lancet 2013;381(9878):1600–2.
7. Kehlet H, Thienpont E. Fast-track knee arthroplasty–status and future challenges. Knee 2013;20(Suppl 1):S29–33.
8. Mertz BG, Kroman N, Williams H, et al. Fast-track surgery for breast cancer is possible. Dan Med J 2013;60(5):A4615.
9. Schultz NA, Larsen PN, Klarskov B, et al. Evaluation of a fast-track programme for patients undergoing liver resection. Br J Surg 2013;100(1):138–43.
10. Balzano G, Zerbi A, Braga M, et al. Fast-track recovery programme after pancreatico-duodenectomy reduces delayed gastric emptying. Br J Surg 2008; 95(11):1387–93.
11. Vanounou T, Pratt W, Fischer JE, et al. Deviation-based cost modeling: a novel model to evaluate the clinical and economic impact of clinical pathways. J Am Coll Surg 2007;204(4):570–9.
12. di Sebastiano P, Festa L, De Bonis A, et al. A modified fast-track program for pancreatic surgery: a prospective single-center experience. Langenbecks Arch Surg 2011;396(3):345–51.
13. Abu Hilal M, Di Fabio F, Badran A, et al. Implementation of enhanced recovery programme after pancreatoduodenectomy: a single-centre UK pilot study. Pancreatology 2013;13(1):58–62.
14. Kennedy EP, Grenda TR, Sauter PK, et al. Implementation of a critical pathway for distal pancreatectomy at an academic institution. J Gastrointest Surg 2009;13(5): 938–44.
15. Kennedy EP, Rosato EL, Sauter PK, et al. Initiation of a critical pathway for pancreaticoduodenectomy at an academic institution–the first step in multidisciplinary team building. J Am Coll Surg 2007;204(5):917–23 [discussion: 923–4].
16. Berberat PO, Ingold H, Gulbinas A, et al. Fast track–different implications in pancreatic surgery. J Gastrointest Surg 2007;11(7):880–7.
17. Nikfarjam M, Weinberg L, Low N, et al. A fast track recovery program significantly reduces hospital length of stay following uncomplicated pancreaticoduodenectomy. JOP 2013;14(1):63–70.

18. Porter GA, Pisters PW, Mansyur C, et al. Cost and utilization impact of a clinical pathway for patients undergoing pancreaticoduodenectomy. Ann Surg Oncol 2000;7(7):484–9.
19. Robertson N, Gallacher PJ, Peel N, et al. Implementation of an enhanced recovery programme following pancreaticoduodenectomy. HPB (Oxford) 2012;14(10): 700–8.
20. Coolsen MM, van Dam RM, Chigharoe A, et al. Improving outcome after pancreaticoduodenectomy: experiences with implementing an enhanced recovery after surgery (ERAS) program. Dig Surg 2014;31(3):177–84.
21. Lassen K, Coolsen MM, Slim K, et al. Guidelines for perioperative care for pancreaticoduodenectomy: Enhanced Recovery After Surgery (ERAS(R)) Society recommendations. Clin Nutr 2012;31(6):817–30.
22. Balshem H, Helfand M, Schunemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol 2011;64(4):401–6.
23. Ypsilantis E, Praseedom RK. Current status of fast-track recovery pathways in pancreatic surgery. JOP 2009;10:646–50.
24. Coolsen MM, van Dam RM, van der Wilt AA, et al. Systematic review and meta-analysis of enhanced recovery after pancreatic surgery with particular emphasis on pancreaticoduodenectomies. World J Surg 2013;37(8):1909–18.
25. Darido EF, Farrell TM. Fast-track concepts in major open upper abdominal and thoracoabdominal surgery: a review. World J Surg 2011;35(12):2594–5.
26. Kagedan DJ, Ahmed M, Devitt KS, et al. Enhanced recovery after pancreatic surgery: a systematic review of the evidence. HPB (Oxford) 2015;17(1):11–6.
27. Spelt L, Ansari D, Sturesson C, et al. Fast-track programmes for hepatopancreatic resections: where do we stand? HPB (Oxford) 2011;13(12):833–8.
28. Measures JCNQC. Specifications Manual for Joint Commission National Quality Core Measures (2010A1). 2010; Available at: https://manual.jointcommission.org/releases/archive/TJC2010B/SurgicalCareImprovementProject.html. Accessed January 31, 2016.
29. Bratzler DW, Hunt DR. The surgical infection prevention and surgical care improvement projects: national initiatives to improve outcomes for patients having surgery. Clin Infect Dis 2006;43(3):322–30.
30. Jones RS, Brown C, Opelka F. Surgeon compensation: "Pay for performance," the American College of Surgeons National Surgical Quality Improvement Program, the Surgical Care Improvement Program, and other considerations. Surgery 2005;138(5):829–36.
31. Measures JCNQC. Prophylactic antibiotic regimen selection for surgery. Available at: https://manual.jointcommission.org/releases/archive/TJC2010B/ProphylacticAntibioticRegimenSelectionForSurgery.html. Accessed January 31, 2016.
32. Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surg Infect (Larchmt) 2013;14(1):73–156.
33. Ceppa EP, Pitt HA, House MG, et al. Reducing surgical site infections in hepatopancreatobiliary surgery. HPB (Oxford) 2013;15(5):384–91.
34. Donald GW, Sunjaya D, Lu X, et al. Perioperative antibiotics for surgical site infection in pancreaticoduodenectomy: does the SCIP-approved regimen provide adequate coverage? Surgery 2013;154(2):190–6.
35. Fong ZV, McMillan MT, Marchegiani G, et al. Discordance between perioperative antibiotic prophylaxis and wound infection cultures in patients undergoing pancreaticoduodenectomy. JAMA Surg 2016;151(5):432–9.

36. Kimmings AN, van Deventer SJ, Obertop H, et al. Endotoxin, cytokines, and endotoxin binding proteins in obstructive jaundice and after preoperative biliary drainage. Gut 2000;46(5):725–31.
37. Klinkenbijl JH, Jeekel J, Schmitz PI, et al. Carcinoma of the pancreas and periampullary region: palliation versus cure. Br J Surg 1993;80(12):1575–8.
38. van der Gaag NA, Kloek JJ, de Castro SM, et al. Preoperative biliary drainage in patients with obstructive jaundice: history and current status. J Gastrointest Surg 2009;13(4):814–20.
39. Mumtaz K, Hamid S, Jafri W. Endoscopic retrograde cholangiopancreaticography with or without stenting in patients with pancreaticobiliary malignancy, prior to surgery. Cochrane Database Syst Rev 2007;(3):CD006001.
40. Salem AI, Alfi M, Winslow E, et al. Has survival following pancreaticoduodenectomy for pancreas adenocarcinoma improved over time? J Surg Oncol 2015; 112(6):643–9.
41. Sewnath ME, Karsten TM, Prins MH, et al. A meta-analysis on the efficacy of preoperative biliary drainage for tumors causing obstructive jaundice. Ann Surg 2002;236(1):17–27.
42. van der Gaag NA, Rauws EA, van Eijck CH, et al. Preoperative biliary drainage for cancer of the head of the pancreas. N Engl J Med 2010;362(2):129–37.
43. Tol JA, van Hooft JE, Timmer R, et al. Metal or plastic stents for preoperative biliary drainage in resectable pancreatic cancer. Gut 2015. [Epub ahead of print].
44. Boulay BR, Parepally M. Managing malignant biliary obstruction in pancreas cancer: choosing the appropriate strategy. World J Gastroenterol 2014;20(28): 9345–53.
45. Fry DE. Colon preparation and surgical site infection. Am J Surg 2011;202(2): 225–32.
46. Holte K, Nielsen KG, Madsen JL, et al. Physiologic effects of bowel preparation. Dis Colon Rectum 2004;47(8):1397–402.
47. Guenaga KF, Matos D, Wille-Jorgensen P. Mechanical bowel preparation for elective colorectal surgery. Cochrane Database Syst Rev 2011;(9):CD001544.
48. Piroglu I, Tulgar S, Thomas DT, et al. Mechanical bowel preparation does not affect anastomosis healing in an experimental rat model. Med Sci Monit 2016; 22:26–30.
49. Gustafsson UO, Scott MJ, Schwenk W, et al. Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS((R))) Society recommendations. World J Surg 2013;37(2):259–84.
50. Lavu H, Kennedy EP, Mazo R, et al. Preoperative mechanical bowel preparation does not offer a benefit for patients who undergo pancreaticoduodenectomy. Surgery 2010;148(2):278–84.
51. Conlon KC, Labow D, Leung D, et al. Prospective randomized clinical trial of the value of intraperitoneal drainage after pancreatic resection. Ann Surg 2001; 234(4):487–93 [discussion: 493–4].
52. Mehta VV, Fisher SB, Maithel SK, et al. Is it time to abandon routine operative drain use? A single institution assessment of 709 consecutive pancreaticoduodenectomies. J Am Coll Surg 2013;216(4):635–42 [discussion: 642–4].
53. Peng S, Cheng Y, Yang C, et al. Prophylactic abdominal drainage for pancreatic surgery. Cochrane Database Syst Rev 2015;(8):CD010583.
54. van der Wilt AA, Coolsen MM, de Hingh IH, et al. To drain or not to drain: a cumulative meta-analysis of the use of routine abdominal drains after pancreatic resection. HPB (Oxford) 2013;15(5):337–44.

55. Bassi C, Dervenis C, Butturini G, et al. Postoperative pancreatic fistula: an international study group (ISGPF) definition. Surgery 2005;138(1):8–13.
56. Van Buren G 2nd, Bloomston M, Hughes SJ, et al. A randomized prospective multicenter trial of pancreaticoduodenectomy with and without routine intraperitoneal drainage. Ann Surg 2014;259(4):605–12.
57. 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):207–14.
58. Kawai M, Tani M, Terasawa H, et al. Early removal of prophylactic drains reduces the risk of intra-abdominal infections in patients with pancreatic head resection: prospective study for 104 consecutive patients. Ann Surg 2006;244(1):1–7.
59. Ljunggren S, Hahn RG, Nystrom T. Insulin sensitivity and beta-cell function after carbohydrate oral loading in hip replacement surgery: a double-blind, randomised controlled clinical trial. Clin Nutr 2014;33(3):392–8.
60. Smith MD, McCall J, Plank L, et al. Preoperative carbohydrate treatment for enhancing recovery after elective surgery. Cochrane Database Syst Rev 2014;(8):CD009161.
61. Yuill KA, Richardson RA, Davidson HI, et al. The administration of an oral carbohydrate-containing fluid prior to major elective upper-gastrointestinal surgery preserves skeletal muscle mass postoperatively–a randomised clinical trial. Clin Nutr 2005;24(1):32–7.
62. Bauer JJ, Gelernt IM, Salky BA, et al. Is routine postoperative nasogastric decompression really necessary? Ann Surg 1985;201(2):233–6.
63. Cheatham ML, Chapman WC, Key SP, et al. A meta-analysis of selective versus routine nasogastric decompression after elective laparotomy. Ann Surg 1995; 221(5):469–76 [discussion: 476–8].
64. Nelson R, Edwards S, Tse B. Prophylactic nasogastric decompression after abdominal surgery. Cochrane Database Syst Rev 2007;(3):CD004929.
65. Nelson R, Tse B, Edwards S. Systematic review of prophylactic nasogastric decompression after abdominal operations. Br J Surg 2005;92(6):673–80.
66. Fisher WE, Hodges SE, Cruz G, et al. Routine nasogastric suction may be unnecessary after a pancreatic resection. HPB (Oxford) 2011;13(11):792–6.
67. Traverso LW, Shinchi H, Low DE. Useful benchmarks to evaluate outcomes after esophagectomy and pancreaticoduodenectomy. Am J Surg 2004;187(5):604–8.
68. Lassen K, Kjaeve J, Fetveit T, et al. Allowing normal food at will after major upper gastrointestinal surgery does not increase morbidity: a randomized multicenter trial. Ann Surg 2008;247(5):721–9.
69. Gerritsen A, Besselink MG, Gouma DJ, et al. Systematic review of five feeding routes after pancreatoduodenectomy. Br J Surg 2013;100(5):589–98 [discussion: 599].
70. Nussbaum DP, Zani S, Penne K, et al. Feeding jejunostomy tube placement in patients undergoing pancreaticoduodenectomy: an ongoing dilemma. J Gastrointest Surg 2014;18(10):1752–9.
71. Friess H, Beger HG, Sulkowski U, et al. Randomized controlled multicentre study of the prevention of complications by octreotide in patients undergoing surgery for chronic pancreatitis. Br J Surg 1995;82(9):1270–3.
72. Suc B, Msika S, Piccinini M, et al. Octreotide in the prevention of intra-abdominal complications following elective pancreatic resection: a prospective, multicenter randomized controlled trial. Arch Surg 2004;139(3):288–94 [discussion: 295].
73. Allen PJ, Gonen M, Brennan MF, et al. Pasireotide for postoperative pancreatic fistula. N Engl J Med 2014;370(21):2014–22.

74. Sarr MG. The potent somatostatin analogue vapreotide does not decrease pancreas-specific complications after elective pancreatectomy: a prospective, multicenter, double-blinded, randomized, placebo-controlled trial. J Am Coll Surg 2003;196(4):556–64 [discussion: 564–5; author reply: 565].
75. Yeo CJ, Cameron JL, Lillemoe KD, et al. Does prophylactic octreotide decrease the rates of pancreatic fistula and other complications after pancreaticoduodenectomy? Results of a prospective randomized placebo-controlled trial. Ann Surg 2000;232(3):419–29.
76. Koti RS, Gurusamy KS, Fusai G, et al. Meta-analysis of randomized controlled trials on the effectiveness of somatostatin analogues for pancreatic surgery: a Cochrane review. HPB (Oxford) 2010;12(3):155–65.
77. Werawatganon T, Charuluxanun S. Patient controlled intravenous opioid analgesia versus continuous epidural analgesia for pain after intra-abdominal surgery. Cochrane Database Syst Rev 2005;(1):CD004088.
78. Popping DM, Elia N, Marret E, et al. Protective effects of epidural analgesia on pulmonary complications after abdominal and thoracic surgery: a meta-analysis. Arch Surg 2008;143(10):990–9 [discussion: 1000].
79. Jorgensen H, Wetterslev J, Moiniche S, et al. Epidural local anaesthetics versus opioid-based analgesic regimens on postoperative gastrointestinal paralysis, PONV and pain after abdominal surgery. Cochrane Database Syst Rev 2000;(4):CD001893.
80. Sugimoto M, Nesbit L, Barton JG, et al. Epidural anesthesia dysfunction is associated with postoperative complications after pancreatectomy. J Hepatobiliary Pancreat Sci 2016;23(2):102–9.
81. Beaussier M, El'Ayoubi H, Schiffer E, et al. Continuous preperitoneal infusion of ropivacaine provides effective analgesia and accelerates recovery after colorectal surgery: a randomized, double-blind, placebo-controlled study. Anesthesiology 2007;107(3):461–8.
82. Bertoglio S, Fabiani F, Negri PD, et al. The postoperative analgesic efficacy of preperitoneal continuous wound infusion compared to epidural continuous infusion with local anesthetics after colorectal cancer surgery: a randomized controlled multicenter study. Anesth Analg 2012;115(6):1442–50.
83. Thompson TK, Hutchison RW, Wegmann DJ, et al. Pancreatic resection pain management: is combining PCA therapy and a continuous local infusion of 0.5% ropivacaine beneficial? Pancreas 2008;37:103–4.
84. Ayad S, Babazade R, Elsharkawy H, et al. Comparison of transversus abdominis plane infiltration with liposomal bupivacaine versus continuous epidural analgesia versus intravenous opioid analgesia. PLoS One 2016;11(4):e0153675.