



Surgery

UNIVERSITY OF TORONTO

Enhanced Recovery after Surgery Protocol for Patients Undergoing Pancreatic Surgery

A Clinical Practice Guideline developed by the HBP Network in
collaboration with the University of Toronto's
Best Practice in Surgery

KS Devitt, AC Wei

Release date: April, 2017

Contents

- Section 1: General information**
- Section 2: Guideline recommendations**
- Section 3: Guideline recommendations and supporting evidence**
- Section 4: External reviewers' comments**

**Best
Practice
in
Surgery**

Acknowledgment

This Guideline is copyrighted by the Best Practice in Surgery. The Best Practice in Surgery welcomes the use of the content of the guidelines as long as you and/or your institution acknowledge the University of Toronto Best Practice in Surgery Program when using the guidelines.

Disclaimer

This guideline has been prepared using best available evidence and expert opinion. However, this guideline only provides recommendations for care and is not to be used to replace independent medical judgment. Best Practice in Surgery takes no responsibility for the use or application of this guideline and its recommendations for the care of patients.

Contact us

For information about the Best Practice in Surgery, access to all of our clinical practice guideline and implementation tools, please visit the Best Practice in Surgery website: www.bestpracticeinsurgery or contact the Best Practice in Surgery at: 416-978-0040 or bestpracticeinsurgery@utoronto.ca

Abbreviations

ACS-NSQIP	American College of Surgeons- National Surgical Quality Improvement Program
CI	confidence interval
ERaS	enhanced recovery after surgery
LMWH	low-molecular-weight heparin
MD	mean difference
NGT	nasogastric tube
NJT	nasojejunal tube
NSAID	nonsteroidal anti-inflammatory drugs
OR	odds ratio
PCA	patient controlled analgesia
POD	postoperative day
PPH	post-pancreatectomy hemorrhage
RD	risk difference
RR	risk ratio
SMD	standardized mean difference
TAP	transverse abdominis-plane
VTE	venous thromboembolism
WMD	weighted mean difference

Section 1. General Information about this Guideline

Aim

The aim of this guideline is to make recommendations on the optimal management of patients undergoing pancreatic surgery and promote the standardization of clinical care within and across institutions.

Outcomes of Interest

The outcomes of interest are decreased complications, enhanced patient recovery, decreased length of hospital stay and increased patient satisfaction.

Target Population

These recommendations apply to adult patients undergoing elective pancreatic surgery.

Intended Users

This guideline is intended for use by hepato-pancreato-biliary surgeons, surgical trainees, anesthesiologists, nurses, dietitians, occupational therapists and physiotherapists involved in the management and care of patients undergoing pancreatic surgery.

Overview of Process

These guideline recommendations are based in part on the Best Practice in Surgery clinical practice guidelines. A further review of evidence was conducted on key elements of a care for patients undergoing pancreatic surgery. The search was executed using electronic indexed sources (MEDLINE, EMBASE, and Cochrane Library). High quality research articles, including randomized controlled trials and systematic reviews, published within 5 years at the time the search was executed, were identified for review to determine best evidence recommendations. Eligible non-randomized prospective studies and retrospective studies were included in the review if there was a paucity of high quality data that met the inclusion criteria. Articles were screened for eligibility based on the following criteria: patients underwent pancreatic surgery and or major abdominal surgery, cases study involved ≥ 50 patients, clinically meaningful outcomes were measured, and the focus was not on transplant patients. Studies with < 50 cases were included if no other study identified from the literature search specifically focused on pancreatic surgery. Where evidence was weak-to-moderate, expert consensus and current practice were used to make recommendations. These recommendations are part of the Best Practice in Surgery initiative in conjunction with the HBP Network.

Rationale for Guideline on the Management of Patients Undergoing Pancreatic Surgery

Surgical process improvement tools (e.g. clinical pathway, fast track programme, or enhanced recovery after surgery (ERaS) protocol) have the capacity to improve quality of care by standardizing process of care and should therefore be utilized to guide postoperative recovery for patients undergoing pancreatic surgery.

Articles were included in the review if they focused on outcomes following the implementation of a surgical process improvement tool during the perioperative period for patients undergoing pancreatic surgery. Two systematic reviews and two prospective studies were identified and analyzed to determine the impact on patient outcomes when compared to conventional care.

The systematic review executed by Kagedan et al¹ included 10 studies, 7 retrospective²⁻⁸ and 3 prospective⁹⁻¹¹. The implementation of an ERaS protocol was associated with a decreased length of hospital stay (7-13 days vs 8-15 days) and hospital costs (\$19 561-\$126 566 vs \$23 112-\$240 242) without negatively affecting morbidity (16-54% vs 29-67%), mortality (0-4% vs 0-3%), reoperation (1-10% vs 2-12%) or readmission rates (4-15% vs 0-25%). The authors concluded the an ERaS protocol may be safely implemented for

pancreatic surgery using best available evidence. The systematic review and meta-analysis by Coolson et al¹² included 8 studies, 5 retrospective²⁻⁶ and 3 prospective⁹⁻¹¹. The results suggested an ERaS protocol may decrease length of hospital stay (7-14 days vs 8-16 days) and hospital costs (\$22 806-\$126 566 vs \$26 393-\$240 242). A meta-analysis of 4 of the included comparative studies,³⁻⁶ which included 984 pancreaticoduodenectomies and 12 total pancreatectomies, suggested an ERaS protocol may significantly reduce overall morbidity (absolute risk difference [95% confidence interval (CI)] 8.2 [2.0, 15.0], $p = 0.008$) with no change to readmission (risk difference (RD) [95% CI] 0.8% [-2.5, 4.1], $p = 0.6$) or mortality rates (RD [95% CI] 0.2% [-1.7, 2.1], $p = 0.8$). The authors concluded that an ERaS protocol for pancreatic surgery may shorten length of hospital stay without compromising morbidity and mortality.

A prospective study by Williamsson et al¹³ compared 50 patients after the implementation of a fast track programme at an academic hospital in Sweden to 50 patients that received conventional care prior to the implementation of the fast track programme. The fast track programme significantly decreased length of hospital stay (10 vs 14 days, $p = 0.001$), hospital costs (€10 400 vs €14 579, $p < 0.001$), and delayed gastric emptying (13 (26%) vs 24 (48%), $p = 0.03$) and had no significant impact on postoperative morbidity (32 (64%) vs 34 (68%), $p = 0.2$) or pancreatic fistula rates (11 (22%) vs 14 (28%), $p = 0.02$). Kobayashi et al¹⁴ conducted a prospective study in Japan which compared 100 patients managed according to a fast track programme to a historical cohort of 90 patients. The implementation of a fast track programme resulted in a significant decrease in length of hospital stay (22 vs 36 days, <0.001), pancreatic fistulas (9 (9%) vs 25 (28%), $p = 0.001$), delayed gastric emptying (2 (2%) vs 10 (9%), $p = 0.04$) and morbidity rates (39 (39%) vs 54 (60%), $p = 0.004$). The authors of both prospective studies concluded that fast track management of perioperative care following pancreatic surgery may reduce complications and decrease length of hospital stay.

In summary, surgical process improvement tools have the potential to reduce length of hospital stay and hospital costs with no deleterious impact on readmission rates, morbidity and mortality; therefore these tools, such as clinical pathways and ERaS protocols, should be utilized to improve quality of care for patients undergoing pancreatic surgery.

Section 2. Summary of Recommendations

1. Preoperative care

- 1.1 Patients and their families should receive education about the surgery and expected recovery prior to their operation. (Level of evidence: Low)
 - 1.1.1 Patients and their families should receive information on: expected length of stay assuming there are no complications; length of preoperative fasting; pain control; early ambulation and feeding; and smoking cessation (if applicable) prior to surgery
- 1.2 Patients should be allowed to eat solid foods until midnight the night before surgery (Level of evidence: High)
- 1.3 Patients should be encouraged to drink clear fluids up to 2 hours before anesthesia administration. Clear fluids include coffee and tea (without milk), and drinks that are high in carbohydrates (i.e. apple juice and pulp-free orange juice) (Level of evidence: High)
 - 1.3.1 Patients should be assessed for gastroesophageal reflux disease, dysphagia symptoms, or other gastrointestinal motility disorders preoperatively as they may require individual recommendations for perioperative fasting (Level of evidence: Low)

2. Intraoperative Care

- 2.1 Perioperative pain control should be multimodal
 - 2.1.1 Minimization of opioid exposure is recommended to reduce opioid-related side effects
 - 2.1.2 NSAIDs (e.g. COX-2 inhibitors) and acetaminophen should be used to reduce opioid consumption (Level of evidence: Low)
 - 2.1.3 The following should also be considered part of the multimodal pain management regimen: intraoperative intravenous lidocaine, intravenous ketamine (especially for patients with chronic pain issues), regional analgesia (Level of evidence: Low-Moderate)
 - 2.1.4 A detailed plan for the transition home should be in place to avoid prolonged use of opioids
- 2.2 Surgical site infection prevention (see Best Practice in Surgery recommendations)
- 2.3 Use of surgical drains
 - 2.3.1 Selective drainage is recommended for patients at high risk of fistula development based on the pancreatic fistula score (Level of evidence: Moderate)
 - 2.3.2 There is insufficient evidence to make recommendations for the use of drains in patients with a moderate to low risk of fistula
 - 2.3.3 If surgical drains are placed, early drain removal is encouraged (Level of evidence: Moderate)
- 2.4 Prophylactic use of nasogastric tubes (NG) for decompression should be avoided except for patients undergoing a pancreaticogastrostomy (Level of evidence: High)

3. Postoperative Care

- 3.1 Urinary catheters should be removed within 48 hours after surgery (Level of evidence: High)
- 3.2 Routine use of somatostatin analogues (e.g. octreotide, pasireotide) are recommended to decrease rate of complications (Level of evidence: Moderate)

- 3.3 Patients should be encouraged to participate in early mobilization once extubated (Level of evidence: Moderate)
 - 3.3.1 Patients should be encouraged to dangle on the side of their bed, walk, or sit in a chair on POD0
 - 3.3.2 Patients should be encouraged to walk at least twice on POD1 and every day until discharge
 - 3.3.3 Patients should be encouraged to sit up in a chair while awake during the day
- 3.4 Patients should resume eating and drinking as soon as possible after surgery (Level of evidence: Moderate)
 - 3.4.1 Patients should be offered clear fluids 2 hours postoperatively provided they are awake, alert and capable of swallowing
 - 3.4.2 Patients should be offered solid food beginning POD1
- 3.5 Patients should be encouraged to chew gum 3x/day for 5 minutes until they are tolerating solid food (Level of evidence: Moderate)
- 3.6 Venous thromboembolism (VTE) prophylaxis is recommended for all patients (Level of evidence: Moderate)
 - 3.6.1 Perioperative VTE prophylaxis is recommended using either unfractionated or fractionated low-molecular-weight heparin (LMWH)
 - 3.6.2 VTE prophylaxis should be continued during postoperative hospitalization
 - 3.6.3 For patients with high thrombosis risk features (e.g. Caprini Risk Assessment Scores ≥ 7), VTE prophylaxis should be extended for 4 weeks postoperatively
- 3.7 There is insufficient evidence to recommend routine use of prokinetic agents to enhance gastrointestinal motility

Section 3. Guidelines Recommendations and Supporting Evidence

1. Preoperative recommendations

Refer to Best Practice in Surgery ERAS for All Clinical Practice Guideline for supporting evidence

2. Intraoperative recommendations

2.1 Perioperative pain control should be multimodal

2.1.1 Minimization of opioid exposure is recommended to reduce opioid-related side effects

2.1.2 NSAIDs (e.g. COX-2 inhibitors) and acetaminophen should be used to reduce opioid consumption

2.1.3 The following should also be considered part of the multimodal pain management regimen: intraoperative intravenous lidocaine, intravenous ketamine (especially for patients with chronic pain), and regional analgesia

2.1.4 A detailed plan for the transition home should be in place to avoid prolonged use of opioids

Opioid-sparing analgesic strategies

Minimization of opioid exposure is recommended to reduce the incidence of opioid-related problems, such as postoperative nausea and vomiting, constipation, pruritus, urinary retention, ileus, sedation and respiratory depression. Opioid-sparing techniques should be used as part of a multimodal analgesia regimen.

Postoperative use of nonsteroidal anti-inflammatory drugs (NSAIDs) and acetaminophen

NSAIDs and COX-2 inhibitors are commonly used as part of a multimodal pain management regimen to improve postoperative analgesia and reduce opioid consumption for patients undergoing major abdominal surgery.¹⁵ However, use of these medications may be associated with anastomotic leakage in some types of procedures (e.g. colorectal surgery).¹⁶ There were no high quality studies identified that evaluated use of NSAIDs following pancreatic surgery. There was one retrospective study by Behman et al¹⁷ that conducted a review of a prospectively maintained database of 251 pancreaticoduodenectomy patients over a 10-year period at one institution. NSAIDs were a component of the multimodal pain management strategy in the early postoperative period for 127 patients. The retrospective review revealed no association between use of any NSAIDs during the early postoperative period and short-term postoperative complications. However, there was an association between COX-2 inhibitors and pancreatic fistulas (20% vs 11%, $p = 0.03$). The authors concluded that caution is warranted concerning the use of COX-2 inhibitors during the postoperative period following pancreaticoduodenectomy. Non-selective inhibitors appear to be safe and had no significant impact on pancreatic fistulas. Further research evaluating the impact of NSAIDs and COX-2 inhibitors as part of the pain management strategy following pancreatic surgery is required to verify the analgesic effect and outcomes.

Acetaminophen has also been shown to have the potential to improve postoperative analgesia and reduce opioid consumption when administered in combination with patient controlled analgesia (PCA) morphine following major surgery.^{18, 19} However, there were no studies identified that examined the use of acetaminophen as part of a postoperative pain management regimen following pancreatic surgery. Therefore the search was expanded to include recent systematic reviews and randomized controlled trials for patients undergoing major abdominal surgery. Bameshki et al conducted a randomized controlled trial at a single institution in Iran which included 60 patients with a post-gastrectomy pain regimen of either morphine plus placebo ($n = 30$) or morphine plus acetaminophen ($n = 30$).²⁰ The authors concluded that the combination of morphine plus acetaminophen reduced total morphine consumption when compared to

morphine plus placebo ($p = 0.001$). There was no significant difference in opioid-related complications, such as nausea and vomiting, pruritus and oxygen desaturation. There were no other studies identified that met the inclusion criteria for these guidelines, however the use of acetaminophen as part of an opioid-sparing analgesic strategy following gastrointestinal surgery (e.g. colorectal surgery) is common practice and should therefore be considered for this patient population.²¹⁻²³

Level of evidence: Low

Lidocaine infusion

There was no evidence available on the effects of lidocaine infusions following pancreatic surgery, therefore the search criteria was expanded to include major abdominal surgery. Four systematic reviews and meta-analyses were identified that examined the use of continuous intravenous perioperative lidocaine infusion for postoperative pain control following major abdominal surgery. Weibel et al²⁴ conducted a systematic review of 45 randomized controlled trials with 2 802 patients to examine the efficacy and safety of intravenous lidocaine for postoperative analgesia and recovery after surgery. The results suggested lidocaine reduced postoperative pain (visual analogue scale, 0-10 cm) at 1-4 hours (mean difference (MD) [95%CI] -0.8 [-1.1, -0.6]) and at 24 hours (MD [95%CI] -0.3 [-0.6, -0.1]) after surgery, but not at 48 hours (MD [95%CI] -0.2, [-0.5, 0.03]). Eleven of these studies were conducted in patients undergoing open abdominal surgery. The meta-analysis of these studies showed a significant impact of lidocaine versus control for early pain management (0-4 hours) ($p < 0.00001$). The authors concluded that lidocaine has the potential to be an alternative to epidural analgesia during postoperative recovery in patients undergoing abdominal surgery, but also recognized that there was limited evidence that lidocaine, when compared to a placebo, had an impact on pain scores and relevant clinical outcomes. The authors further acknowledged the scarcity of data informing the optimal dosage and timing of lidocaine administration. Kranke et al²⁵ reviewed 45 randomized controlled trials that assessed the effects of perioperative lidocaine infusions compared to placebo/no treatment or compared to epidural analgesia on postoperative pain and recovery. Twelve of these randomized controlled trials examined the impact following open abdominal surgery. The meta-analysis reported the same pain scores as Weibel et al. The authors concluded that there was low to moderate evidence to suggest that use of lidocaine compared to placebo has an impact on pain scores and on postoperative nausea. The comparison of intravenous lidocaine versus epidural analgesia revealed no evidence of effect at 24 hours (MD [95%CI] 1.5 [-0.3, 3.3], $p = 0.1$) and at 48 hours (MD [95%CI] 0.98 [-1.2, 3.2], $p = 0.4$) postoperatively. Furthermore, although the impacts were statistically significant, they concluded there was limited evidence to suggest perioperative lidocaine infusions impacts other relevant clinical outcomes compared to a placebo/no treatment; such as time to first flatus (MD [95% CI] -5.5 [-8.0, -3.0], $p < 0.00001$), time to first bowel movements/sound (MD [95%CI] -6.1 [-7.4, -4.9], $p < 0.00001$), risk of paralytic ileus (risk ratio (RR) [95%CI] 0.4, [0.2, 1.0], $p = 0.05$) length of stay (MD [95% CI] -0.3 [-0.6, -0.1], $p = 0.01$), and postoperative opioid consumption (MD [95% CI] -4.2 [-6.4, -1.9], $p < 0.001$). Sun et al²⁶ analyzed 21 randomized controlled trials with 1 108 patients for the efficacy of the administration of lidocaine for postoperative pain management. In 15 of these trials open abdominal surgery was performed. The authors concluded that perioperative systemic lidocaine may reduce postoperative pain intensity, reduce opioid consumption (weighted mean difference (WMD) [95% CI] -7.0 [-10.4, -3.7], $p < 0.0001$), time to first flatus (WMD [95% CI] -6.9 [-9.2, -4.6] $p < 0.00001$), time to bowel movement (WMD [95% CI] -11.7 [-17, -6.5], $p < 0.0001$) and decrease length of stay (WMD [95% CI] -0.5 [-1.0, 0.1], $p < 0.09$). Therefore intravenous lidocaine was recommended as a useful component of a pain management strategy for patients following abdominal surgery.

Khan et al²⁷ conducted a systematic review to determine the appropriate end time for an intraoperative intravenous lidocaine infusion. Seven randomized controlled trials were included in the review; three studies included 160 patients that received an intraoperative intravenous lidocaine infusion and four studies included 202 patients that received a postoperative intravenous lidocaine infusion. The intraoperative group had a significant reduction in pain at rest at 48 hours (standardized mean difference (SMD) [95% CI] -1.2 [1.9, -0.6], $p = 0.004$) and 72 hours (SMD [95% CI] -1.1 [-1.8, -0.4], $p = 0.001$) after surgery and there

was a significant reduction in pain at movement at 24 hours (SMD [95% CI] -0.4 [-0.8, -0.02], $p = 0.04$) after surgery. Additionally, the intraoperative group had a significant reduction in time to return of bowel function (MD [95% CI] -6.5 [-11.1, -1.9], $p = 0.01$). The postoperative lidocaine infusion group had a statistically significant impact on length of hospital stay (MD [95% CI] -1.0 [-1.7, -0.3], $p = 0.01$) but there was no significant reduction in the time to return of bowel function or pain scores at rest or movement at 24, 48 and 72 hours postoperatively. The authors concluded that there was no added benefit in analgesia or reduction in relevant clinical outcomes to an intravenous lidocaine infusion beyond 60 minutes postoperatively.

In summary, variability exists within the evidence regarding the ideal lidocaine regimen, including the timing of initiation and the duration of infusion. However, the evidence suggests perioperative administration of lidocaine may be an appropriate component of a multimodal pain management strategy. The heterogeneity of the aggregated studies suggests further research is required using well-designed studies to determine the most efficacious regimen and to verify the effects on relevant clinical outcomes following pancreatic surgery.

Level of evidence: Low

Intravenous ketamine

Evidence suggests intravenous ketamine may be a useful component in opioid-sparing pain management regimens for patients with opioid tolerance and for the prevention of chronic postsurgical pain.^{21, 28} There were no studies identified that examined intravenous ketamine in patients following pancreatic surgery. The search was expanded to include high quality articles that reviewed intravenous ketamine for postoperative analgesia for patients undergoing major abdominal surgery. Laskowski et al conducted a systematic review that included 70 studies, of which 32 were for abdominal surgery.²⁹ The results of the analysis suggest intravenous ketamine was effective in reducing total opioid requirements (SMD [95% CI] -0.6 [-0.8, -0.5], $p < 0.001$) and delaying the time to first analgesic (SMD [95% CI] 0.9 [0.6, 1.3], $p < 0.001$). The greatest decrease in opioid consumption was in patients undergoing upper abdominal and thoracic surgical procedures (SMD [95% CI] -1.7 [-2.6, -0.9], $p < 0.001$). The perioperative use of ketamine as part of a pain management regime appears safe, however patients in the ketamine treatment group experienced more neuropsychiatric events than patients treated with a placebo ($p = 0.02$). Therefore the risk of side effects should be considered. Further, the optimal dose and route of administration are still unknown and require further investigation.³⁰

Level of evidence: Low

Regional anesthesia

Epidural Thoracic Analgesia

There was limited evidence available on epidurals for pancreatic surgery. Thus, the search strategy was expanded to include high quality studies for patients undergoing major abdominal surgery. Two articles met the pre-defined inclusion criteria, one randomized controlled trial evaluating patients undergoing major abdominal surgery and one retrospective study examining patients following pancreatic surgery.

Ali et al³¹ conducted a randomized controlled trial which assessed the impact of epidural analgesia on the quality of life of patients undergoing major thoracoabdominal surgery. Sixty-eight patients were included in the study; 38 patients were randomized to receive an epidural analgesia and 30 patients to receive PCA. The major findings included mean pain scores that were significantly lower in the epidural group postoperative days (POD) 1, 2 and 3 ($p = 0.004$, $p = 0.003$ and $p = 0.008$). In addition, the physical and mental scores in the epidural group were significantly better than the PCA group for both SF-8 and SF-36 quality of life health surveys ($p < 0.001$). The mean length of hospital stay was shorter in the epidural

group, but this was not statistically significant ($p = 0.4$). The results of this study suggested epidural analgesia was associated with better pain control and short-term quality of life for patients undergoing major thoracoabdominal surgery compared to PCA.

A retrospective review of 42 patients conducted by Choi et al³² assessed whether epidural analgesia for pancreatic surgery helped to improve clinical outcomes. Patients with ($n = 18$) and without epidural ($n = 24$) analgesia were compared. Analgesic regimens were based on physician preference and were therefore not standardized across the 18 patients that received an epidural. Patients in the epidural analgesia group had a significantly lower median pain score (no pain 0 to severe pain 10) on POD 2 (2.3 vs 1.3, $p = 0.03$) but there was no significant difference between the pain scores on POD 1 (1.8 vs 1.2, $p = 0.3$) or POD 3 (0.0 vs 0.4, $p = 0.4$). Patients that received an epidural were more likely to require an intensive care unit admission (10 (42%) vs 14 (77%), $p = 0.02$) but there was no change to overall morbidity (12 (50%) vs 7 (36%), $p = 0.6$), mortality (0 (0%) vs 1 (6%), $p = 0.4$) or length of hospital stay (13 vs 12 days, $p = 0.6$). The authors concluded that epidural analgesia was not associated with a benefit to clinical outcomes; therefore they do not support the use of epidural analgesic in patients undergoing pancreatic surgery except to mitigate postoperative pain.

In summary, there is no strong evidence to support the mandatory use of epidural analgesia. However, studies do suggest superior pain relief for patients undergoing major abdominal surgery. Further research needs to be conducted to assess the efficacy of epidural analgesia following pancreatic surgery. Evidence supports epidural analgesia as part of a multimodal pain management strategy for this patient population and use should be as per the judgment of the treating surgeon and anesthesiologist.

Level of evidence: Moderate

Transverse abdominis-plane (TAP) block

Transverse abdominis-plane block (TAP) technique was first described in detail in 2001.³³ Since then researchers have examined the benefits of TAP block in abdominal surgery compared to epidurals and other forms of regional anesthesia administration. There were no studies identified that specifically examined TAP blocks in patients undergoing pancreatic surgery. Johns et al³⁴ conducted a systematic review and meta-analysis of nine randomized controlled trials containing 413 patients that compared TAP block with either placebo or no TAP block in patients undergoing abdominal surgery. Results suggested TAP block reduced the mean morphine use within the first 24 hours after surgery (MD [95%CI] -23.7 [-38.7, -8.8], $p = 0.002$) and reduced the incidence of postoperative nausea and vomiting (odds ratio (OR) [95%CI] 0.4 [0.2, 0.7], $p = 0.003$). The authors concluded that TAP block have the potential to improve analgesia and reduce opioid-related side effects as part of a multimodal pain management strategy. Charlton et al³⁵ assessed the effects of TAP block on postoperative analgesia requirements following abdominal surgery by conducting a systematic review and meta-analysis of 5 randomized controlled trials. The authors concluded that compared to no TAP block or saline placebo the TAP block resulted in significantly less postoperative requirement for morphine at 24 (MD [95%CI] -22 [-37.9, 6.0], $p = 0.007$) and 48 hours (MD [95%CI] -28.5 [-38.9, -18.1] $p < 0.00001$). There was no significant difference between the two groups for incidents of postoperative nausea and vomiting (RR [95% CI] 0.8 [0.3, 1.8], $p = 0.5$)

In summary, further research is required to validate the evidence supporting the analgesic efficacy of TAP block catheters following pancreatic surgery. The use of TAP block as part of a multimodal pain management strategy should be at the discretion of the treating anesthesiologist and surgeon.

Level of evidence: Moderate

Discharge planning

A detailed plan for the transition to home should be in place to avoid prolonged use of opioids following pancreatic surgery. Patients should be educated regarding use and side effects of any prescribed opioid analgesics at discharge. There should also be a clear weaning plan in place.²³

2.2 Surgical site infection prevention

See supporting evidence available in the Best Practice in Surgery Surgical Site Infection Clinical Practice Guideline.

2.3 Use of surgical drains

2.3.1 Selective drainage is recommended for patients at high risk of fistula development based on the pancreatic fistula score

2.3.2 There is insufficient evidence to make recommendations for the use of drains in patients with a moderate to low risk of fistula

2.3.3 If surgical drains are placed, early drain removal is encouraged

Five systematic reviews were identified and analyzed for patient outcomes following pancreatic surgery. The systematic review and meta-analysis conducted by Dou et al³⁶, Nitsche et al³⁷, Rondelli et al³⁸, and Wang et al³⁹ examined 9, 8, 7, and 5 studies, respectively, all variations of the same nine studies (2 randomized controlled trials^{40, 41} and 7 retrospective studies⁴²⁻⁴⁸). Dou et al³⁶ concluded that omitting prophylactic abdominal drainage may result in higher mortality after pancreatectomy (OR [95%CI] 1.6 [0.9, 2.9], $p = 0.09$) and pancreaticoduodenectomy (OR [95%CI] 2.4 [1.2, 4.7], $p = 0.01$). They found no significant increase in the risk of abdominal abscess with use of prophylactic drainage. Nitsche et al³⁷ results suggested overall morbidity after any kind of pancreatic resection was lower without drains ($p = 0.04$), and found no significant difference in mortality rates. For patients undergoing pancreaticoduodenectomy there were no differences in morbidity ($p = 0.40$) but there were increased rates of intra-abdominal abscesses ($p = 0.04$) and mortality ($p = 0.04$) without intraperitoneal drainage. Rondelli et al³⁸ showed intra-abdominal drainage may increase pancreatic fistulas (OR [95%CI] 2.3 [1.5, 3.5], $p < 0.0001$), total postoperative complications (OR [95%CI] 1.5 [1.3, 1.8], $p < 0.00001$) and re-admission rates (OR [95%CI] 1.3 [1.1, 1.6], $p = 0.01$). Presence or absence of a drain was not found to have a significant correlation to overall mortality rates ($p = 0.09$). Wang et al³⁹ suggested patients without prophylactic drainage after pancreaticoduodenectomy may have significantly higher mortality (OR [95%CI] 2.3 [1.1, 4.9], $p = 0.02$) but fewer overall complications (OR [95%CI] 0.6 [0.5, 0.8], $p = 0.01$), major complications (Clavien grade III-IV) (OR [95%CI] 0.8 [0.6, 0.9], $p = 0.01$), and readmissions (OR [95%CI] 0.8 [0.6, 1.0], $p = 0.04$). The randomized controlled trial by Van Buren et al⁴¹ was terminated early due to findings that suggested routine omission of drains in patients undergoing pancreaticoduodenectomies increased mortality and the severity and frequency of overall complications. McMillan et al⁴⁹ further analyzed the data from Van Buren et al⁴¹ to assess the effect of routine drain placement on the occurrence and severity of clinically relevant postoperative pancreatic fistulas. The authors concluded that patients with moderate (3-6 points) to high (7-10 points) fistula risk based on the Fistula Risk Score⁵⁰ appear to benefit from the use of surgical drains.

The systematic review and meta-analysis conducted by Diener et al⁵¹ examined 4 trials, pertaining to the use of surgical drains after pancreatic surgery. Of these 4 trials, 1 randomized controlled trial⁴⁰ and 1 retrospective study⁴⁴ with a total of 268 patients compared drain versus no drain insertion in patients that had undergone pancreatic cancer surgery. The authors found no significant differences in mortality (OR [95%CI] 1.0 [0.1, 7.0], $p = 1.0$), incidence of postoperative complications (OR [95%CI] 0.8 [0.5, 1.3], $p = 0.4$), pancreatic fistula (OR [95%CI] 0.1 [0.01, 1.8], $p = 0.2$), re-operation and re-intervention rates (OR [95%CI] 1.1 [0.1, 9.7], $p = 0.09$), and length of hospital stay (MD [95%CI] 0.0 [-0.4, 0.4], $p = 1.00$). The remaining 1 randomized controlled trial⁵² and 1 prospective observational study⁵³ with a total of 218 patients compared early drain removal vs late drain removal in patients that had undergone pancreatic surgery. The authors found no significant difference in mortality (OR [95%CI] 0.3 [0.01, 8.2], $p = 0.5$), reduction of postoperative complications (OR [95%CI] 2.7 [1.3, 5.8], $p = 0.009$) or reduction of pancreatic fistula formation after the early removal of drains compared to late removal (OR [95%CI] 0.1 [0.03, 0.6],

p = 0.01). The randomized controlled trial⁵² was re-analyzed by McMillan et al⁵⁴ to identify patients that may benefit from selective drainage. The authors concluded that prophylactic drainage should be avoided for patients with negligible to low fistula risk. Routine drainage was recommended for moderate to high fistula risk patients with a POD 3 drain removal if POD 1 drain fluid amylase is $\leq 5\,000$ U/L. For patients with POD 1 drain fluid amylase $> 5\,000$ U/L or suspected fistula risk based on clinical intuition, drain removal was recommended to be at the discretion of the treating surgeon.

Fong et al⁵⁵ conducted a prospective validation study to determine the appropriate patient population that should be selected for early drain removal (\leq POD 5) following the placement of intraperitoneal drains after pancreatic surgery. The study measured daily postoperative drain amylase levels and correlated them to the development of pancreatic fistulas in two cohorts of patients undergoing pancreatic surgery. The results from first cohort of patients (N = 126) established the drain amylase threshold for the prediction of postoperative pancreatic fistula formation. The results from the second cohort of patients (N = 369) validated the predictive capabilities of the POD 1 drain amylase level and its correlation with the incidence of pancreatic fistulas. In the validation cohort, 2 (0.9%) patients developed a pancreatic fistula out of the 229 (62%) patients that had POD 1 drain amylase values < 600 U/L compared to 44 (31%) out of the 140 (38%) patients that had a POD 1 drain amylase values ≥ 600 U/L. A multivariate analysis identified POD 1 drain amylase level < 600 U/L as the strongest independent predictor of the absence of pancreatic fistula (P < 0.0001). Other variables that had a statistically significant association with the drain amylase volume included pathology, duration of surgery, anastomosis type, body mass index and age-adjusted Charlson index score. The authors concluded that POD 1 drain amylase measurement can be used to stratify patients into low and high risk groups for the development of a pancreatic fistula, and early drain removal (POD 1) can be advocated in patients stratified to the low risk group thus minimizing patient discomfort and morbidity associated with prolonged intraperitoneal drainage.

Witzigmann et al⁵⁶ conducted a randomized controlled trial that was not reviewed in the aforementioned systematic reviews. The study compared 395 patients undergoing pancreatic surgery with pancreaticojejunal anastomosis. Patients were randomized to receive either no drain (N = 193) or intra-abdominal drainage (N = 202). There was no significant difference between surgical (p = 0.7), medical (p = 0.6) or overall morbidity (p = 0.5). Grade B/C pancreatic fistula were significantly lower in the no-drain group (12% vs 6%, p = 0.03). Fistula-associated complications were significantly increased in the drain group (26% vs 13%, p = 0.0008). The reintervention rate was lower in the no-drain group (21% vs 17%). However, postoperative ascites was significantly higher in the no-drain group (1% vs 7%, p = 0.002). The authors concluded that the abandonment of drains did not increase reintervention rates, mortality and overall morbidity. The results of this study suggest routine prophylactic drainage should not be recommended for patients undergoing pancreatic resection with pancreaticojejunal anastomosis.

In conclusion, the 5 systematic reviews provided mixed results with respect to prophylactic intra-abdominal drainage of patients undergoing pancreatic resection. The evidence suggests placement of surgical drains in select patients following pancreatic surgery may reduce postoperative complications but routine drainage is not recommended for this patient population. Therefore, routine omission of intra-abdominal surgical drains cannot be advocated, selective drainage is recommended at the discretion of the treating surgeon.

Level of evidence: Moderate

2.4 Prophylactic use of nasogastric tubes (NGT) for decompression should be avoided except for patients undergoing pancreaticogastrostomy

Two randomized controlled trials and two systematic reviews and meta-analyses were identified. Studies were included if they focused on prophylactic postoperative routine use of nasogastric (NGT) or nasojejunal (NJT) tubes in patients undergoing major abdominal surgery.

The systematic review and meta-analysis by Wei et al⁵⁷ reviewed 8 randomized controlled trials⁵⁸⁻⁶⁵ that compared subjects with and without NGT/NJT decompression after gastrectomy. Patients were randomized to an NGT group (n = 570) and No NGT group (n = 571). There was no significant difference in major complications (RR [95%CI] 1.3 [0.9, 1.8], p = 0.2), minor complications (RR [95%CI] 0.9 [0.6, 1.3], p = 0.6) or time to first flatus (WMD [95%CI] 0.1 [-0.2, 0.4], p = 0.4) between the two groups. There was a decrease in length of hospital stay (WMD [95%CI] 0.8 [0.3, 1.3], p = 0.001) and time to first oral intake (WMD [95%CI] 0.5 [0.3, 0.8], p < 0.001) for patients that did not receive an NGT/NJT. Authors concluded NGT/NJT decompression did not facilitate the recovery of bowel function nor reduce the risk of postoperative complications, and was therefore unnecessary after gastrectomy. Verma and Nelson⁶⁶ conducted a systematic review and a meta-analysis of 37 randomized controlled trials examining prophylactic use of NGT tubes for decompression following abdominal surgical procedures. Included in this review were colorectal, gastroduodenal, biliary, esophageal, and hepatic surgeries. All studies combined included 5711 patients, 2866 patients were randomized to routine NGT use and 2845 patients were randomized to selective or non-routine use of NGT. Patients that did not receive prophylactic NGT decompression following major abdominal surgery were found to have an earlier return of bowel function (MD [95% CI] 0.5 [0.5, 0.6], p < 0.0001) and a reduction in pulmonary complications (OR [95%CI] 1.5 [1.1, 1.9], p = 0.1). There was no change to length of hospital stay (MD [95% CI] 0.5 [0.4, 1.5], p = 0.3), anastomotic leaks (OR [95% CI] 1.1 [0.7, 1.8], p = 0.6) and wound infections (OR [95% CI] 0.8 [0.6, 1.2], p = 0.3). The review examined major outcomes relating to the intended goal of using prophylactic NGT/NJT and concluded that routine use for patients undergoing abdominal surgery should be abandoned in favour of selective use of NGT/NJT decompression.

Pacelli et al⁶³ completed a randomized controlled trial with 270 patients randomized to NG/NJT (n = 134) compared to no NGT/NJT (n = 136). There was no change to length of hospital stay (11 ± 5 days vs 11 ± 8 days, p = 0.9), overall complications (38 (28%) vs 36 (27%), p = 0.5), or persistent decompression (>7 days) and reinsertion (14 vs 18, p = 0.5). For patients that did not receive an NGT there was an increase in time to first flatus (3.5 ± 2 days vs 4.2 ± 2 days, p = 0.02), and increased abdominal distention compared to baseline (2 ± 1 cm vs 3 ± 1 cm, p = 0.0001) but a decreased time to liquid diet (5 ± 2 days vs 4.5 ± 2 days, p = 0.01). Authors concluded that routine placement of an NGT/NJT is not necessary in elective surgery for gastric cancer.

Sapkota et al⁶⁷ conducted a randomized controlled trial for patients undergoing emergency laparotomy for perforation peritonitis, intestinal obstruction and abdominal trauma. Patients that received NGT decompression (n = 61) were compared to a control group that did not receive NGT decompression following an emergency laparotomy (n = 54). There was no significance difference in postoperative complications, specifically gastric upset (34% vs 39%, p = 0.4), wound complications (16% vs 11%, p = 0.3), respiratory complications (12% vs 11%, p = 0.3), and anastomotic leaks (2% vs 2%, p = 0.6). Furthermore, there was no significant difference between the time to first flatus (p = 0.1) and NGT reinsertion rates (3% vs 4%, p = 0.4). The mean length of hospital stay was significantly less for patients that did not receive NGT decompression (8 vs 6 days, p < 0.05). Authors concluded that prophylactic NGT decompression is ineffective at achieving its intended goals and routine use should be questioned.

Patients that have a pancreaticogastrostomy as an alternative to a jejunal anastomosis may require a nasogastric tube to decompress the stomach and relieve tension on the anastomosis after surgery.⁶⁸ Therefore prophylactic use of NGT intubation should be used at the discretion of the treating surgeon when a patient has had a pancreaticogastrostomy.^{68, 69}

In summary, the evidence indicates that the original rationale for using prophylactic NGT intubation (e.g. reduction in wound infections, anastomotic leaks, and pulmonary complications and shorter length of hospital stay) are no longer valid based. As such, its routine use should be avoided following pancreatic surgery, with the exception of patients that have had a pancreaticogastrostomy.

Level of evidence: High

3. Postoperative recovery

3.1 Urinary catheters should be removed within 48 hours after surgery

Studies were included in the review if they focused on routine use of postoperative urinary catheters in patients undergoing major abdominal surgery. One study met this inclusion criteria, a randomized controlled trial by Zmora et al⁷⁰ that included 118 patients who underwent colon and rectal surgery between 2005 and 2008. Patients were divided into three groups each with a different day of urinary catheter discharge. The urinary catheter was removed on either POD 1, 3 or 5. They found that acute urinary retention requiring catheter reinsertion occurred in 12 (10%) patients. More specifically, retention occurred in 6 (15%) patients in whom the catheter was removed on POD 1 compared with 4 (11%) patients whose catheter was removed on POD 5 ($p = 0.4$). A sub-group analysis found that patients with low colorectal anastomosis or coloanal anastomosis (6 cm and below the anal verge) had a significantly increased risk for retention ($p = 0.04$). There was no significant difference between the three groups with regards to symptomatic bacteriuria ($p = 0.3$), urinary tract infections ($p = 0.1$), anastomotic leak ($p = 0.3$), pulmonary complications ($p = 0.8$), or surgical site infections ($p = 0.2$), however, there was a slight trend towards higher rates of the above variables in the group where the urinary catheter was discharged on POD 5. Trickey et al conducted a retrospective study using the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) to identify risk factors for surgical patients who develop postoperative urinary tract infections.⁷¹ The analysis included 8801 patients from the ACS-NSQIP database between 2006 and 2010. 116 (1%) of these patients developed a UTI within 30 days of surgery. When compared to matched controls, patients who developed urinary tract infections were significantly more likely to have had the urinary catheter maintained beyond POD 2 (77 (66%) vs 96 (43%), $p < 0.001$) and to have a longer mean catheter duration (12 vs 5 days, $p < 0.001$).

In summary, the evidence indicates that routine prolonged urinary drainage after pancreatic surgery is not necessary and that rates of urinary tract infections increase among patients whose urinary catheter is maintained beyond POD 2.

Level of evidence: High

3.2 Routine use of somatostatin analogues (e.g. octreotide or pasireotide) are recommended to decrease rate of complications

Studies were included in the review if they focused on routine perioperative administration of somatostatin analogues in adults undergoing pancreatic surgery. One systematic review and meta-analysis and one randomized controlled trial were identified. Gurusamy et al⁷² completed a systematic review which included 21 studies involving 2 348 patients. The goal of this study was to determine whether somatostatin analogues should be used routinely in pancreatic surgery. All studies compared a somatostatin to either no drug or a placebo. There was no significant difference in length of hospital stay ($p = 0.06$), perioperative mortality ($p = 0.2$), reoperation rates ($p = 0.6$), anastomotic leaks ($p = 0.4$), pancreatitis ($p = 0.2$), renal failure ($p = 0.4$), delayed gastric emptying ($p = 0.3$), pulmonary complications ($p = 0.6$) or infected abdominal collections ($p = 0.7$). For patients treated with a somatostatin analogue there was a decrease in overall postoperative complications (RR [95%CI] 0.7 [0.6, 0.8], $p < 0.0001$), pancreatic fistulas (RR [95%CI] 0.7 [0.6, 0.8], $p < 0.00001$), and sepsis (RR [95%CI] 0.4 [0.2, 0.9], $p = 0.002$). The authors concluded that somatostatin analogues may reduce perioperative complications but do not reduce perioperative mortality. Based on the current evidence, the authors recommended somatostatin and its analogues for routine use for patients undergoing pancreatic surgery.

Allen et al⁷³ conducted a randomized controlled trial comparing the somatostatin analogue pasireotide to a placebo for patients undergoing pancreatic resection. There were 300 patients included in the study; 152 patients were randomly assigned to pasireotide and 148 patients to the placebo arm. The rate of grade 3

or higher postoperative pancreatic fistula, leak, or abscess were significantly lower among patients who received pasireotide than among patients who received placebo (RR [95%CI] 0.4 [0.2, 0.8], $p = 0.01$). There was also a significant decrease in readmission rates (26 (17%) vs 43 (29%), $p = 0.02$) but no significant change to length of hospital stay (8 ± 4 days vs 9 ± 7 days, $p = 0.2$).

In summary, evidence regarding the optimal somatostatin analogue is mixed and requires further investigation. However, data suggests somatostatin and its analogues may reduce the incidence of postoperative complications. Therefore, somatostatin and its analogues are recommended for routine use in patients undergoing pancreatic surgery.

Level of evidence: Moderate

3.3 Patients should be encouraged to participate in early mobilization once extubated

3.3.1 Patients should be encouraged to dangle on the side of their bed, walk, or sit in a chair on POD0

3.3.2 Patients should be encouraged to walk at least twice on POD1 and every day until discharge

3.3.3 Patients should be encouraged to sit up in a chair while awake during the day

Studies were included if they focused on routine postoperative early mobilization in patients undergoing major abdominal surgery. One randomized controlled trial and one prospective study were identified and analyzed for patient outcomes. The first trial to evaluate the use of ambulation in the context of a multimodal approach was completed by Lee et al.⁷⁴ Patients who had received laparoscopic colon surgery ($N = 100$) were randomized into a rehabilitation group with early mobilization and diet or to a conventional care group. They measured recovery time by including: tolerance of diet for 24 hours (eat 1/3 or more of their meal), analgesic free after cessation of PCA, safe ambulation (ambulation 600 m without assistance) and afebrile status without major complications. They found that a rehabilitation program resulted in a significant decrease in the median time to recovery after laparoscopic colon surgery (4 (3-5) days vs 6 (5-7) days, $p < 0.0001$). The median time to safe ambulation was significantly shorter in patients that were in the rehabilitation group compared to the patients treated with conventional care (18 (14-21) hours vs 21 (18-24) hours, $p = 0.003$). There was no evidence of an adverse effect on pain scores 1 ($p = 0.7$) and 4 weeks ($p = 0.9$) postoperatively or overall complications ($p = 0.1$). Patients treated in the rehabilitation program had a significantly shorter time to analgesic-free (88 (72-120) hours vs 117 (86-149) hours, $p = 0.02$). The quality of life scores between the two groups were similar at 1 and 4 weeks postoperatively. There were no readmissions or mortality within 1 month of surgery in either group. The authors concluded that a rehabilitation program with early mobilization and diet after laparoscopic colon surgery may reduce recovery time without increasing complications.

In the prospective study by Kibler et al⁷⁵ they implemented a quality improvement strategy to encourage early patient mobilization following colorectal and urologic surgeries at their local academic medical centre. Patient outcomes were collected 6 months prior to the intervention and for a 6-month period after the implementation of the program. In both cohorts patients were divided into two units, a control unit and the intervention unit. There were 1 878 patients in the pre-intervention cohort (1 125 control vs 753 intervention) and 1 748 patients in the post-intervention cohort (1 047 control vs 701 intervention). There was no significant difference between the groups for postoperative complications, hospital costs or length of hospital stay. The distance ambulated increased from 264 to 176 feet/day. The statistical significance of this increase was not reported. There was no reported increase in patient falls and there was significantly less postoperative paralytic ileus in the cohort treated postoperatively on the intervention unit (7.3% vs 4.6%, $p = 0.04$). The quality improvement program was successfully implemented. The authors concluded that early ambulation in patients undergoing colorectal and urologic surgery can be achieved without increasing length of hospital stay, hospital costs or complication rates, and it may reduce paralytic ileus.

In summary, data suggests early mobilization after surgery may provide multiple postoperative benefits. The effect of early mobilization on overall recovery must be taken in context with the other modalities used.

Level of evidence: Moderate

3.4 Patients should resume eating and drinking as soon as possible after surgery

3.4.1 Patients should be offered clear fluids 2 hours postoperatively provided they are awake, alert, and capable of swallowing

3.4.2 Patients should be offered solid food beginning POD1

Studies were included if they focused on routine postoperative early feeding compared to late feeding for patients undergoing major abdominal surgery. Three systematic reviews were included in the evaluation of evidence. Willcutts et al conducted a systematic review and meta-analysis comparing early oral feeding to traditional oral feeding after upper gastrointestinal surgery.⁷⁶ Fifteen studies were included in the analysis with a total of 2 112 patients. Each study's intervention cohort was fed orally earlier than the control cohort. In 12/15 studies oral intake for the intervention cohort was started on POD 1 or earlier. The results revealed no significant difference in anastomotic leak rates (OR [95% CI] 0.8 [0.5, 1.3], $p = 0.5$), pneumonia (OR [95% CI] 0.8 [0.5, 2.6], $p = 0.3$), NGT reinsertion (OR [95% CI] 0.4 [0.1, 1.3], $p = 0.1$), reoperation (OR [95% CI] 0.8 [0.5, 1.3], $p = 0.3$), readmission (OR [95% CI] 1.1 [0.7, 1.9], $p = 0.7$) or mortality rates (OR [95% CI] 1.1 [0.5, 2.6], $p = 0.8$). There was a significant decrease in the postoperative length of hospital stay (WMD [95% CI] -1.4 [-0.7, -2.2], $p < 0.01$). The authors concluded that the evidence does not support delaying oral feeding after upper gastrointestinal surgery. Zhuang et al conducted a meta-analysis of randomized controlled trial that evaluated early oral feeding compared to traditional oral feeding following colorectal surgery.⁷⁷ Seven studies were included in analysis with a total of 587 patients. There was no significant difference between the two cohorts in rates of anastomotic dehiscence (RR [95% CI] 0.5 [0.2, 1.2], $p = 0.1$), pneumonia (RR [95% CI] 0.7 [0.3, 1.6], $p = 0.4$), NGT reinsertion (RR [95% CI] 1.3 [0.8, 2.2], $p = 0.3$), or wound infections (RR [95% CI] 0.7 [0.3, 1.4], $p = 0.3$). There was a significant reduction in total postoperative complications in the intervention cohort (RR [95% CI] 0.7 [0.5, 1.0], $p = 0.04$) and length of stay (WMD [95% CI] -1.6 [-2.8, -0.4], $p = 0.009$). The authors concluded that early oral feeding was safe and effective in this patient population. Liu et al conducted a systematic review and meta-analysis of randomized controlled trials comparing early oral feeding to traditional care for patients undergoing gastric surgery.⁷⁸ Six studies were included in the analysis reporting on 454 patients randomized to either early oral feeding or traditional oral feeding following gastrectomy. There was no significant difference for postoperative complications (RR [95%CI] 0.95 [0.7, 1.3], $p = 0.8$), readmission rates (RR [95%CI] 1 [0.3, 3.3], $p = 1.0$) or incidence of anastomotic leaks (RR [95%CI] 0.3 [0.01, 7.3], $p = 0.5$). Patients randomized to early oral feeding had significantly shorter hospital stays (WMD [95%CI] -2.4 [-3.4, -1.3], $p < 0.0001$) and time to first flatus (WMD [95%CI] -19.9 [-32.0, -7.8], $p = 0.001$). Authors concluded that early oral feeding after gastrectomy seems feasible and safe.

Evidence suggests that early oral feeding is safe and feasible; it may decrease time to first flatus and length of hospital stay without increasing complication rates. Therefore, patients are likely to benefit from early oral feeding during the postoperative recovery period following pancreatic surgery.

Level of evidence: Moderate

3.5 Patients should be encouraged to chew gum 3x/day for 5 minutes until they are tolerating solid food

Studies were included if they focused on routine postoperative administration of chewing gum for gastrointestinal recovery following major abdominal surgery. One systematic review and meta-analysis was identified and analyzed for patient outcomes. Short et al⁷⁹ reviewed 81 studies for patients undergoing abdominal surgery. They found the studies to be small and of poor quality, focusing primarily on colorectal surgery and caesarean sections. There was statistical evidence that use of gum chewing for all surgeries reduced length of hospital stay (0.7 days, $p < 0.00001$), time to first flatus (10 hours, $p < 0.00001$), time

to bowel movement (13 hours, $p < 0.00001$) and time to bowel sounds (5 hours, $p < 0.00001$). The authors concluded that better quality randomized controlled trials in an ERaS setting are necessary but there was some evidence that chewing gum after surgery may help the digestive system to recover. Within the 81 studies included in the systematic review, one study from Sweden evaluated the impact of gum chewing on patient outcomes following pancreatic surgery. Andersson et al⁸⁰ conducted a randomized controlled trial that included 28 patients with one group assigned to chewing gum for 45 minutes 4 times a day plus normal postoperative care ($n = 14$) compared to a group of patients treated according to normal postoperative care with sips of glucose equivalent to the amount present in the chewing gum ($n = 14$). Length of hospital stay decreased from 22 vs 18 days ($p = 0.3$), time to first flatus decreased from 5 vs 4 days ($p = 0.3$), time to first defecation decreased from 9 vs 8 days ($p = 0.9$), time to start clear fluids decreased from 9 vs 5 days ($p = 0.07$) and time to start liquid diet decreased from 9 vs 6 days ($p = 0.3$). Although there was no significant difference between the two groups there was a trend towards improved time to return of gastrointestinal function, thus potentially reducing the impact of postoperative ileus.

Recent evidence supports the use of gum chewing to reduce time to first flatus and first bowel movement in other gastrointestinal procedures.⁸¹ Due to its low risk as part of an intervention bundle, the use of chewing gum should be encouraged starting on POD 1 following pancreatic surgery.

Level of evidence: Moderate

3.6 Venous thromboembolism (VTE) prophylaxis should be used for all patients

3.6.1 Perioperative VTE prophylaxis is recommended using either unfractionated or fractionated low-molecular-weight heparin (LMWH)

3.6.2 VTE prophylaxis should be continued during postoperative hospitalization

3.6.3 For patients with high thrombosis risk features (e.g. Caprini Risk Assessment Scores ≥ 7), VTE prophylaxis should be extended for 4 weeks postoperatively

Patients that are undergoing major abdominal surgery are at an increased risk for venous thromboembolic events (VTE).⁸² Risk factors include age > 60 years, operative times > 2 hours, advanced cancer, previous history of VTE, and > 3 days of planned bed rest.⁸³ There were no randomized controlled trials or systematic reviews identified that focused on VTE prophylaxis following pancreatic surgery. Therefore the search was expanded to include high quality studies for major abdominal surgery.

Akl et al conducted a systematic review of the evidence for the relative efficacy and safety of low-molecular-weight heparin (LMWH) and unfractionated heparin (UFH) for perioperative thromboprophylaxis in patients with cancer.⁸⁴ Sixteen randomized controlled trials were included in the review with 12 890 cancer patients that received preoperative prophylactic anticoagulation. In 8 trials the patients underwent abdominal surgery. The results did not conclusively rule out either a beneficial or harmful effect of LMWH compared to UFH for patient mortality (RR [95%CI] 0.9 [0.7, 1.1], $p = 0.3$), pulmonary embolism (RR [95%CI] 0.7 [0.3, 1.5], $p = 0.4$), symptomatic deep vein thrombosis (RR [95%CI] 0.5 [0.2, 1.3], $p = 0.2$), asymptomatic deep vein thrombosis (RR [95%CI] 0.8 [0.7, 1.0], $p = 0.06$), major bleeding (RR [95%CI] 0.9 [0.5, 1.4], $p = 0.5$), or minor bleeding (RR [95%CI] 0.9 [0.5, 1.8], $p = 0.8$) in patients with cancer. The meta-analysis suggested LMWH was associated with a lower incidence of wound hematoma (RR [95%CI] 0.7 [0.5, 0.9], $p = 0.003$) but a higher volume of intraoperative transfusions (MD [95%CI] 74.3 [47, 102], $p < 0.00001$). There was no statistically significant difference for reoperation for bleeding ($p = 0.8$), intraoperative blood loss ($p = 0.9$), postoperative transfusion ($p = 0.2$), postoperative drain volume ($p = 0.5$) and thrombocytopenia ($p = 0.5$). The authors concluded that the overall quality of evidence was moderate and therefore further trials are required to evaluate the benefits and harms of LMWH and UFH in this patient population.

Farge et al released an international clinical practice guideline for VTE prophylaxis in surgically treated patients with cancer.⁸⁵ The international advisory panel recommended that pharmacologic prophylaxis should be started 12-24 hours preoperatively and continued for at least 7-10 days. They also recommended extended prophylaxis (4 weeks) with LMWH to prevent postoperative VTE after major laparotomy in patients with cancer with a high risk of VTE and a low risk of bleeding. The American Society of Clinical Oncology Clinical Practice also released a guideline to provide recommendations about the prophylaxis and treatment of VTE in patients with cancer, which included patients with cancer undergoing major abdominal surgery.^{86, 87} The authors key recommendations for VTE prophylaxis in patients with cancer included: patients undergoing major cancer surgery should receive prophylaxis starting before surgery and continuing for 7-10 days; extending postoperative prophylaxis up to 4 weeks should be considered in those undergoing major abdominal surgery with high-risk features.

One prospective and two retrospective studies that specifically evaluated the need for and use of VTE prophylaxis medication following pancreatic surgery were identified to supplement the aforementioned recommendations based on abdominal surgical procedures. Hayashi et al⁸⁸ conducted a prospective evaluation of 349 patients that underwent hepatobiliary-pancreatic surgery between 2008 and 2011, 186 underwent a pancreaticoduodenectomy and 120 of these patients received either 4000 IU/day enoxaparin, 1.5mg/day of fondaparinux or 2.5 mg/day fondaparinux at the surgeons discretion until POD 8. The remaining 66 patients did not receive chemical thromboprophylaxis. All patients were of Japanese ethnicity. There was a statistically significant higher incident of postoperative hemorrhage in patients that received chemical thromboprophylaxis compared to patients that did not (35 (29%) vs 4 (6%), RR [95%CI] 4.8 [1.8, 13], $p < 0.05$). There was no significant difference in postoperative complications ($p = 0.3$), length of hospital stay ($p = 0.9$), or grade B/C pancreatic fistulas (RR [95%CI] 1.9 [1.0, 3.5], $p = NS$). For all surgical patients, there were significantly less incidents of VTE in patients that received chemical thromboprophylaxis (6 (3%) vs 11 (8%), RR [95%CI] 0.4 [0.1, 1.0], $p < 0.05$). The authors concluded that chemical thromboprophylaxis is beneficial and safe to use, but further research regarding appropriate dosing is required for the prevention of postoperative hemorrhage and adequate prophylaxis against VTE.

Kokudo et al conducted a retrospective review of a prospectively collected database to analyze the risk factors for pulmonary embolism following pancreatic surgery in Switzerland.⁸⁹ Patients received thromboprophylaxis according to the institutional protocol for pancreas surgery. There was a 7% ($n = 13$) incidence of pulmonary embolism observed following pancreaticoduodenectomy. A multivariate analysis of 187 patients revealed history of thromboembolic events (OR [95%CI] 22.3 [1.5, 330.0], $p = 0.03$), prolonged operative time (> 360 minutes) (OR [95%CI] 5.8 [1.4, 40.0], $p = 0.001$), and Clavien Dindo grade 3 or 4 abdominal complications (OR [95%CI] 10.8 [2.9, 53.0], $p = 0.01$) were independent predictors of pulmonary embolism after a pancreaticoduodenectomy. Tzeng et al conducted a retrospective review of 13 771 elective pancreatectomies between 2005-2010 from the American College of Surgeons-National Surgical Quality Improvement Program (ACS-NSQIP) database.⁹⁰ Overall complications rates included: deep vein thrombosis (2%), pulmonary embolism (1%), VTE (3%), post-pancreatectomy hemorrhage (PPH) (1%), and return to operating room with PPH (0.6%). Approximately 1 in 3 post-pancreatectomy VTE events occurred post-discharge. Independent risk factors for post-discharge VTE were identified as: obesity (OR [95%CI] 1.5 [1.1, 2.2], $p = 0.02$), age ≥ 75 years (OR [95%CI] 1.8 [1.2, 2.6], $p = 0.004$), distal pancreatectomy (OR [95%CI] 2.4 [1.7, 3.4], $p < 0.001$) and organ space infection (OR [95%CI] 2.1 [1.4, 3.3], $p < 0.001$). Of the 136 patients that experienced post-discharge VTE events, 65% experienced at least one of these four identified risk factors. The database did not record usage of VTE chemoprophylaxis nor patients with asymptomatic VTE. The authors concluded that post-pancreatectomy VTE outnumber early haemorrhagic complications, therefore the fear of PPH should not prevent routine administration of

VTE chemoprophylaxis. Furthermore, high-risk patients may benefit from extended (post-discharge) VTE prophylaxis.

In summary, VTE prophylaxis should be considered for patients undergoing pancreatic surgery. For high thrombosis risk patients (e.g. Caprini Risk Assessment Score ≥ 7),⁹¹ recent evidence suggests that extending pharmacologic prophylaxis for 4 weeks postoperatively may be beneficial without increasing the risk of major postoperative hemorrhage.

Level of evidence: Moderate

3.7 There is insufficient evidence to recommend routine use of prokinetic agents to enhance gastrointestinal motility

Studies were included if they focused on routine perioperative administration of prokinetic agents for gastrointestinal recovery following major abdominal surgery. However, insufficient evidence was available to justify making a recommendation regarding the use of prokinetic agents to enhance gastrointestinal motility after pancreatic surgery. Therefore, the administration of prokinetic agents should be at the discretion of the treating surgeon.

Section 4. External Review Process

Reviewer comment: The ERAS protocol of bowel resection includes IV lidocaine infusion as a consideration for situations where an epidural may not be needed or appropriate. My hunch is that it would be appropriate here as well.

Author's response: We have reviewed the literature on lidocaine infusions for pain management following pancreatic surgery and have added these data to the guideline.

Reviewer comment: I was just wondering whether you had a chance to review the impact of VTE prophylaxis for this patient population as well, in particular the use of LMWH/DOACs, unfractionated heparin, incidences of HIT, rate of DVT/PE or other complications if any.

Author's response: We agree with this suggestion and have added the results of this literature review to the guideline.

Reviewer comment: Our main concern is that there is clarity re: route of nutrition, as enteral is generally synonymous with tube feeding in the acute care setting. We are assuming the recommendation is for early oral feeding.

Author's response: Yes, the recommendation is for early oral feeding and we have made some minor revisions to make this clearer in the guideline.

Reviewer comment: There is HUGE variation in the percentage of patients who go on TPN after a Whipple.... this issue is not addressed in the guidelines—can it be added.

Author's response: Recent evidence suggests early feeding is safe and beneficial following pancreatic surgery therefore these guidelines are recommending early feeding in this patient population.

Reviewer comment: Somatostatin analogues—I would state that pasireotide should be used—the data for Octreotide is not so great. I know that Pasireotide is not available, but perhaps this document could be the leverage we need to get this drug for our patients.

Author's response: We have revised the wording to clarify that there is mixed evidence with respect to the preferred somatostatin analogue for this patient population.

Reviewer comment: Epidural statement—it's pretty weak—Buchler has an ongoing RCT looking at complications following epidural, perhaps add that? The QOL outcomes are all pretty meaningless if complications increase.

Author's response: We added evidence from additional studies to strengthen the pain management section.

Reviewer comment: Drains—similarly Buchler presented a drain RCT at American Surgical Association last year---there are some big methodology issues with the trial, but it should be included in the lit review. I would discuss the Macmillan/Vollmer analysis of the Fischer RCT—the risk algorithm seems reasonable.

Author's response: We added the additional analysis by McMillan et al to the evidence regarding surgical drains. We also added the Witzigmann et al randomized controlled trial to the supporting evidence.

Reviewer comment: NG's—can you explicitly state that this is limited to PJ's and NOT PG's?? Otherwise some intrepid intern will pull the NG's on PG's.

Author's response: We revised the wording to explicitly state that NGT requirements following pancreaticogastrostomy may be different than this current recommendation.

Reviewer comment: We have found that removing the Foley's on POD1 leads to a high reinsertion rate, can the guideline suggest discharging the Foley POD1-3?

Author's response: We have revised the guidelines to encourage discharge of urinary catheters within 48 hours after surgery.

Reviewer comment: I am just wondering if it would be worth addressing other aspects of the periop care to be comprehensive. This would align with the format used for the ERAS colorectal guidelines.

Author's response: We have added the relevant perioperative recommendations from the Best Practice in Surgery clinical guidelines.

Reviewer comment: The wording is bit confusing. From the SR I understand that neither routine drainage nor routine omission can be recommended, thus selective drainage to discretion of the surgeon. [2. Routine omission of surgical drains following pancreatic surgery cannot be advocated and selective drainage at the discretion of the treating physician is recommended].

Author's response: We revised the wording to clarify the recommendation.

Reviewer comment: Any recommendation re management of drains when used? Referring to the Bassi RCT re early drain removal based on POD1 drain amylase.

Author's response: We have added evidence and a recommendation regarding management of drains when used.

Reviewer comment: Should it specify for open surgery. If distals are included, most are done laparoscopically and do not require epidural.

Author's response: We have specified open surgery.

Reviewer comment: [RE Somatostatin] Obviously very controversial. Why don't you recommend SOM where the data is by far the strongest? That might help us actually get it.

Author's response: We have revised the wording to clarify that there is mixed evidence with respect to the preferred somatostatin analogue for this patient population.

Reviewer comment: [RE Prokinetic agents] Didn't think there was data for this and again the qualifying statement "at the discretion" is too soft and unnecessary.

Author's response: We have revised the recommendation to clarify that there is insufficient evidence to make a recommendation regarding the use of prokinetic agents.

Reviewer comment: Preoperative fasting guidelines should be recommended here.

Author's response: We have incorporated the fasting guidelines from the Best Practice in Surgery Clinical Guidelines.

Reviewer comment: What about the use of lines- arterial lines and central lines etc.

Author's response: This is currently beyond the scope of this guidelines but will be considered in future versions.

Reviewer comment: There is nothing on fluids and fluid management intraoperatively and postoperatively.

Author's response: Fluid management is currently beyond the scope of this guideline but will be considered in future versions.

References

1. Kagedan DJ, Ahmed M, Devitt KS, Wei AC. Enhanced recovery after pancreatic surgery: a systematic review of the evidence. *HPB : the official journal of the International Hepato Pancreato Biliary Association*. 2015;17(1):11-6.
2. Kennedy E, Grenda T, Sauter P, Rosato E, Chojnacki K, Rosato Jr F, *et al*. Implementation of a Critical Pathway for Distal Pancreatectomy at an Academic Institution. *J Gastrointest Surg*. 2009;13(5):938-44.
3. Kennedy EP, Rosato EL, Sauter PK, Rosenberg LM, Doria C, Marino IR, *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.
4. Vanounou T, Pratt W, Fischer JE, Vollmer JCM, Callery MP. 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.
5. Porter GA, Pisters PWT, Mansyur C, Bisanz A, Reyna K, Stanford P, *et al*. Cost and Utilization Impact of a Clinical Pathway for Patients Undergoing Pancreaticoduodenectomy. *Ann Surg Oncol*. 2000;7(7):484-9.
6. Balzano G, Zerbi A, Braga M, Rocchetti S, Beneduce AA, Di Carlo V. Fast-track recovery programme after pancreatico- duodenectomy reduces delayed gastric emptying. *British Journal of Surgery*. 2008;95(11):1387-93.
7. Nikfarjam M, Weinberg L, Low N, Fink MA, Muralidharan V, Houli N, *et al*. A fast track recovery program significantly reduces hospital length of stay following uncomplicated pancreaticoduodenectomy. *JOP*. 2013;14(1):63-70.
8. Abu Hilal M, Di Fabio F, Badran A, Alsaati H, Clarke H, Fecher I, *et al*. Implementation of enhanced recovery programme after pancreatoduodenectomy: a single-centre UK pilot study. *Pancreatology*. 2013;13(1):58-62.
9. Berberat P, Ingold H, Gulbinas A, Kleeff J, Müller M, Gutt C, *et al*. Fast track--different implications in pancreatic surgery. *J Gastrointest Surg*. 2007;11(7):880-7.
10. di Sebastiano P, Festa L, De Bonis A, Ciuffreda A, Valvano M, Andriulli A, *et al*. A modified fast-track program for pancreatic surgery: a prospective single-center experience. *Langenbecks Archives of Surgery*. 2010;396(3):345-51.
11. Robertson N, Gallacher PJ, Peel N, Garden OJ, Duxbury M, Lassen K, *et al*. Implementation of an enhanced recovery programme following pancreaticoduodenectomy. *HPB : the official journal of the International Hepato Pancreato Biliary Association*. 2012;14(10):700-8.
12. Coolsen MM, van Dam RM, van der Wilt AA, Slim K, Lassen K, Dejong CH. Systematic review and meta-analysis of enhanced recovery after pancreatic surgery with particular emphasis on pancreaticoduodenectomies. *World J Surg*. 2013;37(8):1909-18.
13. Williamsson C, Karlsson N, Stureson C, Lindell G, R. A, Tingstedt B. Impact of a fast-track surgery programme for pancreaticoduodenectomy. *British Journal of Surgery*. 2015;102:1133-41.
14. Kobayashi S, Ooshima R, Koizumi S, Katayama M, Sakurai J, Watanabe T, *et al*. Perioperative Care with Fast-Track Management in Patients Undergoing Pancreaticoduodenectomy. *World Journal of Surgery*. 2014;38(2430-2437).
15. Marret E, Kurdi O, Zufferey P, Bonnet F. Effects of nonsteroidal antiinflammatory drugs on patient-controlled analgesia morphine side effects: meta-analysis of randomized controlled trials. *Anesthesiology*. 2005;102(6):1249-60.
16. Klein M, Gögenur I, Rosenberg J. Postoperative use of non-steroidal anti-inflammatory drugs in patients with anastomotic leakage requiring reoperation after colorectal resection: cohort study based on prospective data. *BMJ*. 2012;345:e6166.
17. Behman R, Karanicolas P, Lemke M, Hanna S, Coburn N, Law C, *et al*. The Effect of Early Postoperative Non-Steroidal Anti-Inflammatory Drugs on Pancreatic Fistula Following Pancreaticoduodenectomy. *J Gastrointest Surg*. 2015;19(9):1632-9.

18. Remy C, Marret E, Bonnet F. Effects of acetaminophen on morphine side-effects and consumption after major surgery: meta-analysis of randomized controlled trials. *Br J Anaesth*. 2005;94(4):505-13.
19. McNicol E, Ferguson M, Haroutounian S, Carr D, Schumann R. Single dose intravenous paracetamol or intravenous propacetamol for postoperative pain *Cochrane Database of Syst Rev*. 2016;CD007126.
20. Bameshki A, Yazdi A, Sheybani S, Boroujerdi H, Gilani M. The Assessment of Addition of Either Intravenous Paracetamol or Diclofenac Suppositories to Patient-Controlled Morphine Analgesia for Postgastrectomy Pain Control. *Anesth Pain Med*. 2015;5(5):e29688.
21. Feldheiser A, Aziz O, Baldini G, Cox B, Fearon K, Feldman L, *et al*. Enhanced Recovery After Surgery (ERAS) for gastrointestinal surgery, part 2: consensus statement for anaesthesia practice. *Acta Anaesthesiol Scand*. 2016;60(3):289-334.
22. Best Practice in General Surgery. Enhanced recovery after surgery guideline: perioperative pain management in patients having Toronto: University of Toronto, 2013 April
23. BC Enhanced Recovery Collaborative. British Columbia Enhanced Recovery Collaborative Opioid-Sparing Technique. British Columbia: Committee SS; 2016
24. Weibel S, Jokinen J, Pace N, Schnabel A, Hollmann M, Hahnenkamp K, *et al*. Efficacy and safety of intravenous lidocaine for postoperative analgesia and recovery after surgery: a systematic review with trial sequential analysis. *Br J Anaesth*. 2016;116(6):770-83.
25. Kranke P, Jokinen J, Pace NL, Schnabel A, Hollmann MW, Hahnenkamp K, *et al*. Continuous intravenous perioperative lidocaine infusion for postoperative pain and recovery. *Cochrane Database Syst Rev*. 2015(7):CD009642.
26. Sun Y, Li T, Wang N, Yun Y, Gan T. Perioperative systemic lidocaine for postoperative analgesia and recovery after abdominal surgery: a meta-analysis of randomized controlled trials. *Dis Colon Rectum*. 2012;55(11):1183-94.
27. Khan J, Yousuf M, Victor J, Sharma A, Siddiqui N. An estimation for an appropriate end time for an intraoperative intravenous lidocaine infusion in bowel surgery: a comparative meta-analysis. *J Clin Anesth*. 2016;28:95-104.
28. Gorlin A, Rosenfeld D, Ramakrishna H. Intravenous sub-anesthetic ketamine for perioperative analgesia. *J Anaesthesiol Clin Pharmacol*. 2016;32(2):160-7.
29. Laskowski K, Stirling A, McKay W, Lim H. A systematic review of intravenous ketamine for postoperative analgesia. *Can J Anaesth*. 2011;58(10):911-23.
30. Brinck E, Tiippana E, Heesen M, Bell R, Straube S, Kontinen V. Perioperative intravenous ketamine for acute postoperative pain in adults (Protocol). *Cochrane Database of Syst Rev*. 2016(Issue 1 Art.No.: CD012033).
31. Ali M, Winter D, Hanly A, O'Hagan C, Keaveny J, Broe P. Prospective, randomized, controlled trial of thoracic epidural or patient-controlled opiate analgesia on perioperative quality of life. *British Journal of Anaesthesia*. 2010;104(3):292-7.
32. Choi D, Schoeniger L. For patients undergoing pancreatoduodenectomy, epidural anesthesia and analgesia improves pain but increases rates of intensive care unit admissions and alterations in analgesics. *Pancreas*. 2010;39(4):492-7.
33. Rafi A. Abdominal field block: a new approach via the lumbar triangle. *Anaesthesia*. 2001;56:1024-6.
34. Johns N, O'Neill S, Ventham N, Barron F, Brady R, T. D. Clinical effectiveness of transversus abdominis plane (TAP) block in abdominal surgery: a systematic review and meta-analysis. *Colorectal Dis*. 2012;14(10):e635-42.
35. Charlton S, Cyna AM, Middleton P, Griffiths JD. Perioperative transversus abdominis plane (TAP) blocks for analgesia after abdominal surgery. *Cochrane Database Syst Rev*. 2010(12):CD007705.
36. Dou C, Liu Z, Jia Y, Zheng X, Tu K, Yao Y, *et al*. Systematic review and meta-analysis of prophylactic abdominal drainage after pancreatic resection. *World J Gastroenterol*. 2015;21(18):5719-34.
37. Nitsche U, Müller T, Späth C, Cresswell L, Wilhelm D, Friess H, *et al*. The evidence based dilemma of intraperitoneal drainage for pancreatic resection - a systematic review and meta-analysis. *BMC Surg*. 2014;14(76).

38. Rondelli F, Desio M, Vedovati M, Balzarotti Canger R, Sanguinetti A, Avenia N, *et al.* Intra-abdominal drainage after pancreatic resection: is it really necessary? A meta-analysis of short-term outcomes. *Int J Surg.* 2014;12 (Suppl 1):S40-7.
39. Wang YC1 SP, Zhu JQ1, Xiong JJ1, Huang W1, Gomatos I1, Nunes QM1, Sutton R1, Liu XB1. Prophylactic intra-peritoneal drain placement following pancreaticoduodenectomy: a systematic review and meta-analysis. *World J Gastroenterol.* 2015;21(8):2150-21.
40. 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):487-93.
41. Van Buren G, 2nd, Bloomston M, Hughes SJ, Winter J, Behrman SW, Zyromski NJ, *et al.* A randomized prospective multicenter trial of pancreaticoduodenectomy with and without routine intraperitoneal drainage. *Ann Surg.* 2014;259(4):605-12.
42. Fisher W, Hodges S, Silberfein E, Artinyan A, Ahern C, Jo E, *et al.* Pancreatic resection without routine intraperitoneal drainage. *HPB.* 2011;13(7):503-10.
43. Mehta VV, Fisher SB, Maithel SK, Sarmiento JM, Staley CA, Kooby DA. 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.
44. Heslin MJ, Harrison LE, Brooks AD, Hochwald SN, Coit DG, Brennan MF. Is intra-abdominal drainage necessary after pancreaticoduodenectomy? *J Gastrointest Surg.* 1998;2:373-8.
45. Correa-Gallego C, Brennan M, D'angelica M, Fong Y, Dematteo R, Kingham T, *et al.* Operative drainage following pancreatic resection: analysis of 1122 patients resected over 5 years at a single institution. *Ann Surg.* 2013;258(6):1051-8.
46. Paulus E, Zarzaur B, Behrman S. Routine peritoneal drainage of the surgical bed after elective distal pancreatectomy: is it necessary? *Am J Surg.* 2012;204(4):422-7.
47. Adham M, Chopin-Laly X, Lepilliez V, Gincul R, Valette P, Ponchon T. Pancreatic resection: drain or no drain? *Surgery.* 2013;154(5):1069-77.
48. Lim C, Dokmak S, Cauchy F, Aussilhou B, Belghiti J, Sauvanet A. Selective policy of no drain after pancreaticoduodenectomy is a valid option in patients at low risk of pancreatic fistula: a case-control analysis. *World J Surg.* 2013;37(5):1021-7.
49. McMillan M, Fisher W, Van Buren G, McElhany A, Bloomston M, Hughes S, *et al.* The value of drains as a fistula mitigation strategy for pancreatoduodenectomy: something for everyone? Results of a randomized prospective multi-institutional study. *J Gastrointest Surg.* 2015;19(1):21-30.
50. Callery M, Pratt W, Kent T, Chaikof E, Vollmer CJ. A prospectively validated clinical risk score accurately predicts pancreatic fistula after pancreatoduodenectomy. *J Am Coll Surg.* 2013;216(1):1-14.
51. Diener MK, Mehr K, Wente MN, Meinhard K, Buchler MW, Seiler CM. Risk-benefit assessment of closed intra-abdominal drains after pancreatic surgery: a systematic review and meta-analysis assessing the current state of evidence. *Langenbecks Arch Surg.* 2011;396:41-52.
52. Bassi C, Molinari E, Malleo G, Grippa 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;252:207-14.
53. 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 104 consecutive patients. *An Surg.* 2006;244:1-7.
54. McMillan M, Malleo G, Bassi C, Butturini G, Salvia R, Roses R, *et al.* Drain Management after Pancreatoduodenectomy: Reappraisal of a Prospective Randomized Trial Using Risk Stratification. *J Am Coll Surg.* 2015;221(4):798-809.
55. Fong ZV, McMillan MT, Marchegiani G, Sahara K, Malleo G, De Pastena M, *et al.* Discordance Between Perioperative Antibiotic Prophylaxis and Wound Infection Cultures in Patients Undergoing Pancreaticoduodenectomy. *JAMA surgery.* 2016;151(5):432-9.
56. Witzigmann H, Diener M, Kienkötter S, Rossion I, Bruckner T, Bärbel W, *et al.* No Need for Routine Drainage After Pancreatic Head Resection: The Dual-Center, Randomized, Controlled PANDRA Trial (ISRCTN04937707). *Ann Surg.* 2016;264(3):528-37.

57. Wei Z, Li J, Li Z, Hao Y, He Y, Chen W, *et al.* Systematic review of nasogastric or nasojejunal decompression after gastrectomy for gastric cancer. *Eur J Surg Oncol.* 2014;40(12):1763-70.
58. Lee J, Hyung W, Noh S. Comparison of gastric cancer surgery with versus without nasogastric decompression. *Yonsei Med J* 2002;43(4):451-6.
59. Doglietto GB PV, Tortorelli AP, *et al.* . Nasojejunal tube placement after total gastrectomy: a multicenter prospective randomized trial. *Arch Surg.* 2004;139(12):1309-13.
60. Hsu S-D, Yu J-C, Chen T-W, *al. e.* Role of nasogastric tube insertion after gastrectomy. *Viszeralmedizin* 2007;23(3):303-6.
61. Li C MJ, Yan M, *et al.* . Nasogastric decompression for radical gastrectomy for gastric cancer: a prospective randomized controlled study. *Dig Surg.* 2011;23(8):167-72.
62. Tavassoli A, Rajabi M, Abdollahi A, *al. e.* Efficacy and necessity of nasojejunal tube after gastrectomy. *Int J Surg* 2011;9(3):233-6.
63. Pacelli F, Rosa F, Marrelli D, Morgagni P, Framarini M, Cristadoro L, *et al.* Naso-gastric or naso-jejunal decompression after partial distal gastrectomy for gastric cancer. Final results of a multicenter prospective randomized trial. *Gastric Cancer.* 2014;17(4):725-32.
64. Yoo C, Son B, Han W, *al. e.* Nasogastric decompression is not necessary in operations for gastric cancer: prospective randomised trial. *Eur J Surg* 2002;168(7):379-83.
65. Wu C, Hwang C, Liu T. There is no need for nasogastric decompression after partial gastrectomy with extensive lymphadenectomy. *Eur J Surg* 1994;160((6e7)):369-73.
66. Verma R, Nelson R. Prophylactic nasogastric decompression after abdominal surgery. *Cochrane Database of Syst Rev.* 2010;3(CD004929).
67. Sapkota R, Bhandari R. Prophylactic Nasogastric Decompression after Emergency Laparotomy. *J Nepal Med Assoc.* 2013;52(191):437-42.
68. Hallet J, Zih F, Deobald R, Scheer A, Law C, Coburn N, *et al.* The impact of pancreaticojejunostomy versus pancreaticogastrostomy reconstruction on pancreatic fistula after pancreaticoduodenectomy: meta-analysis of randomized controlled trials. *HPB : the official journal of the International Hepato Pancreato Biliary Association.* 2015;17(2):113-22.
69. Zhou Y, Yu J, Wu L, Li B. Meta-analysis of pancreaticogastrostomy versus pancreaticojejunostomy on occurrences of postoperative pancreatic fistula after pancreaticoduodenectomy. *Asian J Surg.* 2015;38(3):155-60.
70. Zmora O, Madbouly K, Tulchinsky H, Hussein A, Khaikin M. Urinary bladder catheter drainage following pelvic surgery--is it necessary for that long? *Dis Colon Rectum.* 2010;53(3):321-6.
71. Trickey AW, Crosby ME, Vasaly F, Donovan J, Moynihan J, Reines HD. Using NSQIP to investigate SCIP deficiencies in surgical patients with a high risk of developing hospital-associated urinary tract infections. *Am J Med Qual.* 2014;29(5):381-7.
72. Gurusamy K, Koti R, Fusai G, Davidson B. Somatostatin analogues for pancreatic surgery. *Cochrane Database Syst Rev.* 2013;4.
73. Allen P, Gonen M, Brennan M, Bucknor A, Robinson L, Pappas M, *et al.* Pasireotide for Postoperative Pancreatic Fistula. *The new england journal of medicine.* 2014;370(21):2014-22.
74. Lee T, Kang S, Kim D, Hong S, Heo S, Park K. Comparison of early mobilization and diet rehabilitation program with conventional care after laparoscopic colon surgery: a prospective randomized controlled trial. *Dis Colon Rectum.* 2011;54(1):21-8.
75. Kibler K, Hayes R, Johnson D, Anderson L, Just S, Wells N. Early Postoperative Ambulation: Back to Basics A quality improvement project increases postoperative ambulation and decreases patient complications. *Cultivating Quality.* 2012;112(4):63-9.
76. Willcutts K, Chung M, Erenberg C, Finn K, Schirmer B, Byham-Gray L. Early Oral Feeding as Compared With Traditional Timing of Oral Feeding After Upper Gastrointestinal Surgery: A Systematic Review and Meta-analysis. *Ann Surg.* 2016;264(1):54-63.
77. Zhuang C, Ye X, Zhang C, Dong Q, Chen B, Yu Z. Early versus traditional postoperative oral feeding in patients undergoing elective colorectal surgery: a meta-analysis of randomized clinical trials. *Dig Surg.* 2013;30(3):225-32.

78. Liu X, Wang D, Zheng L, Mou T, Liu H, Li G. Is early oral feeding after gastric cancer surgery feasible? A systematic review and meta-analysis of randomized controlled trials. *PLoS One*. 2014;9(11):e112062.
79. Short V, Herbert G, Perry R, Atkinson C, Ness A, Penfold C, *et al*. Chewing gum for postoperative recovery of gastrointestinal function *Cochrane Database of Syst Rev*. 2015;2.
80. Andersson T, Bjersa K, Falk K, Olsen M. Effects of chewing gum against postoperative ileus after pancreaticoduodenectomy--a randomized controlled trial. *BMC Res Notes*. 2015;10(8):37.
81. Aarts M, Okrainec A, McCluskey S, Siddiqui N, Wood T, Pearsall E, *et al*. Enhanced recovery after surgery guideline: A clinical practice guideline developed by the University of Toronto's best practice in surgery. University of Toronto: University of Toronto, 2014
82. Agnelli G, Bolis G, Capussotti L, Scarpa R, Tonelli F, Bonizzoni E, *et al*. A clinical outcome-based prospective study on venous thromboembolism after cancer surgery: the @RISTOS project. *Ann Surg*. 2006;243(1):89-95.
83. Streiff M, National Comprehensive Cancer Center Network. The National Comprehensive Cancer Center Network (NCCN) guidelines on the management of venous thromboembolism in cancer patients. *Thromb Res*. 2010;125 (Suppl 2):S128-33.
84. Akl EA, Kahale L, Sperati F, Neumann I, Labedi N, Terrenato I, *et al*. Low molecular weight heparin versus unfractionated heparin for perioperative thromboprophylaxis in patients with cancer. *Cochrane Database Syst Rev*. 2014(6):CD009447.
85. Farge D, Debourdeau P, Beckers M, Baglin C, Bauersachs RM, Brenner B, *et al*. International clinical practice guidelines for the treatment and prophylaxis of venous thromboembolism in patients with cancer. *J Thromb Haemost*. 2013;11(1):56-70.
86. Lyman GH, Khorana AA, Falanga A, Clarke-Pearson D, Flowers C, Jahanzeb M, *et al*. American Society of Clinical Oncology guideline: recommendations for venous thromboembolism prophylaxis and treatment in patients with cancer. *J Clin Oncol*. 2007;25(34):5490-505.
87. Lyman G, Bohlke K, Khorana A, Kuderer N, Lee A, Arcelus J, *et al*. Venous thromboembolism prophylaxis and treatment in patients with cancer: american society of clinical oncology clinical practice guideline update 2014. *J Clin Oncol*. 2015;33(6):654-6.
88. Hayashi H, Morikawa T, Yoshida H, Motoi F, Okada T, Nakagawa K, *et al*. Safety of postoperative thromboprophylaxis after major hepatobiliary-pancreatic surgery in Japanese patients. *Surg Today*. 2014;44(9):1660-8.
89. Kokudo T, Uldry E, Demartines N, Halkic N. Pulmonary embolism: specific risk factor after pancreas resection? *Pancreas*. 2014;43(6):891-4.
90. Tzeng C, Katz M, Lee J, Fleming J, Pisters P, Vauthey J, *et al*. Predicting the risks of venous thromboembolism versus post-pancreatectomy haemorrhage: analysis of 13 771 NSQIP patients. *HPB : the official journal of the International Hepato Pancreato Biliary Association*. 2014;16(4):373-83.
91. Arcelus J, Candocia S, Traverso C, Fabrega F, Caprini J, Hasty J. Venous thromboembolism prophylaxis and risk assessment in medical patients. *Semin Thromb Hemost*. 1991;17(Suppl 3):313-8.