Editorial

Pancreaticoduodenectomy for pancreatic cancer: perspective from the United States

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Introduction

Despite being a relatively rare cancer, pancreatic cancer is the third leading cause of cancer death in the United States with over 41,000 patients succumbing to the disease in 2016 alone (1). In fact, pancreatic cancer is projected to be the second most common cause of cancer deaths by 2030 (2).

Approximately 75% of all pancreatic cancers arise in the head of the pancreas. Among patients with resectable disease, a pancreaticoduodenectomy (PD) is required for complete extirpation of the tumor among eligible patients and offers the best chance for long-term survival. The surgical resection of the head of the pancreas was first performed by Walther Kausch in Germany in 1909 but later popularized by Allen Whipple (3,4). Over the past several decades, PD has become a safe operation with recent perioperative mortality rates quoted at less than 1% (5,6). Perhaps equally important as the surgical treatment of pancreatic cancer, a comprehensive evaluation and multi-disciplinary treatment team including medical oncologists, gastroenterologists, pathologists, and radiation oncologists are necessary for the treatment of this deadly disease. As such, this article will focus on the multi-disciplinary approach to the patient with pancreatic cancer requiring PD in the United States.

Preoperative workup

All patients presenting with known or suspected pancreatic cancer are required to undergo high-resolution pancreas-specific imaging. Based on the available data (7) and practice preferences of the surgeons at our institution, multi-detector thin-slice pancreas protocol CT scans are performed. MRI is utilized if patients have a contraindication to CT scan (i.e., dye allergy) or for closer evaluation of small indeterminate liver or pancreatic lesions unable to be characterized following CT scan. Patients are seen in our multi-disciplinary pancreas clinic, which is attended by pancreatic surgeons, radiologists, gastroenterologists, pathologists, and medical oncologists. Each individual case is thoroughly reviewed during our multi-disciplinary conference. A treatment decision is created based on individual patient and disease-related factors. Preoperative endoscopy is often unnecessary except for patients requiring preoperative biliary drainage or to obtain a biopsy for those patients set to receive neoadjuvant chemotherapy. As previous studies have shown that preoperative biliary drainage/stent placement may cause an increase in perioperative complications (8), this modality is used sparingly at our institution and often only when total bilirubin >10 mg/dL or when cholangitis is suspected.

Neoadjuvant chemotherapy

Patients with clearly resectable disease most commonly proceed directly to PD without any neoadjuvant therapy. An ongoing randomized controlled clinical trial at our institution, however, is currently testing a granulocyte-macrophage colony-stimulating factor (GM-CSF) secreting vaccine in combination with cyclophosphamide in the neoadjuvant and adjuvant setting (9). Though several clinical trials evaluating the impact of neoadjuvant chemotherapy among patients with resectable disease remain ongoing (10), the standard of care remains to proceed with PD without neoadjuvant therapy in the absence of a clinical trial protocol.

Patients with locally advanced and borderline resectable disease are commonly referred for neoadjuvant chemotherapy, though the benefit of such an approach remains indeterminate without level 1 evidence. Current guidelines by the National Comprehensive Cancer Network recommend neoadjuvant therapy for borderline resectable disease. Several retrospective studies have evaluated the use of neoadjuvant chemotherapy among patients with locally advanced pancreatic cancer with varying results (11-16). Despite a consensus by the International Study Group of Pancreatic Surgery, variations in the definitions of borderline resectable and locally advanced pancreatic cancer remain (17). As such, resectability rates following neoadjuvant chemotherapy vary widely in the literature.

Among patients with initially unresectable disease, radiographic and pathologic response to neoadjuvant chemotherapy may lead to resectability in a subset of patients. In a systematic review of 57 studies, Gillen et al reported that 33.2% of patients were able to undergo resection after neoadjuvant therapy. However none of the included trials involved the administration of the now commonly utilized FOLFIRINOX chemotherapy regimen (18). More recently, Sadot *et al.* found that nearly one-third of patients with stage 3 locally unresectable diseases that received FOLFIRINOX ultimately underwent resection in a single institution review (19). Furthermore, median overall survival was significantly improved among patients who responded to FOLFIRINOX, potentially indicating favorable tumor biology. In other recently published data, Hackert *et al.* found that the neoadjuvant administration of FOLFIRINOX resulted in a 61% resection rate among patients with locally advanced pancreatic cancer as compared to only 46% among those receiving gemcitabine and radiation (20). In a meta-analysis involving 13 studies and 253 patients, Petrelli *et al.* found a R0 resection rate of 40% with the use of FOLFIRINOX-based neoadjuvant chemotherapy in borderline or unresectable pancreatic cancer (21). Based on these and other available data, it is the preference of our institution to use FOLFIRINOX for neoadjuvant chemotherapy, if tolerable by the patient, reserving a regimen of gemcitabine/protein-bound paclitaxel or others for those with dose-limiting toxicities or non-response to therapy.

Neoadjuvant chemoradiotherapy

Neoadjuvant radiation therapy in conjunction with chemotherapy has shown utility in many gastrointestinal cancers and is also used in the management of locally advanced and borderline resectable pancreatic cancer. The impact of the addition of radiotherapy to standard neoadjuvant chemotherapy regiments has been evaluated in numerous studies with wide-ranging results (14,22,23). In a retrospective analysis by Stessin *et al.* using Surveillance, Epidemiology, and End Results (SEER) data, median survival was significantly improved with neoadjuvant radiotherapy (22). In a multi-institutional study involving our own institution, the use of radiation therapy in conjunction with gemcitabine/oxaliplatin was well tolerated and resulted in an R0 resection in 84% of patients (23). In a meta-analysis involving 11 studies with 4,400 patients, Gillen *et al.* reported that neoadjuvant chemoradiotherapy resulted in a resectability rate of 74%; this rate dropped to 33% among those initially deemed unresectable (18). Interestingly, patients who had their cancer converted to resectable disease after neoadjuvant therapy had a median survival of 21 months, which was equivalent to that of patients who initially presented with resectable disease (18). Taken together, our team routinely offers neoadjuvant radiotherapy in addition to chemotherapy among patients with unresectable locally advanced disease without distant metastasis.

Preoperative preparation

Epidural placement is utilized based patient and provider preferences. All patients receive 5,000 units of subcutaneous heparin approximately one hour prior to incision (24). Aerobic and anaerobic antibiotic prophylaxis is administered within one hour prior to incision and continued for 24 hours postoperatively (25). Hair is trimmed prior to incision using a razor and a chlorhexidine-based solution is used as surgical antiseptic.

Surgical approach and technique

Minimal invasive PD

Operative approach is based on both patient-specific factors (patient body habitus, performance status, patient preference) and surgeon preference and experience. Recent data has shown that the use of minimally invasive techniques for complex pancreatic surgery throughout the United States is increasing (26). Laparoscopic PD has been shown to be a safe and cost-effective operation (27-29). In a review of 108 patients undergoing laparoscopic PD,

Croome *et al.* found total laparoscopic PD resulted in a shorter hospital length of stay and a longer progression-free survival as compared to patients undergoing open PD (30). Even among patients requiring major venous resection, laparoscopic PD was found to be safe and feasible (31).

Robotic PD has gained popularity in recent years. In one of the largest analysis of robotic PD, Zureikat *et al.* found robotic PD to be a safe and feasible operation (32). As with most new technology, there appears to be a learning curve as Boone et al found statistical improvements in several quality metrics following robotic PD with increasing number of cases (33). In a recent multi-institutional comparison of open versus robotic PD, robotic PD was associated with lower blood loss and reductions in major complications (34). At our institution, both laparoscopic PD and robotic PD are offered and an operative approach is decided upon after a thorough discussion with the patient. Regardless of the operative approach, intra-operative resection and reconstruction techniques remain similar.

Open PD

Due to the high-sensitivity of high-resolution imaging, diagnostic laparoscopy is not routinely performed. We utilize a midline incision from the sub-xiphoid process and extending to the level of the umbilicus. Several variations in PD are possible and are discussed below:

- Pylorus-preserving *vs.* classic PD: several randomized trials have shown equivalent outcomes between pylorus-preserving and classic PD and thus we consider both techniques to be equivalent and choose it based on surgeon's preference (35,36);
- Extended lymphadenectomy: as many randomized trials and systemic reviews have shown a lack of benefit and an increase in postoperative complications, extended lymphadenectomy is not routinely performed (37-41);
- Major venous resection: resection of the portal vein/superior mesenteric vein is occasionally necessary to achieve an R0 resection. Major venous resection (SMV/PV) is performed in approximately 5% of all cases at our institution and is getting more common (6). Primary repair *vs.* patch venoplasty is performed depending on the amount of vein resected and the potential flow compromise of the repaired vessel. In instances that require the entire vein to be resected, a primary end-to-end anastomosis is performed after mobilization of the SMV/PV if feasible. If this is not technically possible due to a long-segment involvement, an interposition graft using allograft femoral vein is often used for better size match.

  Riediger *et al.* reported their experience in 53 patients with vein resection and showed that this technique is safe with no increase in postoperative morbidity (42). Many other series have also confirmed the feasibility of vein resection during PD (43-45);
- Pancreaticojejunostomy *vs.* pancreaticogastrostomy: though several trials have shown mixed results between pancreaticojejunostomy and pancreaticogastrostomy reconstruction (46,47), the preference at our institution is to reconstruct the pancreatic remnant using a pancreaticojejunostomy technique. Pancreatic reconstruction is performed using a two-layer duct to mucosa pancreaticojejunostomy at our institution. Postoperative pancreatic fistula (POPF) can be significantly reduced by meticulous anastomosis with optimization of blood supply at the pancreaticojejunostomy (48);
- Gastrojejunostomy: the antecolic location of gastrojejunostomy has been shown to reduce the incidence of delayed gastric emptying in several publications and is the preferred method of enteric reconstruction (49,50). Furthermore, a side-to-side anastomosis is also preferred, as previous studies have shown this to reduce delayed gastric emptying as compared to an end-to-side anastomosis (51);
- Pancreatic drainage: though there remains to be consensus as to the necessity of routine intraperitoneal drainage following PD (52-54), routine intraperitoneal drainage with closed suction drains is commonly used at our institution.

Postoperative care

All patients are admitted to the intensive care unit postoperatively. A nasogastric tube is left in overnight and removed on the morning postoperative day 1. An enhanced recovery after surgery (ERAS) pathway is followed and includes a stepwise increase of diet, early ambulation, and minimization of narcotics. Early drain removal is encouraged after minimal drainage (<50 mL/24 hours) and low drain amylase levels (<3 times of serum amylase) following postoperative day 3. Based on randomized trial results from our institution (55), the use of erythromycin to prevent delayed gastric emptying is used at the discretion of the surgeon. Similarly, octreotide or Pasireotide may

be utilized in patients with high-risk for pancreatic fistula including those with soft glands and small pancreatic ducts (56, 57).

Complications

In our recent series of PD of 1,687 patients with pancreatic ductal adenocarcinoma, the overall complication rate was 41% (6). The most common complications following open PD include delayed gastric emptying (DGE) (16%), wound complications/surgical site infection (11%), and POPF (6%) (6). The incidence of wound complications and DGE after minimal invasive PD is much lower comparing to open PD (58,59). DGE and wound complications are often related to POPF. In the absence of POPF, the management of DGE is mainly supportive. Nasogastric tube is used to decompress the stomach if DGE persists or is severe. Parental nutrition support is rarely needed but utilized if necessary. Based on our institutions randomized controlled trial (55), patients with DGE may benefit from prokinetics such as metoclopramide and erythromycin.

Follow-up

The average length of stay after PD is 7 days. Patients are seen for follow-up appointments following hospital discharge at 2 to 3 weeks and then every 3 months thereafter. The overwhelming majority of patients receive adjuvant chemotherapy +/– radiotherapy based on previous clinical trial results (18,60-62). Several clinical trials are ongoing evaluating different combinations of systemic chemotherapy as well as the safety and efficacy of targeted agents and immunotherapy (63). Postoperative surveillance imaging scans and laboratory studies (including CA 19-9 levels) are performed every 3–6 months to evaluate for disease recurrence.

Conclusions

Pancreatic cancer is an aggressive cancer with increasing incidence in the United States. PD for pancreatic cancer can be performed in a safe manner that offers the best hope for long-term survival. Complications following PD, however, are common. Further experience with minimally invasive techniques, as well as ongoing trial results in various neoadjuvant and adjuvant chemotherapy, immunotherapy, and targeted therapy regiments may result in improved future patient outcomes.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Howlader N, Noone AM, Krapcho M, et al. editors. SEER Cancer Statistics Review, 1975-2013, National Cancer Institute. Bethesda, MD. Available online: http://seer.cancer.gov/csr/1975_2013/. Based on November 2015 SEER data submission, posted to the SEER web site, April 2016.
2. Rahib L, Smith BD, Aizenberg R, et al. Projecting cancer incidence and deaths to 2030: the unexpected burden of thyroid, liver, and pancreas cancers in the United States. Cancer Res 2014;74:2913-21.
3. Kausch W. Das carcinoma der papilla duodeni und seine radikale entfeinung. BeitrZ Clin Chir 1912;78:439-86.
4. Whipple AO, Parsons WB, Mullins CR. Treatment of Carcinoma of the Ampulla of Vater. Ann Surg 1935;102:763-79.
5. Gleeson EM, Shaikh MF, Shewokis PA, et al. WHipple-ABACUS, a simple, validated risk score for 30-day mortality after pancreaticoduodenectomy developed using the ACS-NSQIP database. Surgery 2016;160:1279-87.
6. He J, Ahuja N, Makary MA, et al. 2564 resected periampullary adenocarcinomas at a single institution: trends over three decades. HPB (Oxford) 2014;16:83-90.
7. Soriano A, Castells A, Ayuso C, et al. Preoperative staging and tumor resectability assessment of pancreatic cancer: prospective study comparing endoscopic ultrasonography, helical computed tomography, magnetic resonance imaging, and angiography. Am J Gastroenterol 2004;99:492-501.
8. 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;362:129-37.
9. Jaffee EM, Hruban RH, Biedrzycki B, et al. Novel allogeneic granulocyte-macrophage colony-stimulating factor-secreting tumor vaccine for pancreatic cancer: a phase I trial of safety and immune activation. J Clin Oncol 2001;19:145-56.
10. Kim SM, Eads JR. Adjuvant and Neoadjuvant Therapy

for Resectable Pancreatic and Periampullary Cancer. Surg Clin North Am 2016;96:1287-300.
11. Ferrone CR, Marchegiani G, Hong TS, et al. Radiological and surgical implications of neoadjuvant treatment with FOLFIRINOX for locally advanced and borderline resectable pancreatic cancer. Ann Surg 2015;261:12-7.
12. Palmer DH, Stocken DD, Hewitt H, et al. A randomized phase 2 trial of neoadjuvant chemotherapy in resectable pancreatic cancer: gemcitabine alone versus gemcitabine combined with cisplatin. Ann Surg Oncol 2007;14:2088-96.
13. Arvold ND, Ryan DP, Niemierko A, et al. Long-term outcomes of neoadjuvant chemotherapy before chemoradiation for locally advanced pancreatic cancer. Cancer 2012;118:3026-35.
14. Allendorf JD, Lauerman M, Bill A, et al. Neoadjuvant chemotherapy and radiation for patients with locally unresectable pancreatic adenocarcinoma: feasibility, efficacy, and survival. J Gastrointest Surg 2008;12:91-100.
15. Rose JB, Rocha FG, Alseidi A, et al. Extended neoadjuvant chemotherapy for borderline resectable pancreatic cancer demonstrates promising postoperative outcomes and survival. Ann Surg Oncol 2014;21:1530-7.
16. McClaine RJ, Lowy AM, Sussman JJ, et al. Neoadjuvant therapy may lead to successful surgical resection and improved survival in patients with borderline resectable pancreatic cancer. HPB (Oxford) 2010;12:73-9.
17. Bockhorn M, Uzunoglu FG, Adham M, et al. Borderline resectable pancreatic cancer: a consensus statement by the International Study Group of Pancreatic Surgery (ISGPS). Surgery 2014;155:977-88.
18. Gillen S, Schuster T, Meyer Zum Buschenfelde C, et al. Preoperative/neoadjuvant therapy in pancreatic cancer: a systematic review and meta-analysis of response and resection percentages. PLoS Med 2010;7:e1000267.
19. Sadot E, Doussot A, O'Reilly EM, et al. FOLFIRINOX Induction Therapy for Stage 3 Pancreatic Adenocarcinoma. Ann Surg Oncol 2015;22:3512-21.
20. Hackert T, Sachsenmaier M, Hinz U, et al. Locally Advanced Pancreatic Cancer: Neoadjuvant Therapy With Folfirinox Results in Resectability in 60% of the Patients. Ann Surg 2016;264:457-63.
21. Petrelli F, Coinu A, Borgonovo K, et al. FOLFIRINOX-based neoadjuvant therapy in borderline resectable or unresectable pancreatic cancer: a meta-analytical review of published studies. Pancreas 2015;44:515-21.
22. Stessin AM, Meyer JE, Sherr DL. Neoadjuvant radiation is associated with improved survival in patients with resectable pancreatic cancer: an analysis of data from the surveillance, epidemiology, and end results (SEER) registry. Int J Radiat Oncol Biol Phys 2008;72:1128-33.
23. Kim EJ, Ben-Josef E, Herman JM, et al. A multi-institutional phase 2 study of neoadjuvant gemcitabine and oxaliplatin with radiation therapy in patients with pancreatic cancer. Cancer 2013;119:2692-700.
24. Gould MK, Garcia DA, Wren SM, et al. Prevention of VTE in nonorthopedic surgical patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012;141:e227S-77S.
25. Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm 2013;70:195-283.
26. Ejaz A, Sachs T, He J, et al. A comparison of open and minimally invasive surgery for hepatic and pancreatic resections using the Nationwide Inpatient Sample. Surgery 2014;156:538-47.
27. Mesleh MG, Stauffer JA, Bowers SP, et al. Cost analysis of open and laparoscopic pancreaticoduodenectomy: a single institution comparison. Surg Endosc 2013;27:4518-23.
28. Asbun HJ, Stauffer JA. Laparoscopic vs open pancreaticoduodenectomy: overall outcomes and severity of complications using the Accordion Severity Grading System. J Am Coll Surg 2012;215:810-9.
29. Boggi U, Amorese G, Vistoli F, et al. Laparoscopic pancreaticoduodenectomy: a systematic literature review. Surg Endosc 2015;29:9-23.
30. Croome KP, Farnell MB, Que FG, et al. Total laparoscopic pancreaticoduodenectomy for pancreatic ductal adenocarcinoma: oncologic advantages over open approaches? Ann Surg 2014;260:633-8; discussion 638-40.
31. Kendrick ML, Sclabas GM. Major venous resection during total laparoscopic pancreaticoduodenectomy. HPB (Oxford) 2011;13:454-8.
32. Zureikat AH, Moser AJ, Boone BA, et al. 250 robotic pancreatic resections: safety and feasibility. Ann Surg 2013;258:554-9; discussion 559-62.
33. Boone BA, Zenati M, Hogg ME, et al. Assessment of quality outcomes for robotic pancreaticoduodenectomy: identification of the learning curve. JAMA Surg 2015;150:416-22.
34. Zureikat AH, Postlewait LM, Liu Y, et al. A Multi-institutional Comparison of Perioperative Outcomes of Robotic and Open Pancreaticoduodenectomy. Ann Surg 2016;264:640-9.
35. Seiler CA, Wagner M, Sadowski C, et al. Randomized prospective trial of pylorus-preserving vs. Classic

duodenopancreatectomy (Whipple procedure): initial clinical results. J Gastrointest Surg 2000;4:443-52.
36. Lin PW, Lin YJ. Prospective randomized comparison between pylorus-preserving and standard pancreaticoduodenectomy. Br J Surg 1999;86:603-7.
37. Yeo CJ, Cameron JL, Sohn TA, et al. Pancreaticoduodenectomy with or without extended retroperitoneal lymphadenectomy for periampullary adenocarcinoma: comparison of morbidity and mortality and short-term outcome. Ann Surg 1999;229:613-22; discussion 622-4.
38. Yeo CJ, Cameron JL, Lillemoe KD, et al. Pancreaticoduodenectomy with or without distal gastrectomy and extended retroperitoneal lymphadenectomy for periampullary adenocarcinoma, part 2: randomized controlled trial evaluating survival, morbidity, and mortality. Ann Surg 2002;236:355-66; discussion 366-8.
39. Riall TS, Cameron JL, Lillemoe KD, et al. Pancreaticoduodenectomy with or without distal gastrectomy and extended retroperitoneal lymphadenectomy for periampullary adenocarcinoma--part 3: update on 5-year survival. J Gastrointest Surg 2005;9:1191-204; discussion 1204-6.
40. Michalski CW, Kleeff J, Wente MN, et al. Systematic review and meta-analysis of standard and extended lymphadenectomy in pancreaticoduodenectomy for pancreatic cancer. Br J Surg 2007;94:265-73.
41. Sun J, Yang Y, Wang X, et al. Meta-analysis of the efficacies of extended and standard pancreatoduodenectomy for ductal adenocarcinoma of the head of the pancreas. World J Surg 2014;38:2708-15.
42. Riediger H, Makowiec F, Fischer E, et al. Postoperative morbidity and long-term survival after pancreaticoduodenectomy with superior mesenterico-portal vein resection. J Gastrointest Surg 2006;10:1106-15.
43. Chu CK, Farnell MB, Nguyen JH, et al. Prosthetic graft reconstruction after portal vein resection in pancreaticoduodenectomy: a multicenter analysis. J Am Coll Surg 2010;211:316-24.
44. Hristov B, Reddy S, Lin SH, et al. Outcomes of adjuvant chemoradiation after pancreaticoduodenectomy with mesenterico-portal vein resection for adenocarcinoma of the pancreas. Int J Radiat Oncol Biol Phys 2010;76:176-80.
45. Zhang J, Qian HG, Leng JH, et al. Long mesentericoportal vein resection and end-to-end anastomosis without graft in pancreaticoduodenectomy. J Gastrointest Surg 2009;13:1524-8.
46. Bassi C, Falconi M, Molinari E, et al. Reconstruction by pancreaticojejunostomy versus pancreaticogastrostomy following pancreatectomy: results of a comparative study. Ann Surg 2005;242:767-71, discussion 771-3.
47. Shen Y, Jin W. Reconstruction by Pancreaticogastrostomy versus Pancreaticojejunostomy following Pancreaticoduodenectomy: A Meta-Analysis of Randomized Controlled Trials. Gastroenterol Res Pract. 2012;2012:627095.
48. Strasberg SM, Drebin JA, Mokadam NA, et al. Prospective trial of a blood supply-based technique of pancreaticojejunostomy: effect on anastomotic failure in the Whipple procedure. J Am Coll Surg 2002;194:746-58; discussion 759-60.
49. Hartel M, Wente MN, Hinz U, et al. Effect of antecolic reconstruction on delayed gastric emptying after the pylorus-preserving Whipple procedure. Arch Surg 2005;140:1094-9.
50. Nikfarjam M, Kimchi ET, Gusani NJ, et al. A reduction in delayed gastric emptying by classic pancreaticoduodenectomy with an antecolic gastrojejunal anastomosis and a retrogastric omental patch. J Gastrointest Surg 2009;13:1674-82.
51. Nakamura T, Ambo Y, Noji T, et al. Reduction of the Incidence of Delayed Gastric Emptying in Side-to-Side Gastrojejunostomy in Subtotal Stomach-Preserving Pancreaticoduodenectomy. J Gastrointest Surg 2015;19:1425-32.
52. 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;259:605-12.
53. Poon RT, Fan ST, Lo CM, et al. External drainage of pancreatic duct with a stent to reduce leakage rate of pancreaticojejunostomy after pancreaticoduodenectomy: a prospective randomized trial. Ann Surg 2007;246:425-33; discussion 433-5.
54. Conlon KC, Labow D, Leung D, et al. Prospective randomized clinical trial of the value of intraperitoneal drainage after pancreatic resection. Ann Surg 2001;234:487-93; discussion 493-4.
55. Yeo CJ, Barry MK, Sauter PK, et al. Erythromycin accelerates gastric emptying after pancreaticoduodenectomy. A prospective, randomized, placebo-controlled trial. Ann Surg 1993;218:229-37; discussion 237-8.
56. Ma LW, Dominguez-Rosado I, Gennarelli RL, et al. The Cost of Postoperative Pancreatic Fistula Versus the Cost of

Pasireotide: Results from a Prospective Randomized Trial. Ann Surg 2017;265:11-6.
57. Allen PJ, Gonen M, Brennan MF, et al. Pasireotide for postoperative pancreatic fistula. N Engl J Med 2014;370:2014-22.
58. Kendrick ML, Cusati D. Total laparoscopic pancreaticoduodenectomy: feasibility and outcome in an early experience. Arch Surg 2010;145:19-23.
59. Beissel JM, Kendrick ML, Podratz KC, et al. Pancreaticoduodenectomy in optimal primary cytoreduction of epithelial ovarian cancer: A case report and review of the literature. Gynecol Oncol Rep 2014;10:25-7.
60. Oettle H, Neuhaus P, Hochhaus A, et al. Adjuvant chemotherapy with gemcitabine and long-term outcomes among patients with resected pancreatic cancer: the CONKO-001 randomized trial. JAMA 2013;310:1473-81.
61. Neoptolemos JP, Stocken DD, Bassi C, et al. Adjuvant chemotherapy with fluorouracil plus folinic acid vs gemcitabine following pancreatic cancer resection: a randomized controlled trial. JAMA 2010;304:1073-81.
62. Klinkenbijl JH, Jeekel J, Sahmoud T, et al. Adjuvant radiotherapy and 5-fluorouracil after curative resection of cancer of the pancreas and periampullary region: phase III trial of the EORTC gastrointestinal tract cancer cooperative group. Ann Surg 1999;230:776-82; discussion 782-4.
63. Li D, O'Reilly EM. Adjuvant and Neoadjuvant Therapy for Pancreatic Cancer. Surg Oncol Clin N Am 2016;25:311-26.

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