Pancreatic Cancer Care Guidelines

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If patient has clinical suspicion of pancreas cancer, we suggest the following:

- CT abdomen with contrast
- Referral to gastroenterology with MD experienced in EUS
  - EUS encouraged unless results not thought to change management
    - Mandatory in patients who are borderline, unresectable, or non-visualized on preoperative CT (NCCN 12.2)
    - May not be necessary in patients with tissue diagnosis and clearly resectable on imaging
  - Tissue confirmation should be attempted on all right sided lesions (2009 AHPBA consensus guidelines)
  - EUS biopsy preferred over percutaneous (NCCN 12.2)
  - ERCP & placement of durable stent is discouraged except in the following scenarios:
    - if neoadjuvant or non-surgical therapy planned
    - if surgery will be delayed > 2 weeks
    - if fevers, chills, severe pruritis or other clinical evidence of cholangitis
    - Short metal stents at the discretion of gastroenterologists, non-consensus recommendation
- Serum CA 19-9 (blood test that is elevated in many patients with pancreas cancer)
  - Do not measure in patients with elevated bilirubin. In these cases, measure only after biliary compression reduces bilirubin to normal; or if no preoperative stenting is performed, then measure CA 19-9 postoperatively to follow for recurrence (NCCN 12.2) as the preoperative measurement will be inaccurate.

Tests we recommend in the evaluation of pancreas cancer prior to surgery:

- Pancreatic protocol CT
  - Triphasic study with visualization SMA and SMV, 3 mm cuts*
  - New study if triphasic not done or inadequate or > 8 weeks old
  - Acceptable alternative: MRI
- Chest CT
- PET/CT not necessary except if suspicion of otherwise occult metastases:
  - if non regional lymphadenopathy
  - if CA 19-9 > 180 in setting of normal bilirubin
- Preoperative separate staging laparoscopy with peritoneal washings only in rare circumstances:
  - Equivocal PET/CT (SUV 1-3, enlarged nodes) and suspicion for peritoneal spread
- Presentation at our liver and pancreas cancer conference

How we classify cases of pancreatic cancer, using 3 levels of tumor extent:

- Resectable
  - No distant metastases
  - Mesenteric veins and arteries free of tumor, without abutment, narrowing, encasement, thrombosis
  - No adenopathy in celiac, SMA regions or left of the aorta
Clear fat planes around celiac axis, hepatic artery, SMA

- Borderline resectable
  - No distant metastases
  - Venous involvement of the SMV/portal vein demonstrating tumor abutment with impingement and narrowing of the lumen, encasement of the SMV/portal vein but without encasement of the nearby arteries, or short-segment venous occlusion resulting from either tumor thrombus or encasement but with suitable vessel proximal and distal to the area of vessel involvement, allowing for safe resection and reconstruction. Isolated jejunal or ileal vein suitable for distal venous reconstruction
  - Gastroduodenal artery encasement up to the hepatic artery with either short segment encasement or direct abutment of the hepatic artery, without extension to the celiac axis
  - Tumor abutment of the SMA not to exceed greater than 180 degrees of the circumference of the vessel wall

- Locally advanced
  - Distant metastases, greater than 180 degrees SMA encasement, any celiac abutment, non-reconstructible SMV/portal occlusion, aortic invasion or encasement

- Positive peritoneal cytology on staging laparoscopy with no visualized metastases
  - Not suitable for resectable or borderline classification as published management guidelines not consistent with NCCN Guidelines 2.2012, consider systemic therapy initially, delayed local therapy may be appropriate[1]

### Treatment of resectable tumors
(tumors that don’t require treatment before surgery, unless under protocol)

1. Enter into clinical trial if eligible, discuss with patient
   - Gough study (all pancreatic mass cases)
   - Neoadjuvant (none open 3.2013; protocol under discussion but not yet written)
   - Post-operative (ACOSOG/A5041; RTOG 0848)

2. Biliary decompression optional, see previous discussion

3. Tissue confirmation not available, repeat EUS and/or laparoscopy with u/s guided core biopsy, unless suspicious mass or resection otherwise indicated

4. Surgical resection

5. Post-operative adjuvant therapy, Gemcitabine based

### Treatment of borderline resectable tumors
(tumors that have limited growth into surrounding blood vessels of the intestine—specific definition discussed later)

- Offer therapy under protocol if available
  - Gough trial
  - Chemoradioimmunotherapy protocol Crocenzi (IRB pending)
  - ACOSOG/Alliance trial when open—Matt Katz PI
Treatment of locally advanced tumors
(tumors that completely surround blood vessels of the intestine)

- Clinical trial
  - Gough trial
  - Chemoradioimmunotherapy protocol Crocenzi (IRB pending)
  - FOLFIRINOX on ACOSOG trial if available
- FOLFIRINOX off protocol for excellent functional status patients if intent curative
- Gemcitbine based combination therapy with concurrent gem/RT if off protocol
- Salvage surgery for major responders if under protocol or ambivalence regarding initial staging or M1 by cytology only

Preoperative care

- Routine preoperative labs plus CA 19-9
- Advise oral intake of Impact Advanced Recovery™ 8 fl oz/237 ml per day for 7 days prior to surgery.
- Review of imaging, including arterial, venous anatomy and staging studies with team at fellows conference (Wednesday pm and Thursday am)
- Offer entry into tissue studies and other relevant protocols, discuss study plans and pre-operative studies and labs with Trinh Stephens--HPB clinic coordinator

Day of surgery, preparation

- Review imaging at time of surgery, with films displayed in OR, discuss vascular anatomy, and if secondary procedures planned
- Discussion of plans for specimen handling for pathology and research as part of the time out process just before surgery begins. Telephone contact with appropriate lab personnel before starting case—Talicia/Ben
  - Office: 503 215-4236
  - Talicia’s cell: 503-896-8555
  - Ben’s cell: 503-318-1854
  - Pippa’s cell: 646-320-8488
- Avoidance of epidural catheter. Use of submuscular pain pumps or local blocks for pain control encouraged. Intrathecal narcotic injection optional in routine case, not difficult cases or pts treated with neoadjuvant therapy.
- Positioning, tuck right arm and bed at 90 degrees if robotic case.

Day of surgery, operative care

- Laparoscopic evaluation of abdomen and liver u/s prior to open surgery
- Culture bile if pancreatic stent placed pre op
- Consider external stenting of high risk anastomoses (soft gland, small duct < 3 mm)
- Drain pancreas unless low risk of leaking (firm gland, duct > 3 mm)
- Avoid NG[2]
• Feeding jejunostomy selectively (high risk of leak)
• Use LMH on formulary sc every day, starting day after surgery, and scd’s per high risk criteria until d/c or 30 days if vein reconstruction
• Famotadine 20 mg IV bid, transition to omeprazole when taking po
• If not firm pancreas with duct < 3 mm: Octreotide intraop at time of assessing anastomosis 100 mcg sc and 100 mcg every 8 hours post op for 5 days or until fistula low volume < 50 ml/day.
• Operative note includes the following:
  o pancreatic texture (soft, medium, firm)
  o pancreatic duct size
  o location of drain placement.
• Clear liquid diet, d/c foley pod 2

Post-operative care
• Full liquid diet pod 3 and drain amylase if applicable
• Remove drain(s) if amylase less than 3 times normal serum level and clinical pancreatic or lymphatic leak not suspected, regardless of volume
• Oral pain medication pod 3,4
• Probe any indurated/erythematous part of open incision early and pack without starting antibiotics unless infection documented or strongly suspected
• Laboratory tests as indicated clinically
• Pancreatic enzyme replacement when tolerating regular diet, creon 24,000 U with meals
• CT scan if any suspicion of leak (any day) or abscess (POD 5 or later), or elevated WBC or fever without suspicion of leak, with percutaneous drainage as indicated, empiric antibiotics (zosyn or directed antibiotic if bile culture done) for significant post op inflammation, 5 days or longer if indicated
• Expected median day of d/c is day 7
• D/C medications include creon, omeprazole

Pathologic analysis of specimens
• Specimens are generally kept sterile until research staff can dissect tissue for Gough study. Planning for research staff presence at time of tissue availability should be discussed with the operative team before the surgery starts. There should be either direct communication between the surgeon and pathologist for proper orientation and margin identification, or the surgeon should identify the important margins with a clearly understood and documented method, written on the pathology requisition, for example: stitch on SMA margin, safety pin on the retroperitoneal/uncinate margin, frozen section on pancreatic duct margin and bile duct margin (see SOP: Liver and Pancreas Tumor Acquisition)
• Posterior Margin: This margin is from the posterior caudad aspect of the pancreatic head that merges with the uncinate margin and that appears to be covered by loose connective tissue. Radial rather than en face sections of this margin will more clearly demonstrate whether it is involved by tumor. In some instances this margin can be included in the same section as the SMA margin section
• **Portal Vein Groove Margin:** This is the smooth-surfaced groove on the posterior-medial surface of the pancreatic head that rests over the portal vein. Radial rather than en face sections of this margin will more clearly demonstrate whether it is involved by tumor and also will provide the distance of the tumor from the margin. As is true for the posterior margin, in some instances this margin can be included in the same section as the SMA margin section.

• **U Portal Vein Margins:** If an en bloc partial or complete vein resection is added to the surgical specimen it should be marked separately. En face proximal and distal end margins of the vein should be separately submitted as Proximal Portal Vein Margin and Distal Portal Vein Margin. A section documenting tumor invasion into the vein wall should also be submitted. If feasible, this section should be a full thickness of the vein wall demonstrating the depth of tumor invasion as this has been shown to have prognostic value.

• **Pancreatic Neck (transection) Margin:** This is the en face section of the transected pancreatic neck. The section should be placed into the cassette with true margin facing up so that the initial section into the block represents the true surgical margin.

• **Bile Duct Margin:** This is the en face section of the bile duct end. The section should be removed from the unopened duct and placed into the cassette with true margin facing up so that the initial section into the block represents the true surgical margin.

• **Other margins analyzed in Whipple specimens include the proximal and distal enteric margins (en face sections) and anterior surface (closest representative).** The anterior surface is not a true margin, but identification and reporting of this surface when positive may portend a risk of local recurrence, and so should be reported in all cases. Collectively, these pancreatic tissue surfaces constitute the circumferential transection margin. Designating the various specific margins with different colored inks will allow recognition on microscopy.

**Follow-up**

- Surgery clinic 1 – 2 weeks post op, 3 months post op x 2, every 6 months.
- Need post-operative blood draw at first follow up for Gough study.
- Medical oncology referral and treatment per NCCN guidelines
  - RTOG 0848, examines whether the addition of erlotinib and/or delayed radiation therapy to gemcitabine adjuvant chemotherapy improves survival as compared to gemcitabine alone following R0 or R1 resection of head of pancreas adenocarcinoma (including adenocarcinoma of the head, neck, and uncinate process).
  - Gemcitabine based chemotherapy +/- radiation off protocol

**References**