North-East London Cancer Network & Barts and the London HPB Centre
PROTOCOL FOR MANAGEMENT OF PANCREATIC CANCER
(OCTOBER 2009)

I. PRE-REFERRAL GUIDELINES

Screening

1. Offer genetic counseling, genetic testing and regular follow-up at a specialist centre to patients with hereditary pancreatitis, familial pancreatic cancer and other familial cancer syndromes (e.g. ovarian and breast cancer syndrome)
2. Keep patients with familial adenomatous polyposis on endoscopic follow-up and if they have stage 4 duodenal polyposis, offer surgical resection (pancreato-duodenectomy)
3. Consider pancreatic cancer as a possibility in patients with adult-onset diabetes (<2 years' duration) who have no predisposing features (obesity, steroids) or family history
4. Exclude pancreatic cancer in patients with an unexplained attack of acute pancreatitis
5. Keep patients with chronic pancreatitis under surveillance

Obstructive jaundice on initial presentation

1. Check LFTS, Clotting
2. Use Ultrasound as initial screening tool. Following that…
    - CBD Stones confirmed: ERCP or laparoscopic bile duct stone management as per local expertise
    - CBD stone suspected but not visualised, pancreatic head not visualised: MRI with MRCP
    - Pancreatic head mass or suspicion thereof: CT scan (chest, abdomen and pelvis)

II. MDT PROCESS AND PRE-OPERATIVE WORK-UP

Staging of tumour with CT

1. Do a triple phase CT using pancreatic protocol
2. Evaluate all CT Scans at an MDT with HPB input.
3. All patients undergoing surgery for suspected cancer should be triaged as
    - Definitely irresectable
    - Definitely resectable
    - Doubtful resectability based on vascular invasion (Patients triaged to groups 2 and 3 should be audited for resectability rate)
4. CT scan report should specify:
    - Site of tumour: bile duct, head, neck, uncinate, body, tail
    - Size of tumour

- Local invasion: vessels (SMA, SMV, PV, IVC), duodenum, stomach, liver hilum, colon
- Metastasis: liver, peritoneum, distant lymph nodes (celiac etc.,)

5. For tumours of the pancreatic head,
   - Involvement of the portal or superior mesenteric vein by tumour is not an absolute contraindication to surgery and the decision on resectability should be made by a HPB surgeon and radiologist.
   - Major arterial involvement (SMA/Coeliac/Common hepatic), liver metastases and disseminated peritoneal disease are contraindications to resectional surgery.
   - Lymph node metastases within the operative field are not a contraindication to resection but distant nodal enlargement (i.e. coeliac nodes) precludes curative resection

5. For tumours of the pancreatic body and tail, involvement of the splenic artery or vein is not a contraindication to resection
6. CT scan should be within 4 weeks of a scheduled operation.

Role of additional investigations

1. ERCP: ERCP is preferable to PTC in relieving obstructive jaundice in patients with pancreatic cancer. Points to consider:
   - Obtain bile for cytology and brushings from the stricture
   - Avoid stenting provided patient is fit for surgery and surgery possible within 2 weeks and Bilirubin < 250 mg
   - Use plastic rather than metal stents in patients with resectable tumours, ot if if resectability not yet assessed at MDT (or at the very least, if placing metal stents do not insert them right up to the liver hilum)
2. PTC: If ERCP fails and biliary drainage is necessary, do a PTC
3. EUS: Indications are
   - Mass not seen on CT scan, but high suspicion of carcinoma
   - To assess vascular invasion in borderline cases
   - Unresectable tumour and need for tissue diagnosis
   - Coeliac plexus block
4. Laparoscopy: Only in selected cases (peritoneal disease, possible liver metastasis) discussed at MDT. No standard role for laparoscopic ultrasound in assessing vessel encasement.
5. PET: Role in diagnostic work-up doubtful, To be re-assessed in the light of more literature
6. MRI/MRCP: No routine role in diagnostic work-up.
7. CA-19.9: Baseline pre-operative value should be at minimal jaundice state where possible
8. Biopsy:
   - Avoid transperitoneal biopsy in patients with potentially resectable tumours
   - If EUS is being done, try and obtain tissue diagnosis
   - Try to obtain histological confirmation of cancer in all patients being referred for chemotherapy and/or radiotherapy, and preferably in patients being

referred for palliative care

9. Anaesthetic fitness particularly in elderly, frail or unfit patients should be assessed by anaesthetists and Cardio-pulmonary exercise testing (CPET) used where appropriate.

Note on unusual and rare tumours

1. Cystic tumours of the pancreas
   - These can often be differentiated from inflammatory cysts on the basis of the clinical presentation and the radiological appearances
   - Consider EUS-guided aspiration (or failing that, percutaneous aspiration) of a sample of cyst fluid, and test that for CEA level, amylase level, and cytology.
   - Mucinous cystic tumours have a high CEA level in the cyst fluid. They carry a potential for malignant transformation. Consider surgical resection.
2. Neuroendocrine tumours
   - These are rare tumours, and should be managed by a specialist endocrine and HPB team
   - Patients with multiple endocrine neoplasia syndromes require genetic testing, counseling and follow-up
   - Additional tests are often warranted including serum assays of gut hormones and chromogranin, MR, EUS, radionuclide scans (octreotide, MIBG), and angiography with calcium stimulation and hepatic venous sampling
   - Aggressive resectional surgery may be appropriate in some patients with a seemingly high tumour load

III. SURGERY

Resections for pancreatic cancer should only be performed at the designated regional Centre. Standard peri-operative protocol at Barts and the London for resection of tumours of the **pancreatic head** is as follows:

1. Have HDU/ITU bed available
2. 4 units cross-match
3. No role for extended lymphadenectomy (sampling of lymph nodes where appropriate)
4. Portal vein or Superior mesenteric venous resection to be done only for patients with definite evidence of venous invasion
5. No role for vascular arterial resections
6. Pancreatic anastomosis: to be decided on by surgeon, depending on gland texture (soft,friable,firm etc) and other anatomical considerations
7. Octreotide:100 mcg subcutaneously 8 hrly, to start pre-op & continue to day 7
8. Drain fluid amylase on day 4-5.
9. Post-op oral feed within day 4, provided condition stable. No routine jejunosotomy or NG /NJ feeds.

10. No TPN except in clinically significant pancreatic leaks
11. Aim discharge by day 14 (Audit discharge dates).
12. Consider pancreatic enzyme supplements.
13. If patient found to have inoperable disease:
    - Perform a biliary bypass (preferably using the CBD rather than the gall bladder) and a duodenal bypass.
    - Also consider coeliac plexus block (50% ethanol)
    - Obtain tissue diagnosis if none obtained so far

14. Note on **splenectomy**: If a patient is likely to undergo total pancreatectomy, or a distal pancreatectomy for a tumour of the pancreatic body/tail, counsel the patient about the consequences of splenectomy and administer pre-splenectomy vaccines. After surgery, put on antibiotic prophylaxis.

IV. HISTOPATHOLOGY

1. Comply with the minimum dataset as recommended by Royal College of Pathologists (our current reporting exceeds this).
2. Discuss all resected patients and biopsied patients at MDT and make appropriate adjuvant/palliative treatment decisions in conjunction with oncologists.

V. FOLLOW-UP SCHEDULE for patients with **resected** cancers

1. 1st surgical outpatients: 4 weeks.
    - Check wound, general recovery.
    - Do baseline post-operative CA-19.9 and routine bloods.
    - Refer for adjuvant chemotherapy/chemoradiotherapy as appropriate. All referrals to be discussed at MDT and sent to local oncology clinicians. (See below)
    - Assuming adjuvant treatment is commenced immediately and takes six months to complete, there should be no HPB Centre follow-up until the 6th month, to avoid duplication of assessments (clinical and investigational).
    - Watch for clinical symptoms of steatorrhea and treat as appropriate
    - General principles of shared care:
        - All letters to be copied to appropriate clinicians
        - Investigations as per trial protocol

2. 2nd surgical outpatient appointment: 6 months, to coincide with CT scan (ideally on day of visit to HPB Centre). Also, CA19.9 and routine bloods
3. 3-monthly surgical follow-up thereafter for the first 2 years; CT scans at 12, 18 and 24 months
4. 6-monthly follow-up over the 3rd, 4th and 5th years, with CT Scans annually.

VI. ADJUVANT THERAPY FOR PANCREAS CANCER

1. No role for routine **neo-adjuvant** therapy.Neo-adjuvant chemotherapy or chemoradiation may be considered in a small group of selected

patients with locally advanced disease, or within the context of clinical trials
2. Resected patients who have received neo-adjuvant therapy should not be included in adjuvant therapy trials
3. Resected patients with R0/R1/R2 tumours should be offered adjuvant chemotherapy (Gemcitabine).
4. Resected patients with R1/R2 tumours may be considered for adjuvant chemoradiation

VII. ADVANCED PANCREATIC CANCER

1. Patients should be considered for entry into the Telovac study. There will be (from Nov/Dec 2009) a Cancer Research UK Phase I/IIa Trial of an oral Notch Inhibitor (MK-0752) in Combination with Gemcitabine in patients with Stage 4 Metastatic Pancreatic Cancer

2. Palliation of gastric outlet obstruction: Consider Surgical bypass or failing that Duodenal stents

3. Pain relief

4. Referral to Palliative Care