Upper Gastrointestinal Cancer (Suspected)
Part 2

Effective Date: April 2, 2016

Disclaimer
The Family Practice Oncology Network (FPON) developed this clinical practice guideline following a documented guideline adaptation process. The recommendations in this guideline were adapted with permission from the BC Cancer Agency – Gastrointestinal Cancer Management Guidelines, and unless otherwise stated, are based primarily on evidence sourced and evaluated by the BC Cancer Agency, as well as expert clinical opinion. Additional sources of evidence were evaluated and cited as indicated. Recommendations were finalized following an external peer review. This guideline is intended to give guidance to practitioners on the clinical management of upper gastrointestinal cancer, and is not designed to replace clinical decision-making, or to be considered a standard of care.

SCOPE

Part 2 of this guideline outlines recommendations for the prevention, screening, diagnosis, treatment and follow-up of upper gastrointestinal (GI) malignancies, including pancreatic cancer, neuroendocrine tumours (NETs) of the pancreas and duodenum, and cancer of the extrahepatic biliary tract. The primary target audience for this guideline is community general practitioners providing first contact or primary health care.

KEY RECOMMENDATIONS

- Screening for upper GI cancers, including extrahepatic biliary and pancreatic cancers, is not recommended, but should be considered for certain high risk groups. Details on selection of these patients is included within the guideline (see *Screening*)[1,2,3]
- Painless jaundice should be considered pancreatic cancer until proven otherwise[1]
- If pancreatic cancer is suspected investigations should be expedited
- There is no evidence that routine imaging or laboratory investigations including Ca 19-9 are useful in detecting recurrent metastatic disease[1,3]
- Patients facing potentially life-limiting conditions may benefit from advance care planning (see *Resources)*

PREVENTION

The risk of many of these cancers increases with smoking.[4,5,6] Diabetes, chronic pancreatitis, and excessive alcohol consumption are all risk factors for pancreatic cancer.[4,6,7] As with many other cancers, preventative measures include reducing alcohol intake, maintaining a healthy weight and smoking cessation.[4]

SCREENING

There are no recommended screening guidelines for pancreatic or bile duct cancer.[1,2,3] The incidence of these cancers is low (e.g. the incidence of pancreatic cancer in B.C. is 12.55 cases per 100,000 population).[8] Screening with EUS or MRI may be indicated in patients at high risk (see *Risk Factors*) for pancreatic cancer.[1,7,9,10,11]

Background and Risk Factors

- *Pancreatic Cancer*

  Pancreatic cancers are of exocrine or endocrine origin. Exocrine tumors are the most common type of pancreatic cancer, of which 85% are adenocarcinoma.[1] Approximately 10% are adenosquamous carcinoma, and the remaining are endocrine tumours (pNETs) amounting to < 4% of all pancreatic neoplasms.[1,12] Pancreatic exocrine carcinomas are associated with poor prognosis, and patients are often asymptomatic until late in the course of the disease.[1] Ampullary cancers have a better prognosis than pancreatic adenocarcinoma.[1] The incidence of pancreatic cancer increases significantly from the age of 60.[8]

  Non-hereditary risk factors include smoking, chronic pancreatitis, diabetes mellitus, obesity, and a possible association with *Helicobacter pylori* infection.[4,13,14,15,16] Hereditary pancreatic cancer account for 5-10% of cases.[10,17,18,19] Some of these hereditary risk factors include:

  - Individuals with two or more first degree relatives with pancreatic carcinoma[18]
  - Carriers of BRCA1 and BRCA2 mutations[20,21]
  - Carriers of p16 mutations[10]
  - Patients with Lynch syndrome with affected first degree relatives[10]
  - Patients with Peutz-Jeghers syndrome[10]

- *Neuroendocrine Tumours*

  Neuroendocrine tumours arise from the diffuse neuroendocrine system of the gut.[12] They are rare and include NETs of the stomach, duodenum and pancreas.[12] Pancreatic NETs (pNETs) are rare and can occur at any age, and in both sexes equally.[12] Pancreatic neoplasms can occur as part of four hereditary conditions:

  - Multiple endocrine neoplasia type 1 (MEN1)[12,22]
  - von Hippel-Lindau disease (VHL)[12,22]
  - Neurofibromatosis 1 (NF-1; von Recklinghausen disease)[12,22]
  - Tuberous sclerosis complex (TSC)[12,22]

  The most common association of pNETs is with MEN1.[12,22]

- *Bile Duct Cancer*

  Cholangiocarcinoma may present as obstructive jaundice, or be mistaken for hepatocellular carcinoma or metastatic disease from an unknown primary site. Over 90% of bile duct carcinomas are adenocarcinomas.[23] The incidence of bile duct cancer peaks in the seventh decade and occurs slightly more frequently in men than in women.[23] Prevalence is higher in South East Asia, and may be related to chronic parasitic infection of the liver (i.e. liver flukes - *Clonorchis sinensis* and *Opisthorchis viverrini).*[23]

  Risk factors for bile duct cancer in Western populations include:

  - Inflammatory bowel disease[24]
  - Primary sclerosing cholangitis[23]
  - Congenital choledochal cysts[23]
  - Possible exposure to environmental toxins (i.e. dioxins, asbestos, nitrosamines, Thorotrast)[23,25]

  The incidence of cholangiocarcinoma in patients with underlying primary sclerosing cholangitis is 8-40%.[23]

DIAGNOSIS

Diagnosis is difficult as many of the symptoms of these cancers are non-specific and can mimic benign or other malignant conditions (e.g. ovarian cancer, gastric cancer, primary peritoneal cancer).

- ***Signs and Symptoms***

  In pancreatic cancer, the two most common presenting symptoms are abdominal pain and jaundice.[26] Painless jaundice is considered to be pancreatic cancer until proven otherwise. Persistent abdominal pain and ongoing weight loss should prompt appropriate investigations. Other non-specific symptoms include:

  - Fatigue, anorexia, weight loss, dull epigastric pain, early satiety
  - Abdominal pain, back pain, or weight loss are usually signs of late-stage disease

  NETs present as functional or nonfunctional tumours. Functional tumours are characterized by excess hormone production resulting in clinical syndromes (e.g. carcinoid syndrome), and are named according to the hypersecreted hormone (e.g. insulinomas, gastrinomas).[12] Alternatively, non-functional tumours are not due to excess hormone production, and present due to tumour bulk; tumours are slow growing and metastatic disease is usually present at diagnosis. The patient may present with intermittent abdominal discomfort for months or years, often interpreted to be a functional disorder[12]

- ***Investigations***

  While the incidence of these cancers is low, it is important to maintain a high index of suspicion in patients with persistent symptoms.

- If cancer is suspected, investigations should be expedited (i.e. urgent request for abdominal imaging)
- Initial investigations, depending on level of clinical suspicion, should include abdominal imaging (i.e. US/CT scan), and blood work (CBC, creatinine, liver function tests)
- CA 19-9 serum antigen is the tumour marker for pancreaticobiliary malignancy, however, this marker is not specific for these cancers

➢ ***Indications for Referral to a Specialist***
A person should be ***referred urgently*** to a specialist if they have:

- obstructive jaundice
- an upper abdominal mass

STAGING

The TNM classification system is the international standard. Refer to the BC Cancer Agency gastrointestinal guidelines (see *Resources*), for a link to staging diagrams and definitions for T, N, and M descriptors.

TREATMENT

Treatment is as recommended by the surgeon and the oncologist/BC Cancer Agency team.

➢ *Pancreatic Cancer*
Surgical treatment offers the only potential cure for resectable carcinoma of the pancreas. Adjuvant therapy may be offered following surgery. Surgery, chemotherapy, or radiation therapy may be indicated for palliation.

➢ *Neuroendocrine Tumours*
A multidisciplinary approach to the treatment of NETs is recommended.[12] Patients with resectable NETs can expect a good intermediate term prognosis. Resectable NETs are managed by endoscopic or surgical resection. Unresectable metastatic disease may benefit from debulking for palliation. For gastrin-producing NETs, proton pump inhibitors should be used to control acid-related symptoms.[12]

➢ *Biliary Tract Cancer*
Surgery of resectable tumours is the only potentially curative treatment available.[3] The role of adjuvant chemotherapy remains undefined.[3] Patients with advanced disease may achieve a prolonged period of palliation through surgical, endoscopic and radiological drainage procedures.[3] In a palliative setting, chemotherapy may provide a benefit.[3]

FOLLOW-UP

At the discretion and direction of the oncologist, the patient may be discharged to the primary care provider.

Follow-up care may include the following:

- Surveillance for recurrent disease or late effects of treatment when indicated
- Monitoring and treating complications and/or side effects
- Providing patient support
- Symptom management, best supportive care and the involvement of palliative services

There is no evidence that routine imaging or laboratory investigations including Ca 19-9, are useful in detecting recurrent metastatic disease. Early detection of asymptomatic metastases does not enhance survival. Investigations should be performed based the clinical presentation of a patient who is suspected of having recurrent or metastatic disease.[1,3]

Patients with a life-limiting disease or illness may benefit from the development of an advance care plan (ACP) (see *Resources*) that incorporates the patient's values and personal goals, indicates potential outcomes, and outlines linkages with other healthcare professionals that would be involved in the care and their expected roles. The ACP is an opportunity to also identify the patient's alternate substitute decision maker or legal health representative.

Specific recommendations will be provided in the patient's discharge letter. At any time the patient and/or primary care provider may consult with the BC Cancer Agency for any follow-up questions or concerns.

RESOURCES

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➢ PHYSICIAN AND PATIENT RESOURCES

- **BC Cancer Agency**, www.bccancer.bc.ca
  - Gastrointestinal Clinical Practice Guidelines www.bccancer.bc.ca/HPI/CancerManagementGuidelines/Gastrointestinal/default.htm
  - Hereditary Cancer Program, for referrals: 604-877-6000 (ext. 672198), www.screeningbc.ca/Hereditary/ForHealthProfessionals/Default.htm
  - Hereditary Cancer Program Referral Form
- **BC Guidelines**, BCGuidelines.ca
  - *Dyspepsia with or without Helicobacter pylori Infection – Clinical Approach in Adults – December 2009*
  - *Palliative Care for the Patient with Incurable Cancer or Advanced Disease*
    - *Part 1: Approach to Care – 2010*
    - *Part 2: Pain and Symptom Management – 2011*
    - *Part 3: Grief and Bereavement – 2011*
- **British Columbia Ministry of Health**
  - *My Voice – Expressing my Wishes for Future Health Care Treatment – Advance Care Planning Guide*, available at www.health.gov.bc.ca/library/publications/year/2013/MyVoice-AdvanceCarePlanningGuide.pdf
  - Provincial advance care planning resources are available at www.gov.bc.ca/advancecare
- **HealthLink BC**, www.healthlinkbc.ca , 8-1-1 (toll free in B.C.), 7-1-1 TTY (Deaf and hearing-impaired)

➢ ABBREVIATIONS

ACP – advance care plan
CA 19-9 – cancer antigen 19-9
CBC – complete blood count
CT – computerized tomography
GI – gastrointestinal
NETs – neuroendocrine tumours
pNETs – pancreatic neuroendocrine tumours
PPIs – proton pump inhibitors
TSH – thyroid stimulating hormone
US - ultrasound

➢ ASSOCIATED DOCUMENTS

The following document accompanies this guideline:

- Family Practice Oncology Network – *Upper Gastrointestinal Cancer (Suspected) – Part 1* (available at www.bccancer.bc.ca/health-professionals/networks/family-practice-oncology-network/guidelines-protocols).

➢ RENEWAL DATE

This guideline will be reviewed 3-5 years following the effective date, unless changes in clinical evidence warrant an earlier revision.

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