Upper Gastrointestinal Cancer (Suspected)
Part 2
External Review

Effective Date: TBD

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.
- Painless jaundice should be considered to be pancreatic cancer until proven otherwise.
- 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.\(^1\),\(^2\)
- 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.\(^3\),\(^4\) Excessive alcohol consumption, as well as the presence of diabetes and chronic pancreatitis increase the risk of pancreatic cancer.\(^3\) As with many other cancers, preventative measures include reducing alcohol intake, maintaining a healthy weight, and smoking cessation.

SCREENING
There are no recommended screening guidelines for pancreatic or bile duct cancer.\(^2\),\(^5\) 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, and bile duct cancer 1-2 cases per 100 000 population).\(^6\),\(^7\) Screening with EUS or MRI may be indicated in patients at high risk (see Risk Factors) for pancreatic cancer.\(^5\),\(^8\)

Risk Factors
The incidence of pancreatic cancer increases significantly from the age of 60.\(^6\) Non-hereditary risk factors include smoking, chronic pancreatitis, diabetes mellitus, obesity, and Helicobacter pylori infection.\(^3\) Hereditary pancreatic cancer account for 5-10% of cases.\(^5\) People at higher risk include:\(^5\)
- individuals with two or more first degree relatives with pancreatic carcinoma
- carriers of BRCA2 mutations
- carriers of p16 mutations
- patients with Lynch syndrome with affected first degree relatives
- patients with Peutz-Jeghers syndrome

Pancreatic NETs (pNETs) are rare and can occur at any age, and in both sexes equally.\(^9\)
Pancreatic neoplasms can occur as part of four hereditary conditions:\(^9\)
- multiple endocrine neoplasia type 1 (MEN1),
- von Hippel-Lindau disease (VHL),
- neurofibromatosis 1 (NF-1; von Recklinghausen disease), and
- tuberous sclerosis complex (TSC)

The most common association of pNETs is with MEN-1 (80\%).\(^9\)

Bile duct cancer occurs equally in men and women, and incidence peaks in the sixth and seventh decade.\(^7\) Prevalence is higher in South East Asia, and may be related to chronic infection with *Clonorchis sinensis* and *Opisthorchis viverrini*.\(^10\) Risk factors for bile duct cancer in Western populations include:\(^10\)
- inflammatory bowel disease
- primary sclerosing cholangitis
- congenital choledochal cysts
- possible exposure to environmental toxins (i.e. dioxins, asbestos, nitrosamines, Thorotrast)

The incidence of cholangiocarcinoma in patients with underlying primary sclerosing cholangitis is 9-40\%.\(^10\)

**DIAGNOSIS**

**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.\(^11\) Approximately 10% are adenosquamous carcinoma; the remainder are endocrine tumours (pNETs) amounting to <4% of all pancreatic neoplasms.\(^9\) Pancreatic exocrine carcinomas are associated with poor prognosis,\(^12\) and patients are often asymptomatic until late in the course of the disease. Ampullary cancers have a better prognosis than pancreatic adenocarcinoma.\(^11\)

**Neuroendocrine Tumours**

Neuroendocrine tumours arise from the diffuse neuroendocrine system of the gut.\(^13\) They are rare and include NETs of the stomach, duodenum and pancreas.

**Bile Duct Cancer**

Intrahepatic cholangiocarcinoma is often mistaken for hepatocellular carcinoma, or metastatic disease from an unknown primary site.\(^14\) Over 90% of bile duct carcinomas are adenocarcinomas.\(^14\)

**Signs and Symptoms**

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

In pancreatic cancer, the two most common presenting symptoms are abdominal pain and jaundice.\(^15\) Other non-specific symptoms are included below:
- Painless jaundice is considered to be pancreatic cancer until proven otherwise.
- Fatigue, anorexia, weight loss, dull epigastric pain, early satiety.\(^12\)
- Abdominal pain, back pain or weight loss are usually signs of late-stage disease.\(^8\)
- Persistent abdominal pain and ongoing weight loss should prompt appropriate investigations.
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).\textsuperscript{13}
- Non-functional tumours are not due to excess hormone production, and alternatively 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.\textsuperscript{13}

**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 (urgent request for abdominal imaging).
- Initial investigations should include abdominal imaging (US and CT scan), and bloodwork (CBC, creatinine, liver function tests, tumour markers).
- CA 19-9 serum antigen is the tumour marker for pancreatico-biliary malignancy, however, this marker is not specific to these cancers.\textsuperscript{14}

**Indications for Referral to a Specialist**
- A person should be referred urgently to a specialist if they have obstructive jaundice.
- A person with an upper abdominal mass should be referred urgently to a specialist.

**STAGING**
The TNM classification system is the international standard. Refer to the BC Cancer Agency gastrointestinal guidelines (Refer to 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.\textsuperscript{9,13} 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.\textsuperscript{13}

*Biliary Tract Cancer*
Surgery of resectable tumours is the only potentially curative treatment available.\textsuperscript{16} The role of adjuvant chemotherapy remains undefined.\textsuperscript{16} Patients with advanced disease may achieve a prolonged period of palliation through surgical, endoscopic and radiological drainage procedures.\textsuperscript{16} In a palliative setting, chemotherapy may provide a benefit.\textsuperscript{16}

**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 on the clinical presentation of a patient who is suspected of having recurrent or metastatic disease.1,2

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

REFERENCES

2 BC Cancer Agency. Cancer Management Guidelines – Gastrointestinal – 9 Gall Bladder, Extrahepatic and Intrahepatic (Peripheral), and Cholangiocarcinoma Cancer Management Guidelines. 9b.7 Follow-up [in press; cited 2015 February 6].
RESOURCES
  o Gastrointestinal Clinical Practice Guidelines
  o Hereditary Cancer Program, for referrals: 604-877-6000 (ext. 672198),
    http://www.screeningbc.ca/Hereditary/ForHealthProfessionals/Default.htm
● BC Guidelines, BCGuidelines.ca
  o Dyspepsia with or without Helicobacter pylori Infection – Clinical Approach in Adults –
    December - 2009
  o 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
  o My Voice – Expressing my Wishes for Future Health Care Treatment – Advance Care
    Planning Guide
  o Provincial advance care planning resources are available at www.gov.bc.ca/advancecare
● Healthlink BC, www.healthlinkbc.ca - (toll free in B.C.) 8-1-1 , or TTY (Deaf and hearing-impaired)
  7-1-1

ACRONYMS
ACP – advance care plan  
CBC – complete blood count  
CT – computed tomography  
GI – gastrointestinal  
US – ultrasound

ASSOCIATED DOCUMENTS
The following documents accompany this guideline:
● Family Practice Oncology Network – Upper Gastrointestinal Cancer (Suspected) – Part 1 (insert
  hyperlink)
● Hereditary Cancer Program Referral Form

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

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 cited as indicated. These recommendations
were finalized following a clinical external review.