Pancreatic Cancer – Established

Disclaimer

Contents

Background................................................................................................................................................. 2
  About Pancreatic Cancer .......................................................................................................................... 2
  Red flags .................................................................................................................................................. 2

Assessment.................................................................................................................................................. 2
  Cancer treatment summary letter ........................................................................................................... 2
  Diagnostic and staging results .................................................................................................................. 3
  Side-effects of chemotherapy or radiation therapy .................................................................................. 3

Management.............................................................................................................................................. 4
  General Practitioner Role ....................................................................................................................... 4
  Management of biliary obstruction ......................................................................................................... 5
  Considerations for surgery ...................................................................................................................... 5
  Treatment options for localised pancreatic cancer (stages 1 and 2) without distant metastases .......... 5
  Treatment regimens for inoperable or metastatic pancreatic cancer (stages 3 and 4) ......................... 6
  Treatments for progressive disease ....................................................................................................... 6
  Psychological care ................................................................................................................................... 7
  Palliative care .......................................................................................................................................... 7
  Follow-up .................................................................................................................................................. 7

Referral....................................................................................................................................................... 7

Information................................................................................................................................................. 7
  For health professionals ......................................................................................................................... 7
  For patients .............................................................................................................................................. 8

References.................................................................................................................................................. 8
Background

About Pancreatic Cancer

- Pancreatic cancer is a disease with poor prognosis compared with many other cancers with median survival of 11 to 20 months from diagnosis and 5 year survival is poor.
- Pancreatic cancer presents late, with only 20% being confined to the pancreas at diagnosis.
- 20% of pancreatic cancer originates in pancreatic cysts.
- About 3000 cases are diagnosed in Australia per year.
- The incidence is rising particularly in women, probably due to dietary factors including paucity of fruit and vegetables and increasing dependence on high fat/cholesterol foods. Smoking, alcohol excess, age, and genetic factors also increase the risk.
- While it is the 9th (women) or 10th (men) most common cancer in Australia, it is the 5th most common cause of cancer-related deaths.
- Low numbers of cases in Aboriginal and Torres Strait Islander populations make analysis difficult, but incidence seems similar to the non indigenous population, and mortality a little higher perhaps due to remoteness of location and delay in diagnosis.
- Despite advances, treatment for pancreatic cancer has moderate efficacy at best and the disease is regarded as incurable.
- Surgery offers the only potential for cure, however, only 15% of cases are candidates for surgical resection. 5 year survival after successful resection is 15% with median survival 15 to 24 months.
- Immunotherapy has yet to demonstrate benefit in pancreatic cancer.

Red flags

- Acute biliary obstruction
- Ascending cholangitis – pain, fever, jaundice
- Haematemesis or melaena from radiotherapy

Assessment

1. Refer to the cancer treatment summary letter, if available, from the treating team. Check that assessment agrees with the treatment plan chosen after considering co-morbidities. Contact the relevant GP Liaison Unit for queries about Specialist to general practitioner correspondence.

Cancer treatment summary letter

Most importantly should include:

- risk of recurrence and intentions of treatment.
- goals and quantitative benefit of proposed treatment.
- what the patient has been told.

Usually includes:

- diagnostic tests performed and results.
- tumour characteristics and other factors determining prognosis.
- type and date of treatments and a treatment summary.
- expectations of disease course, including expected discharge from oncology services.
- interventions and treatment plans from other health professionals.
- a process for rapid re-entry to specialist medical services for suspected recurrence.
- a list of symptoms that might need prompt investigation.
➢ a list of supportive care services provided and a plan for community care services, including what each service is to provide.
➢ contact information for key care providers.

2. Familiarise yourself with:

<table>
<thead>
<tr>
<th>Diagnostic and staging results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Investigations for pancreatic cancer diagnosis and staging</strong></td>
</tr>
<tr>
<td>➢ FBE, electrolytes and urea, LFTs,</td>
</tr>
<tr>
<td>➢ Imaging – Pancreatic protocol CT, CT Chest, MRI, MRCP</td>
</tr>
<tr>
<td>➢ Gastroscopy, ERCP, or endoscopic ultrasound results.</td>
</tr>
<tr>
<td>➢ Peritoneal cytology/histology results – positive results when present indicate metastatic peritoneal disease</td>
</tr>
<tr>
<td>➢ Serum biomarkers: cancer antigen 19-9 (CA 19-9) is elevated, has false positives (in jaundiced patients) and negatives.</td>
</tr>
<tr>
<td>➢ CA 19-9 should never be used as a screening test.</td>
</tr>
</tbody>
</table>

• the patient's [Eastern Cooperative Oncology Group (ECOG) performance status](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5776036/). Patients of ECOG status 3 or 4 are deemed unsuitable for major surgery or palliative chemotherapy.

3. Assess for red flags and side-effects of chemotherapy. If any red flags, notify the oncology team. See [GP Fact sheet common chemotherapy side effects](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5776036/).

4. Ask about any other side-effects of chemotherapy or radiation therapy, if relevant.

<table>
<thead>
<tr>
<th>Side-effects of chemotherapy or radiation therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>➢ Systemic side-effects:</td>
</tr>
<tr>
<td>o Asthma, urticaria</td>
</tr>
<tr>
<td>o Pneumonitis (gemcitabine)</td>
</tr>
<tr>
<td>o Flu-like illness 1 or 2 days after gemcitabine</td>
</tr>
<tr>
<td>o Photosensitivity</td>
</tr>
<tr>
<td>➢ Neurological side-effects – Peripheral neuropathy</td>
</tr>
<tr>
<td>➢ Chest pain or angina due to coronary artery vasospasm (non-ST-elevation myocardial infarction (NSTEMI) may result) after 5 FU therapy</td>
</tr>
<tr>
<td>➢ Fluid retention and oedema with gemcitabine</td>
</tr>
<tr>
<td>➢ Thromboembolism</td>
</tr>
<tr>
<td>➢ <strong>Gastrointestinal side-effects</strong></td>
</tr>
<tr>
<td>o Mouth ulcers</td>
</tr>
<tr>
<td>o Nausea</td>
</tr>
<tr>
<td>o Vomiting</td>
</tr>
<tr>
<td>o Haematemesis or melaena</td>
</tr>
<tr>
<td>o Diarrhoea</td>
</tr>
<tr>
<td>➢ Febrile neutropenia</td>
</tr>
<tr>
<td>➢ <strong>Radiotherapy side-effects</strong></td>
</tr>
<tr>
<td>o Local radiation injury</td>
</tr>
<tr>
<td>o Gastrointestinal problems as above</td>
</tr>
</tbody>
</table>
5. Take a **history** and assess for evidence of progressive disease or complication.

**History**
- Increasing pain, usually in the upper or middle abdomen and back
- Unexplained nausea, anorexia, or weight loss
- Jaundice or itch – related to biliary obstruction and may be associated with cholangitis
- Polyuria, polydipsia – may mean the onset of diabetes
- Steatorrhea – may be associated with pancreatic exocrine insufficiency
- Vomiting – may mean gastric outlet obstruction
- Abdominal distention – may mean malignant ascites
- Symptoms of venous (peripheral or portal) thrombosis and or pulmonary embolism
- Psychological – depression and anxiety are common due to the severity of the diagnosis

- **Symptoms and signs of decompensated liver failure**
  - Fatigue
  - Malaise
  - Anorexia
  - Nausea
  - Weight loss or oedematous changes
  - Jaundice or neurological signs of hepatotoxicity

Report any of the above to the treating oncology team.

6. If concerned about neutropenia or biliary obstruction, consider performing FBE and LFTs.

**Management**

**General Practitioner Role**

*The predominant role of the general practitioner during active treatment is to:*

- provide psychosocial support and lifestyle advice.
- monitor medication compliance and side-effects.
- provide dietary advice and support.
- manage co-morbidities and intercurrent illnesses.
- identify complications of treatment e.g., infection associated with neutropenia.
- avoid or defer minor procedures e.g., routine cervical screening during chemotherapy treatment.

1. Consider cultural sensitivities and resources for those of Aboriginal and Torres Strait Islander origin or other cultures. Ask the patient their ethnicity.

2. Consider palliative care involvement early to improve communication, symptom control, and quality of life, and to help reduce hospital admissions.
   - Ensure that discussion with the patient are consistent with the poor survival from the disease.
   - Even when completely resected, patients with tumours < 2 cm with no lymph node or other metastasis still have a 5-year survival of only around 20%.

3. Discuss **advance care planning** with the patient.
4. Management options depend on intent, and are modified based on patient factors, predominantly overall [ECOG performance status](#). Patients of ECOG status 3 or 4 are not surgical candidates and usually not offered palliative chemotherapy as risk-to-benefit ratio is unfavourable.

### Management of biliary obstruction

- As 60% pancreatic carcinoma occur in the head or uncinate process. Many patients present with obstructive jaundice.
- Consider early referral to a pancreatic surgeon for biliary drainage via endoscopic retrograde cholangio-pancreatography (ERCP), if possible. This is required before chemotherapy can be given.

### Considerations for surgery

- Pancreatic cancers are grouped as:
  - Resectable
  - Borderline resectable
  - Locally advanced
  - Metastatic
- Patients considered borderline resectable, or resectable, who are ECOG 1 to 2, and who are fit, may be considered for surgery
- Patients considered borderline resectable may be given neoadjuvant chemotherapy then re-staged for consideration for surgery.
- See also Cancer Research UK – [Pancreatic Cancer Risk Factors](#)

### Treatment options for localised pancreatic cancer (stages 1 and 2) without distant metastases

#### Surgery

- Whipple's procedure (pancreatico-duodenectomy for tumours in head or uncinate process) (ECOG status 1 or 2 only)
- Distal or subtotal pancreatectomy and splenectomy for tumours of the pancreatic tail or body. Pre and post splenectomy vaccinations are required.5
- Unfortunately, surgical findings often result in restaging a pancreatic cancer as inoperable. Recovery from surgery is often protracted.

#### Chemotherapy

- Chemotherapy may be given before surgery to increase resectability or after surgery.
  - Gemcitabine alone (a nucleoside analogue chemotherapy agent)
  - Gemcitabine and capecitabine (DNA targeting cytotoxic)
  - Folfirinox regime
Treatment regimens for inoperable or metastatic pancreatic cancer (stages 3 and 4)

Pancreatic cancer is not as sensitive to chemotherapy or radiotherapy as other tumour types. Median survival with treatment is 2 to 6 months and intent is not curative, however individual results vary.

**Treatment regimens** are based on a determination of [ECOG performance status](#).

**Treatment for inoperable or metastatic pancreatic cancer**

Overall outcome is improved with fitness, but interestingly not tumour response to treatment. Survival times roughly double, but are still only measured in months.

<table>
<thead>
<tr>
<th>ECOG 0 to 1</th>
<th>ECOG 1 to 2, or aged &gt; 75 years with lower ECOG</th>
<th>ECOG 2 to 3</th>
<th>ECOG 3 to 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initially gemcitabine and paclitaxel.</td>
<td>Initially gemcitabine and paclitaxel.</td>
<td>Single agent gemcitabine or less often single agent 5-FU or capecitabine.</td>
<td>Chemotherapy unsuitable</td>
</tr>
<tr>
<td>Then on progression, FOLFIRINOX.</td>
<td>Then on progression, FOLFIRINOX or irinotecan as single agent.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Then on further progression single or double agent from choices below.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Treatments in above table**

- **FOLFIRINOX (modified) treatment** – used in fit patients:
  - 5-fluorouracil (5-FU), irinotecan, oxaliplatin (both are DNA targeting cytotoxics) with leucovorin, which enhances effect of 5-FU
  - Treatment as day stay, then ambulatory home treatment with 5-FU over 24 hours via central line, repeated every 2 weeks for a total of 6 or 12 cycles. Varied based on tumour, regimen and tolerance.
  - See also [Pancreatic Cancer Action](#)
- **FOLFOX (modified)** – fluorouracil (5-FU) (given as per FOLFIRINOX above) with leucovorin and oxaliplatin, and folinic acid chemotherapy
- Gemcitabine (a nucleoside analogue chemotherapy agent) and nab-paclitaxel (a cytotoxic chemotherapy agent)
- Gemcitabine monotherapy

**Treatments for progressive disease**

- If evidence of progressive local invasive disease, request either:
  - [urgent or routine hepatobiliary and upper GI surgery referral](#), or
  - [urgent or routine oncology referral](#) within 2 weeks.
- If any red flags or complications resulting from above procedures or treatments, request any of:
  - [Immediate gastroenterology referral or admission](#)
  - [Immediate hepatobiliary and upper GI surgery referral or admission](#)
  - [Immediate oncology referral or admission](#)
In addition to chemotherapy, which may provide symptom relief, quality of life may also be improved by:
- surgical (stent) or radiologic biliary decompression.
- relief of gastric outlet obstruction.
- pain control (management may include radiotherapy.

Monitoring is usually performed by clinical assessment with FBE, LFTs, CT imaging, and CA 19-9 levels.

If disease progresses despite a treatment regimen, usually treatment is changed to one of the other modalities, but there is little evidence for survival benefit once progression has occurred.

If progression occurs monotherapy or combination chemotherapy, FOLFOX (modified) or single agent irinotecan may be implemented as a second-line option.

Immunotherapy has yet to demonstrate benefit in pancreatic cancer.

Psychological care

Consider, if appropriate, referral to a clinical psychologist using a Mental Health Care plan.

Palliative care

- Refer early to Specialist Palliative Care Services (SPCS) in established pancreatic cancer.
- Holistic care combining psychological, psychosocial, physical and existential care is paramount due to the poor prognosis.

Follow-up

- Long-term follow-up is unfortunately a rarity.
- Palliative care services constitute the usual follow-up.
- See Cancer Survivorship Care.

Referral

- If evidence of progressive local invasive disease, request either:
  - urgent or routine hepatobiliary and upper GI surgery referral, or
  - urgent or routine oncology referral within 2 weeks.
- If any red flags or complications resulting from above procedures or treatments, request any of:
  - Immediate gastroenterology referral or admission
  - Immediate hepatobiliary and upper GI surgery referral or admission
  - Immediate oncology referral or admission

- Refer early to Specialist Palliative Care Services (SPCS) in established pancreatic cancer.
- Consider Mental Health Care plan and referral to a clinical psychologist.

Information

For health professionals

- American Cancer Society – Pancreatic Cancer
- Cancer Council Australia:
For patients

- Cancer Council:
  - Cancer: What to expect
  - Pancreatic Cancer: What to Expect
- Cancer Council Victoria – Aboriginal Communities: Information
- National Indigenous Cancer Network – About Cancer
- Pancare Foundation – About Pancreatic Cancer

References


Select bibliography


Last Reviewed: November 2019
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