

# Optimal care pathway for people with biliary cancer

## Quick reference guide



Support: Assess supportive care needs at every step of the pathway and refer to appropriate health professionals or organisations.

The optimal care pathways describe the standard of care that should be available to all cancer patients treated in Australia. The pathways support patients and carers, health systems, health professionals and services, and encourage consistent optimal treatment and supportive care at each stage of a patient's journey. Seven key principles underpin the guidance provided in the pathways: patient-centred care; safe and quality care; multidisciplinary care; supportive care; care coordination; communication; and research and clinical trials.

This quick reference guide provides a summary of the *Optimal care pathway for people with biliary cancer*. Biliary cancer includes cancer of the gallbladder and biliary tract cancer (also called cholangiocarcinoma).

Please note that not all patients will follow every step of the pathway.

## Step 1: Prevention and early detection

### Prevention

The causes of biliary cancer are not fully understood, and there is currently no clear prevention strategy.

### Risk factors

There are very few people at high risk. People with the following risk factors are at increased risk:

#### Gallbladder cancer

- Gallstones
- Having gallbladder polyps
- History of long-term inflammation of the gallbladder
- First-degree or immediate relative (mother, father, sibling or child) having gallbladder cancer
- Inherited genetic conditions such as abnormalities of the liver, gallbladder or bile ducts
- Obesity
- Smoking
- Being from East Asia or South America.

#### Biliary tract cancer

- Medical history of long-term inflammation of the bile duct such as primary sclerosing cholangitis
- Biliary cysts
- Inherited genetic conditions such as abnormalities of the liver, gallbladder or bile ducts
- Chronic liver disease such as cirrhosis, hepatitis B infection and hepatitis C infection
- Infection with a liver fluke parasite (linked to bile duct cancer cases in Africa and Asia)

- Genetic changes such as hereditary nonpolyposis colorectal cancer syndrome (Lynch syndrome), characterised by abnormalities of the mismatch repair genes (MMR) *MLH1*, *MSH2*, *MSH6* and *PMS2*, as well as mutations in *BRCA1/2*
- Exposure to Thorotrast, which is a radioactive compound that was used in x-rays from the 1930s to the 1950s
- Exposure to asbestos
- Being from East Asia or South America
- Pre-existing inflammatory bowel disease such as chronic ulcerative colitis
- Older age
- Diabetes
- Obesity.

### Early detection

Being aware of the risk factors and who is at high risk can guide monitoring and referral to a specialist.

### Screening recommendations

Routine screening for biliary cancer is not currently recommended in either the general population or in relatives of people with biliary cancer.

For people at higher risk, such as those with primary sclerosing cholangitis, long-term inflammation of the gallbladder or gallbladder polyps (6–10 mm), consider annual surveillance using ultrasound. Consider cholecystectomy for patients with gallbladder polyps over 10 mm.

### Checklist

- Current and past medical history discussed, including any genetic and inherited conditions.
- Recent weight changes discussed, and the patient's weight recorded.
- Alcohol intake discussed and recorded and support for reducing alcohol consumption offered if appropriate.
- Smoking status discussed and recorded, and brief smoking cessation advice offered to smokers.
- Physical activity recorded.
- Referral to a dietitian considered.
- Referral to a physiotherapist or exercise physiologist considered.
- Education on being sun smart considered.
- Any recent travel to Asia or Africa where liver fluke exposure may occur, discussed.
- Potential exposure to Thorotrast and asbestos noted.

## Step 2: Presentation, initial investigations and referral

Many cases present with non-specific symptoms or are asymptomatic until advanced stages of the disease.

The following signs and symptoms should be investigated:

- jaundice (requires urgent investigation) with or without darkened urine, pale bowel movements and itchy skin
- unexplained nausea or vomiting
- unexplained weakness
- unexplained loss of appetite and weight loss
- fevers and chills
- pain in the right side of the abdomen.

### Initial investigations

The patient's GP should take a thorough medical history to check for any risk factors and symptoms that suggest biliary cancer.

Where there is a suspicion of biliary cancer, consider:

- abdominal CT scan and/or abdominal ultrasound
- serum CA 19-9, liver function tests, full blood examination, biochemistry and coagulation screen (INR/APTT).

Where jaundice is present, the following should be performed, reviewed and the patient referred to a specialist doctor urgently:

- liver function tests and coagulation screen (INR/APTT)
- abdominal ultrasound
- CT of the abdomen and pelvis including a multiphase scan of the liver, provided this does not delay urgent referral.

### Referral options

At the referral stage, the patient's GP or other referring doctor should advise the patient about their options for referral, waiting periods, expertise, if there are likely to be out-of-pocket costs and the range of services available. This will enable patients to make an informed choice of specialist and health service.

### Communication

#### The GP's responsibilities include:

- explaining to the patient and/or carer who they are being referred to and why
- supporting the patient and/or carer while waiting for specialist appointments
- informing the patient and/or carer that they can contact the Cancer Council on 13 11 20 and/or the Pancare Foundation on 1300 881 698 and/or the Liver Foundation on 1800 841 118.

### Checklist

- Signs and symptoms recorded.
- Patient urgently referred to a biliary cancer specialist.
- Supportive care needs assessment completed and recorded, and referrals to allied health services actioned as required.
- Patient notified of support services such as the Cancer Council 13 11 20 and/or the Pancare Foundation on 1300 881 698 and/or the Liver Foundation on 1800 841 118.
- Referral options discussed with the patient and/or carer including cost implications.

### Timeframe

Patients who present with jaundice should be referred for tests immediately and followed up rapidly.

Other symptoms require investigations to be completed and reviewed by a GP **within two weeks** of the first appointment.

Patients with suspected or proven biliary cancer should be immediately referred and seen by a gastroenterologist, hepatologist, oncologist or hepatopancreatobiliary (HPB) surgeon with expertise in biliary cancer management and linked to a multidisciplinary team **within two weeks** of referral to the specialist.

## Step 3: Diagnosis, staging and treatment planning

### Diagnosis and staging

The minimum diagnostic procedure that should be completed before the multidisciplinary meeting (MDM) is a CT scan. The other tests can be performed under the direction of the MDM and should not delay presentation of a patient with suspected biliary cancer to the MDM. If the remaining staging tests reveal contrary information the patient may be re-presented to the MDM for further consideration.

Diagnosis of a mass is primarily by imaging. Contrary to the situation with most cancers, definitive tissue diagnosis before multidisciplinary planning is not recommended. Biopsy approaches may be complex but are generally required where there is diagnostic uncertainty, or where tissue is required for systemic therapy (such as chemotherapy) or clinical trials. This should be facilitated and overseen by the MDM process. Final pathology may, rarely, prove benign, despite appropriate work-up.

Contrast-enhanced CT scan of the chest, abdomen and pelvis, including multiphase CT scan of the liver is recommended (to be completed first if not already performed).

The following investigations are suggested and can occur under the direction of the MDM:

- contrast-enhanced MRI liver and magnetic resonance cholangiopancreatography (MRCP)
- endoscopic ultrasound (EUS)
- FDG-PET. (This can be useful in some cases but is not necessary in all cases. It may be a useful tool, for example, to evaluate evidence of spread of intrahepatic tumours or equivocal findings on radiology.)

Urgent stenting is **not** recommended if the patient's symptoms are mild. An appropriate diagnostic work-up should take place first. Stenting should not be done before the patient is reviewed at an MDM to determine if the tumour is resectable.

Staging for biliary cancer is vital to determine if the disease is resectable or non-resectable because the treatment pathways are different and preparation for resectable disease is highly specific.

A laparoscopy may be included in staging for resectable biliary cancer. Obtain a core biopsy for diagnostic pathology and molecular profiling before starting systemic or locoregional therapies.

### Genetic testing

Inherited genetic conditions causing biliary cancer are uncommon.

The types of genetic changes linked with an increased risk of biliary cancer include Lynch syndrome, characterised by abnormalities of the mismatch repair genes (MMR) *MLH1*, *MSH2*, *MSH6* and *PMS2*, as well as mutations in *BRCA1/2*.

Patients with a strong family history of cancer should be referred to a familial cancer clinic to determine whether the tumour is part of an inherited predisposition to cancer.

### Treatment planning

Patients with proven or suspected biliary cancer should be discussed at an MDM **within two weeks** of the initial specialist review. The MDM can occur after the minimum diagnostic tests; the full range of tests should not delay presentation at an MDM.

### Research and clinical trials

Consider enrolling the patient in clinical trials where available and appropriate. Search for a trial <[www.australiancancertrials.gov.au](http://www.australiancancertrials.gov.au)>.

### Communication

#### The lead clinician's<sup>1</sup> responsibilities include:

- discussing a timeframe for diagnosis and treatment options with the patient and/or carer
- explaining the role of the multidisciplinary team in treatment planning and ongoing care
- encouraging discussion about the diagnosis, prognosis, advance care planning and palliative care while clarifying the patient's wishes, needs, beliefs and expectations, and their ability to comprehend the communication
- providing appropriate information and referral to support services as required
- communicating with the patient's GP about the diagnosis, treatment plan and recommendations from MDMs.

### Checklist

- Diagnosis confirmed.
- Performance status and comorbidities measured and recorded.
- Patient discussed at an MDM and decisions provided to the patient and/or carer.
- Clinical trial enrolment considered.
- Supportive care needs assessment completed and recorded and referrals to allied health services actioned as required.
- Patient referred to support services (Cancer Council, Pancare Foundation, Liver Foundation) as required.
- Treatment costs discussed with the patient and/or carer.

### Timeframe

Diagnostic and staging investigations that the MDM has recommended should be completed **within two weeks** of referral.

<sup>1</sup> Lead clinician – the clinician who is responsible for managing patient care. The lead clinician may change over time depending on the stage of the care pathway and where care is being provided.

## Step 4: Treatment

### Establish intent of treatment

- Curative
- Anti-cancer therapy to improve quality of life and/or longevity without expectation of cure
- Symptom palliation

A treatment plan may also be informed by genomic testing. Genomics-informed cancer care can improve the experience of people affected by cancer by optimising the treatment response and minimising treatment toxicity.

### Treatment options

#### Surgery

- For resectable disease surgical resection offers the best long-term survival chance in patients with biliary cancer. Palliative surgery for metastatic cancer is not usually recommended.

#### Intrahepatic biliary cancer

- Partial hepatectomy (liver resection) is recommended.

#### Perihilar biliary cancers

- Right extended hepatectomy or left hemi-hepatectomy is recommended.

#### Distal biliary cancer

- Pancreaticoduodenectomy (Whipple's procedure) is recommended.

#### Gallbladder cancer

- Cholecystectomy including removing surrounding tissue such as the lymph nodes, adjacent bile ducts and part of the liver is recommended.

### Liver transplantation

- In the case of intrahepatic biliary cancer, consider a liver transplant for lesions smaller than 2 cm.
- For perihilar biliary cancer, consider a liver transplant for lesions no larger than 3 cm.
- For both sites of biliary cancer, there needs to be clear evidence that there are no metastasis including lymph node metastasis before considering a liver transplant.

### Locoregional therapy

#### Radiation therapy

- External beam radiation therapy (EBRT), chemoradiation (CRT) or stereotactic body radiotherapy / stereotactic ablative radiotherapy (SBRT/SABR) may be appropriate.
- Radiotherapy may be considered for patients with:
  - unresectable/locally advanced biliary cancer after completing systemic therapy and the disease is stable
  - intrahepatic biliary cancer with or without vascular involvement for patients in whom surgery is contraindicated
  - metastatic intrahepatic biliary cancer to reduce the risk of liver failure from local disease progression.
- Adjuvant CRT may be considered after margin positive resection (R1) or resection of node-positive disease.
- Adjuvant CRT may be considered following R0 resection of T2 or N1 gallbladder cancer.

#### Intra-arterial treatment

- May be either transarterial chemoembolisation (TACE), selective internal radiation therapy (SIRT) or hepatic arterial infusion chemotherapy (HAIC).

#### Thermal ablation

- Radiofrequency ablation (RFA) or microwave ablation (MWA) may be appropriate.
- Consider this for patients with intrahepatic biliary cancer no greater than 3 cm who have contraindications to surgery.

### Checklist

- Intent of treatment established.
- Risks and benefits of treatments discussed with the patient and/or carer.
- Treatment plan discussed with the patient and/or carer.
- Treatment plan provided to the patient's GP.
- Treating specialist has adequate qualifications, experience and expertise.
- Supportive care needs assessment completed and recorded, and referrals to allied health services actioned as required.
- Early referral to palliative care considered.
- Advance care planning discussed with the patient and/or carer.

## Step 4: Treatment continued

### Systemic therapy

- Adjuvant chemotherapy is recommended for all patients following resection for biliary cancer.
- Palliative chemotherapy is recommended for most patients with advanced biliary cancer, unless contraindicated by frailty or comorbidities.
- There are several approved targeted therapies available to treat patients with locally advanced, unresectable or metastatic biliary cancer, with more undergoing clinical trials. Molecular profiling is advised for all patients to guide appropriate targeted and immunotherapy choice.

### Palliative care

Early referral to palliative care can improve quality of life and in some cases survival. Referral should be based on need, not prognosis. For more, visit the Palliative Care Australia website <[www.palliativecare.org.au](http://www.palliativecare.org.au)>.

### Communication

#### The lead clinician and team's responsibilities include:

- discussing treatment options with the patient and/or carer including the intent of treatment as well as risks and benefits
- discussing advance care planning with the patient and/or carer where appropriate
- communicating the treatment plan to the patient's GP
- helping patients to find appropriate support for exercise programs where appropriate to improve treatment outcomes.

### Timeframes

- Surgery should be undertaken **within four weeks** of the MDM, depending on urgency.
- Systemic therapy for unresectable biliary cancer should begin **within four weeks** of the MDM, depending on urgency.
- Adjuvant chemotherapy in postoperative care should begin **within eight weeks** of surgery, depending on the patient's recovery.
- Radiation therapy should begin **within four weeks** of the MDM, depending on urgency.
- Adjuvant radiotherapy in postoperative care should begin **within eight weeks** of surgery, depending on the patient's recovery.

## Step 5: Care after initial treatment and recovery

### Provide a treatment and follow-up summary to the patient, carer and GP outlining:

- the diagnosis, including tests performed and results
- tumour characteristics
- treatment received (types and date)
- current toxicities (severity, management and expected outcomes)
- interventions and treatment plans from other health professionals
- potential long-term and late effects of treatment and care of these
- supportive care services provided
- a follow-up schedule, including tests required and timing

- contact information for key healthcare providers who can offer support for lifestyle modification
- a process for rapid re-entry to medical services for suspected recurrence.

### Communication

#### The lead clinician's responsibilities include:

- explaining the treatment summary and follow-up care plan to the patient and/or carer
- informing the patient and/or carer about secondary prevention and healthy living
- discussing the follow-up care plan with the patient's GP.

### Checklist

- Treatment and follow-up summary provided to the patient and/or carer and the patient's GP.
- Supportive care needs assessment completed and recorded and referrals to allied health services actioned as required.
- Patient-reported outcome measures recorded.

## Step 6: Managing recurrent, residual or metastatic disease

### Detection

Most residual or recurrent disease will be detected via routine follow-up/imaging or by the patient presenting with symptoms.

### Treatment

All patients should be evaluated for referral to the original multidisciplinary team. In managing people with recurrent, residual or metastatic biliary cancer, the treatment aim is to relieve pain and any unnecessary side effects to ensure optimal quality of life.

Treatment will depend on the location and extent of disease, previous management and the patient's preferences.

### Advance care planning

Advance care planning is important for all patients to consider but especially those with advanced disease. It is a voluntary process that allows them to plan for their future health and personal care by thinking about their values and preferences. This can guide future

treatment if the patient is unable to speak for themselves.

### Survivorship and palliative care

Survivorship and palliative care should be addressed and offered early. Early referral to palliative care can improve quality of life and in some cases survival. Referral should be based on need, not prognosis.

### Communication

The lead clinician and team's responsibilities include explaining the treatment intent, likely outcomes and side effects to the patient and/or carer and the patient's GP.

### Checklist

- Treatment intent, likely outcomes and side effects explained to the patient and/or carer and the patient's GP.
- Supportive care needs assessment completed and recorded and referrals to allied health services actioned as required.
- Advance care planning discussed with the patient and/or carer.
- Patient referred to palliative care if appropriate.
- Routine follow-up visits scheduled.

## Step 7: End-of-life care

### Palliative care

Consider a referral to palliative care. Ensure advance care directives have been explained and the patient has been offered an opportunity to develop one if they choose. If the patient has an advance care directive, ensure it is shared with treating teams and is used to guide care decisions if the patient cannot speak for themselves.

### Voluntary assisted dying

Voluntary assisted dying is legislated by state and territory governments, so it is essential to know the rules around this choice in the state or territory where the patient lives.

### Communication

#### The lead clinician's responsibilities include:

- being open about the prognosis and discussing palliative care options with the patient
- establishing transition plans to ensure the patient's needs and goals are considered in the appropriate environment.

### Checklist

- Supportive care needs assessment completed and recorded, and referrals to allied health services actioned as required.
- Patient referred to palliative care.
- Advance care directives (if any) are shared and considered in care decisions.

Visit our guides to best cancer care webpage <[www.cancer.org.au/cancercareguides](http://www.cancer.org.au/cancercareguides)> for consumer guides. Visit our OCP webpage <[www.cancer.org.au/health-professionals/optimal-cancer-care-pathways](http://www.cancer.org.au/health-professionals/optimal-cancer-care-pathways)> for the optimal care pathway and instructions on how to import these guides into your GP software.