Optimal care pathway for people with hepatocellular carcinoma

Quick reference guide

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 hepatocellular carcinoma (HCC).*

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

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

Step 1: Prevention and early detection

Prevention

Timely diagnosis for viral hepatitis B (HBV) and C (HCV) can reduce the risk of infection developing into cancer. Vaccination is the best prevention for HBV. Strategies to curb alcohol intake and reduce obesity (and hence type 2 diabetes and non-alcoholic fatty liver disease) will also reduce future HCC burden.

Risk factors

The major risk factors for developing HCC are:

- cirrhosis of the liver of any cause
- history of moderate to heavy alcohol intake
- obesity
- HBV infection (particularly for those with an extended period of exposure, childhood-acquired and high viral load, increasing age, ethnicity (African, Asian or Aboriginal) and male gender).

The risk factors for developing HCC in people with HCV are:

- chronic HCV infection with advanced fibrosis
- a family history of HCC.

Other risk factors for HCC include male gender, increasing age, HBV and HCV viral co-infection, non-alcoholic fatty liver disease, type 2 diabetes, iron overload, aflatoxin exposure and tobacco smoking.

Screening recommendations

Australia does not have a population screening program for HCC. Base surveillance for HCC in high-risk groups on 6-monthly liver ultrasound with or without alpha-fetoprotein (AFP).

All patients with cirrhosis should be in a screening program. In patients with HBV (without cirrhosis), screening should begin according to the following guide:

- African-background patients from age 20
- Asian-background males from age 40
- Asian-background females from age 50
- Caucasian patients from age 50.

Family history

Patients who have chronic viral hepatitis or a family history of HCC have an increased risk of HCC and need to undergo regular 6-monthly surveillance with ultrasound.

Checklist

- ❑ Family history obtained and recorded
- ❑ Vaccination for HBV if indicated
- ❑ Recent weight changes discussed and 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

Step 2: Presentation, initial investigations and referral

Signs and symptoms included in the tables below are based on best available evidence on how patients may present to their general practitioner (GP) with hepatocellular carcinoma (HCC).

Signs and symptoms

Patients presenting to their GP with the following signs and symptoms should be investigated. Signs and symptoms have been categorised by higher, moderate and lower risk, underpinned by primary care evidence. See referral and safety netting section for more detail on appropriate next steps.

Checklist

- ❑ Signs and symptoms recorded
- ❑ Supportive care needs assessment completed and recorded, and referrals to allied health services actioned as required

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

Step 2: Presentation, initial investigations and referral continued

Higher-risk symptoms About 3-5 out of 100 people with a higher-risk symptom are likely to have HCC	N/A*
Moderate-risk symptoms About 1-2 out of 100 people with one of these symptoms are likely to have HCC	Abdominal mass Raised alkaline phosphatase (ALP)
Lower-risk symptoms Less than one out of 100 people with this symptom is likely to have HCC	Abdominal pain (especially right upper quadrant pain)

* N/A: There is no evidence of specific symptoms which place patients at a higher risk of having HCC

Signs, symptoms and symptom combinations

Presenting to general practice with a combination of signs and symptoms may increase a patient's risk of having HCC. This table demonstrates the single symptoms associated with HCC, and how the risk changes when presenting with more than one symptom. Signs and symptoms have been categorised by higher, moderate and lower risk, underpinned by primary care evidence.

	Single symptoms	Symptom combinations
Higher-risk symptoms About 3-5 out of 100 people with a higher-risk symptom or combination are likely to have HCC	N/A	N/A
Moderate-risk symptoms About 1-2 out of 100 people with one of these symptoms or combinations are likely to have HCC	Abdominal mass Raised ALP	• Abdominal bloating with any of the following: – low albumin – raised ALP – raised bilirubin – unexplained anaemia • Abdominal pain with either: – low albumin – raised ALP
Lower-risk symptoms Less than one out of 100 people with this symptom is likely to have HCC	Abdominal pain	

These recommendations are generated from evidence in populations primarily aged >40 years. The risk of an undiagnosed cancer increases with age for all signs and symptoms.

Given the limited evidence on symptomatic presentations of HCC in general practice, the following have not been included in the above table but can be symptoms or signs of HCC:

- a hard mass on the right side of the abdomen
- unexplained weight loss
- worsening liver failure (jaundice, ascites, portal hypertension)
- constitutional symptoms including night sweats and anorexia.

Underlying risk factors outlined in Step 1 (e.g., known cirrhosis of the liver, hepatitis B virus (HBV) infection, chronic hepatitis C virus (HCV) infection with advanced fibrosis, family history of HCC, and a history of moderate to heavy alcohol intake) should be considered in the presence of signs and symptoms of HCC and could be used to lower the threshold for initial investigation.

Initial investigations include

- ultrasound of the liver
- alpha-fetoprotein (AFP) test
- liver function tests, full blood count, urea and electrolytes.

Checklist continued

- ❑ Patient notified of support services such as Cancer Council 13 11 20
- ❑ Referral options discussed with the patient and/or carer including cost implications

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

Step 2: Presentation, initial investigations and referral continued

- investigations for causes of underlying liver disease including viral hepatitis, alcohol abuse, haemochromatosis (iron overload) and metabolic dysfunction-associated fatty liver disease (MAFLD [fatty liver])
- quad-phase computed tomography (CT) scan of the liver (if appropriate).

Safety netting

For patients with low-to-moderate-risk symptoms, further investigation to identify an underlying cause is appropriate. All patients should be provided with safety-netting advice, including a planned timeframe for follow-up that is agreed with the patient, and the need for patient-initiated follow-up if new symptoms develop, if symptoms persist or worsen, or if the patient has further concerns.

Referral options

At the referral stage, the patient's GP or other referring doctor should, where possible, 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 Cancer Council on 13 11 20 for additional support.

Timeframe

Conduct tests **within 2 weeks** of a patient presenting with symptoms. Patients should see a specialist linked to a multidisciplinary team **within 2 weeks** of GP referral.

Step 3: Diagnosis, staging and treatment planning

The multidisciplinary team should manage diagnosis, staging and treatment planning where possible.

Diagnosis

The following sequence of investigations is suggested:

- four-phase contrast-enhanced liver CT scan
- MRI with contrast in patients who cannot tolerate appropriate CT contrast or where diagnostic uncertainty remains after CT scan
- contrast-enhanced ultrasound in select cases where CT and MRI are not suitable (e.g. poor renal function).

If diagnostic uncertainty still remains, consider a liver biopsy.

Staging

Staging should use validated staging protocols such as the Barcelona Clinic Liver Cancer guidelines.

Staging parameters include radiological imaging (tumour size, number and location of lesions, metastases and vascular invasion), Eastern Cooperative Oncology Group (ECOG) status and a liver function assessment using the Child–Pugh or a similar scoring system.

Treatment planning

Within 2 weeks of finding a suspected HCC, refer the patient to a specialist multidisciplinary team where possible.

Research and clinical trials

Consider enrolment where available and appropriate. Search for a trial <www.australiancancertrials.gov.au>.

Communication

The lead clinician's[1] 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 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 (such as Cancer Council) as required
- ❑ Treatment costs discussed with the patient and/or carer

Timeframe

Complete diagnostic investigations **within 4 weeks** of the initial referral.

1 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.

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

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.

In many cases the severity of the co-existing liver disease affects the treatment options and needs to be treated appropriately.

Surgery – resection or transplant

Only a small number of cases are suited to surgery. A resection may benefit patients with compensated liver disease. A liver transplant may benefit patients who also have cirrhosis, including those with decompensation, and for patients with a tumour volume within accepted international guidelines.

Local ablative therapies

Radiofrequency ablation, microwave ablation, percutaneous ethanol, percutaneous acetic acid injections, stereotactic radiation therapy or image-guided cryoablation may be appropriate.

Regional therapies

Transarterial chemoembolisation, transarterial embolisation or selective internal radiation therapy may be appropriate.

Localised therapies

These are the most common treatment for early-stage HCC and have curative intent.

They may benefit patients:

- with unresectable disease (due to the size or location of the tumour)
- with small tumour(s) (lesions 5 cm or smaller)
- awaiting liver transplant
- with small, recurrent tumours.

Treating advanced HCC

The standard treatment for patients with advanced HCC is systemic therapies. First-line approved systemic therapy in Australia for advanced HCC is either sorafenib or lenvatinib. Other combination therapies are being evaluated.

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>.

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.

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

Timeframe

Begin treatment **within 4 weeks** of the multidisciplinary meeting.

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

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 or by the patient presenting with symptoms.

Treatment

Evaluate each patient for whether referral to the original multidisciplinary team is appropriate. 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 but especially those with advanced disease. It 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 referral to palliative care if not already involved. Ensure that an advance care directive is in place. An important part of care at this stage is good symptomatic management of the liver disease such as ascites, infection, encephalopathy and variceal bleeding.

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 directive in place

Visit our guides to best cancer care webpage <www.cancercareguides.org.au> for consumer guides. Visit our OCP webpage <www.cancer.org.au/OCP> for the optimal care pathway and instructions on how to import these guides into your GP software.

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