

Palliation

Treating Patients with Inoperable Biliary Tract and Primary Liver Tumors

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KEYWORDS

- Palliation • Cholangiocarcinoma • Hepatocellular carcinoma • Systemic therapies
- Targeted therapies • Chemoembolization • Endoscopic therapies

KEY POINTS

- Hepatocellular carcinoma and cholangiocarcinoma are frequently unresectable because of advanced local disease.
- Patients with unresectable tumors may be amenable to ablation techniques administered through multiple routes and techniques of administration.
- Palliation should also include restoring biliary drainage, pain management, improving nutritional status and fat absorption, and improving pruritus.
- Systemic chemotherapy and sorafenib are palliative options used in conjunction with locoregional therapies or as sole therapeutic options.

Hepatocellular carcinoma (HCC) and cholangiocarcinoma (CCA) account for nearly all primary liver tumors.^{1,2} Resection is the most effective therapy for both tumors but is frequently not possible, often because of advanced local disease.^{3,4} Patients with unresectable tumors have a poor prognosis, with median survival often 3 to 6 months.⁵ Although several treatment options exist, these are not curative approaches and rather palliative.

HCC is the most common primary liver tumor, representing 90% of primary liver cancers. Cirrhosis is associated with HCC in almost 90% of the cases.^{6,7} Chronic hepatitis B virus and hepatitis C virus contribute to HCC development in approximately 80% of cases. The mean annual incidence of HCC in cirrhotic patients is 3% to 4%, and this figure increases proportionally with liver function impairment.⁸ Less than 20% of these tumors are amenable to definitive surgical management,

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because of advanced intrahepatic disease or other medical conditions that prohibit major surgery. Locoregional therapies have been recommended in patients with HCC as a form of palliation.⁹ Locoregional therapies include radiofrequency ablation (RFA), percutaneous ethanol injection (PEI), cryoablation, microwave ablation, transarterial chemoembolization (TACE), hepatic artery infusion (HAI), radioembolization (⁹⁰Y), and bland embolization.

CCA is the second most common primary liver cancer after HCC and comprises 10% of primary liver cancers. CCA can be subdivided into cancers affecting the intrahepatic, perihilar, and extrahepatic biliary tree. At presentation, most CCAs are perihilar (50%–60%), 20% are intrahepatic, 20% are distal extrahepatic, and 5% are multifocal.¹⁰ Most patients with CCA have no known risk factors; however, there seems to be an association with chronic inflammation of the biliary epithelium and diseases such as primary sclerosing cholangitis, chronic infection with liver flukes, hepatolithiasis, and viral hepatitis.¹¹ Surgical resection offers the approach for long-term survival, but few patients are operative candidates.¹² Palliative strategies include surgical, percutaneous, and endoscopic techniques to decompress the biliary system and locoregional palliative therapies.

STRATEGY

The selection of the best treatment is dependent on the status of the underlying liver and the tumor stage. Although HCC is rare in a noncirrhotic liver, these patients are the most likely candidates for liver resection. In most cases in which cirrhosis underlies HCC, the degree of functional impairment often precludes safe surgery.¹³ CCA develops in the background of cirrhosis in only 10% of patients; however, most CCA cases are deemed unresectable at presentation.

Most patients are not candidates for resection because of advanced tumors, tumor location near major intrahepatic vessels precluding a negative-margin resection, multifocal tumors, or poor hepatic functional reserve. Liver function is assessed through the Child-Turcotte-Pugh classification, and this is combined with a detailed evaluation of tumor extent. There are multiple staging systems for liver cancer, such as the TNM (Tumor, Node, Metastases), Okuda, CLIP (Cancer of the Liver Italian Program), and BCLC (Barcelona Clinic Liver Cancer) staging. These assessments examine the liver for characteristics such as multifocality, vascular invasion, and extrahepatic disease.^{13,14} In addition, the general condition and performance status of the patient is assessed. Patients with high-risk tumors, multiple comorbid conditions and poor performance status may be candidates for palliative treatment alone.

Even in centers with extensive experience in hepatic resection, the resection rate for HCC is in the range of 10% to 37%.^{15–17} In patients with unresectable HCC disease, liver transplantation should always be considered. Select patients may also be amenable to ablation techniques administered through multiple routes and techniques of administration. These options are reported to offer potential long-term benefit.¹⁸ TACE and sorafenib administration are palliative approaches that have been shown to have a positive impact on survival.^{19–21}

Treatment protocols for intrahepatic CCAs (ICCs) are not as common as those for HCC. Nevertheless, there is a clear role for hepatic resection when feasible, and chemoembolization has been used successfully in unresectable patients.^{22,23} CCA is diagnosed at late stages in most patients and resection is possible in only 15% to 20% of cases.²⁴ If the disease is deemed unresectable, palliation should include restoring biliary drainage to reduce risk of cholangitis, pain management, improving nutritional status and fat absorption, and improving pruritus.²⁵

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