Hilar Cholangiocarcinoma: expert consensus statement

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Abstract
An American Hepato-Pancreato-Biliary Association (AHPBA)-sponsored consensus meeting of expert panelists met on 15 January 2014 to review current evidence on the management of hilar cholangiocarcinoma in order to establish practice guidelines and to agree consensus statements. It was established that the treatment of patients with hilar cholangiocarcinoma requires a coordinated, multidisciplinary approach to optimize the chances for both durable survival and effective palliation. An adequate diagnostic and staging work-up includes high-quality cross-sectional imaging; however, pathologic confirmation is not required prior to resection or initiation of a liver transplant trimodal treatment protocol. The ideal treatment for suitable patients with resectable hilar malignancy is resection of the intra- and extrahepatic bile ducts, as well as resection of the involved ipsilateral liver. Preoperative biliary drainage is best achieved with percutaneous transhepatic approaches and may be indicated for patients with cholangitis, malnutrition or hepatic insufficiency. Portal vein embolization is a safe and effective strategy for increasing the future liver remnant (FLR) and is particularly useful for patients with an FLR of <30%. Selected patients with unresectable hilar cholangiocarcinoma should be evaluated for a standard trimodal protocol incorporating external beam and endoluminal radiation therapy, systemic chemotherapy and liver transplantation. Post-resection chemoradiation should be offered to patients who show high-risk features on surgical pathology. Chemoradiation is also recommended for patients with locally advanced, unresectable hilar cancers. For patients with locally recurrent or metastatic hilar cholangiocarcinoma, first-line chemotherapy with gemcitabine and cisplatin is recommended based on multiple Phase II trials and a large randomized controlled trial including a heterogeneous population of patients with biliary cancers.

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Evaluation and staging of suspected hilar cholangiocarcinoma

Epidemiology and clinical presentation
Hilar cholangiocarcinoma (Hilar CC) is a rare malignancy, approximately 7000 cases of which are diagnosed per year in North America. Its incidence has remained stable over the past three decades. Among bile duct cancers, however, it is the most common type. Known risk factors include primary sclerosing cholangitis (PSC), liver fluke infestation (Clonorchis sinensis and Opisthorchis viverrini) and hepatolithiasis, but most cases are sporadic without an apparent inciting factor.1 Patients typically present with cachexia, fatigue and jaundice, often reflecting locally advanced or metastatic disease. Approximately 90% of patients present with biliary symptoms, including, most commonly, painless jaundice. Up to 10% will have concomitant cholangitis.2 The tendency toward presentation at an advanced stage and the historical lack of effective systemic
agents explain the resultant poor survival rates: most patients succumb within a year of diagnosis.

**Initial evaluation**

The goals of preoperative evaluation are to rule out benign causes of hilar obstruction, to identify patients with early-stage disease who may benefit from surgical therapy, and to provide palliative biliary drainage and systemic treatment to those with advanced disease and preserved performance status.

Pathologically, there are three subtypes of extrahepatic bile duct adenocarcinoma, including the sclerosing (>70%), nodular (20%) and papillary (5–10%) subtypes.1,3 The vast majority of hilar CC are mucinous adenocarcinomas with a nodular or sclerosing growth pattern that involves the rich lymphatic plexus around the bile ducts early in the course of disease. Over time, hilar lesions can progress locally with the formation of a mass that frequently involves critical hilar vascular structures. Less commonly, patients present with a papillary form that tends to have an endobiliary growth pattern and a more favourable prognosis.

**Laboratory and imaging work-up**

In the absence of cholangitis, the work-up of the jaundiced patient typically starts with laboratory investigation and imaging. Carbohydrate antigen (CA) 19-9 levels may not be accurate in the setting of hyperbilirubinaemia, but may be relevant later in the evaluation after biliary decompression. In addition, 10% of patients may be Lewis antigen non-producers and thus will not secrete CA 19-9.4 An elevated immunoglobulin G4 (IgG4) level may suggest eosinophilic cholangiopathy (lymphoplasmacytic cholangiopathy).5,6 Ultrasonography demonstrates intrahepatic biliary dilatation with a decompressed distal bile duct and gallbladder, isolating the obstruction to the common hepatic duct and/or hilum. High-quality cross-sectional imaging before bile duct instrumentation is the single most important and accurate step in the diagnostic algorithm. Depending on institutional expertise this may be accomplished with thin-slice, high-resolution computed tomography (CT) or magnetic resonance imaging/magnetic resonance cholangiopancreatography (MRI/MRC).7 The diagnostic and staging accuracy of both modalities significantly diminish after biliary stent placement as a result of decompression and imaging artefacts.

Conventional CT has a tumour detection rate of 60–69% and accuracy in determining resectability of 44–80%.7 Based on this, conventional CT has limited value in hilar CC and its main purpose is to determine the extent of extrahepatic disease. By contrast, high-resolution CT has been shown to accurately predict resectability in most hilar CC, which is beneficial in avoiding non-therapeutic laparotomies.7 The preferred technique is by helical high-resolution CT with at least arterial and portovenous phases with rapid intravenous contrast bolus (5 ml/s for a total of 150 ml). The section thickness should be 2.5 mm reconstructed at 1.25 mm and the radiologic interpretation should focus on the location and extent of biliary involvement (Bismuth–Corlette classification), involvement of the hepatic arteries, portal veins, peritoneum and adjacent structures, and intrahepatic metastases.

The advantages of MRI with MRCP include a clearer delineation of the intrahepatic extension of the tumour within the bile ducts and higher diagnostic specificity as MRI is better able to diagnose some non-malignant aetiologies of hilar obstruction. The main disadvantage of MRI refers to its lack of accuracy in determining vascular invasion and therefore resectability. Other disadvantages of MRI are the complexity of the multiple protocols, the requirement for a high level of patient cooperation in terms of motion and breathing in order to achieve optimal images, and lack of information regarding the extent of extrahepatic disease, including regional adenopathy, peritoneal metastases and distant metastases, although diffusion-weighted imaging strengthens the performance of MRI in these areas. When both are well performed, the accuracy of MRI and CT in predicting resectability should exceed 75%.

Hilar cholangiocarcinomas tend not to be fludeoxyglucose (FDG)-avid, with the result that positron emission tomography (PET) has low sensitivity for the diagnosis of cholangiocarcinoma as the cause of a hilar biliary obstruction. For patients with a confirmed diagnosis, sensitivity rises for the detection of regional and distant disease, but rarely adds to the information available from other staging modalities. Some studies suggest that PET findings may change the treatment protocol in a small subset of hilar CC patients, but rarely does this occur in the absence of previous suspicious findings and/or an unexplained elevation in the CA 19-9 level.8,9

**Endobiliary procedures**

The most common presentation of hilar CC is jaundice. Many patients will undergo biliary drainage during the preoperative preparatory phase. In patients without suspicion for a benign cause of hilar biliary obstruction (e.g. Mirizzi syndrome, eosinophilic cholangiopathy, intrahepatic gallstones, liver flukes, etc.), preoperative pathologic confirmation is not required prior to resection or transplantation, although confirmation is mandatory prior to chemotherapy or radiation in most instances. Provided that neoadjuvant protocols are available, patients with suspicious regional lymphadenopathy should be considered for endoscopic ultrasound (EUS) or laparoscopic fine needle aspiration (FNA) of any suspicious nodes. Percutaneous or laparoscopic biopsy of the primary tumour is not recommended in patients who are candidates for liver transplantation because of the high risk for disseminated disease following these procedures.10 In a trial incorporating neoadjuvant chemoradiotherapy followed by liver transplantation, the small number of patients who underwent a transperitoneal FNA confirming adenocarcinoma had an extremely high rate of peritoneal seeding at the time of operative staging.
During biliary stenting, brushings can be attempted to confirm diagnosis. Because of the fibrotic nature of these tumours, endobiliary washing/brushing yields a definitively positive result in approximately 40% of patients with hilar CC. Use of fluorescent in situ hybridization (FISH) targeting pericentromeric regions of chromosomes 3, 7 and 17 can significantly enhance the sensitivity of brush biopsy. Trisomy and tetrasomy are indeterminate criteria for malignancy. Polysomy is diagnostic of malignancy, with sensitivity of 50% and specificity of >95%. It is notable that clinical evaluation without the use of FISH accurately predicts the presence of malignancy among resected patients approximately 90% of the time. When resection is undertaken with a presumptive diagnosis of hilar CC, a benign aetiology is identified in approximately 10% of cases.

Staging and classification

Bismuth and Corlette described their criteria for categorizing perihilar bile duct cancers in 1975. This initial classification of carcinomas of the hilus described the extent to which the common hepatic duct, duct confluence, and left and right ducts were involved by tumour. The descriptions correlate with the operations required for complete extirpation and establishment of biliary continuity. Subsequent classification by Jarnagin et al. incorporated vascular involvement, resulting lobar atrophy, and extension to secondary biliary radicles. This system is a useful framework for defining the resectability of hilar lesions but describes the characteristics of only the primary hilar tumour. The Mayo Clinic classification system includes additional factors such as the size and multifocality of the primary tumour, the nodal and extraregional metastatic burden, and clinical features such as jaundice and performance status. Finally, the American Joint Commission on Cancer (AJCC) Cancer Staging Manual includes a tumour–node–metastasis (TNM) staging classification for perihilar bile ducts which is primarily used in resected patients. The seventh edition of the AJCC manual has recently been evaluated and allows for a better overall prediction of survival because of a refined T-stage with better stratification of prognosis for resected patients.

Consensus statements

- The minimum diagnostic and staging work-up in suspected hilar CC includes CA 19-9 level and high-quality cross-sectional imaging (preferably before biliary stenting) of the chest, abdomen and pelvis.
- Pathologic confirmation is not required prior to proceeding with attempted resection or initiation of a liver transplantation protocol, provided that benign aetiologies have been excluded and a complete staging evaluation has been completed.
- Percutaneous or laparoscopic biopsy of the primary tumour is not recommended in patients who may be candidates for transplantation because there is a high incidence of disseminated disease following those procedures.
- Imaging by FDG-PET lacks the sensitivity and specificity required in a routine staging tool for patients with hilar CC.

Surgical treatment of hilar CC

Definition of resectability

Resection of the involved intra- and extrahepatic bile ducts, as well as the associated hepatic lobe and caudate lobe, is the standard of care for suitable patients, although many patients present with unresectable disease. Five-year survival rates following resection generally range from 25% to 50%, with regional metastasis limiting long-term survival. Survival is highly correlated with resection margin status. Median survival and 5-year survival among patients with a negative margin (R0) resection range from 27 months to 58 months and from 27% to 45%, respectively. Among patients with a positive microscopic or gross margin, median survival and 5-year survival are markedly worse, ranging from 12 months to 21 months and from 0% to 23%, respectively.

The primary principle underpinning the criteria for unresectability is the requirement for biliary reconstruction options and adequate hepatic parenchyma. Patients in whom the tumour extends into the liver and without a target for restoring biliary continuity are unresectable. Patients with evidence of hepatic atrophy of the anticipated remnant lobe or sector will not have adequate parenchyma for recovery. With these principles in mind, any of the following criteria categorize a non-metastatic hilar cancer as unresectable: (i) bilateral segmental ductal extension; (ii) unilateral atrophy with either contralateral segmental ductal or vascular inflow involvement, and (iii) unilateral segmental ductal extension with contralateral vascular inflow involvement. The improved margin-negative resection rates and survival associated with caudate lobectomy for patients with Bismuth-Corlette type III and IV lesions have been demonstrated in several retrospective series. Although some authors have described acceptable outcomes in patients undergoing portal vein resection and reconstruction in the setting of main portal vein involvement, these operations should be undertaken by only the most experienced centres with the appropriate hepatobiliary and vascular surgery expertise. Vascular resections should not be performed routinely in hilar CC and the decision to resect the portal vein should be determined intraoperatively based on vascular extension.

At the time of operative exploration, 20-50% of patients have been found to be unresectable based on previously published series; however, the rate of resectability should continue to diminish as the sensitivity of contemporary imaging continues to improve. A margin-negative resection is achieved in 70-80% of patients submitted to resection in these series. In summary, although the criteria for resectability are well defined, complete preoperative assessment does not
eliminate the risk for non-therapeutic laparotomy or incomplete surgical resection.

**Perioperative preparation**

In light of the significant risk for postoperative adverse events, considerable attention has been dedicated to developing strategies for improving the patient’s condition at the time of surgery. Portal vein embolization (PVE) is used to increase the size of the future liver remnant (FLR) and has been shown to be effective in inducing lobar hypertrophy with minimal risk. A meta-analysis published in 2008 reviewed 37 publications involving 1140 patients undergoing PVE in preparation for major hepatectomy and found that the FLR increased by an average of 8–27% with no mortality and with morbidity of <3%. If the FLR after PVE is ≤20% or the degree of hypertrophy is ≤5%, liver resection should be considered high-risk and may be contraindicated. Portal vein embolization of the segment IV branch improves the hypertrophy of segments II and III. Biliary drainage should be established before PVE in the case of biliary dilatation of the FLR.

A more widely debated subject concerns the use and route of preoperative biliary decompression in the jaundiced patient, with proponents citing improved liver function from the relief of preoperative biliary decompression in the jaundiced patient, whereas detractors cite improved liver function from the relief of preoperative biliary decompression in the jaundiced patient. Studies that have utilized rigorous patient selection have shown excellent results, with 5-year recurrence-free survival rates of 65–70% in patients with unresectable tumours. The risks for disease progression and recurrence have been identified, and this multimodal therapy has been successfully applied at many centres.

**Role of liver transplantation**

Although liver transplantation alone was found to be a dismal failure in patients with hilar CC, it has evolved to represent a promising option in patients with unresectable lesions when it is used in combination with neoadjuvant chemoradiotherapy. Studies that have utilized rigorous patient selection have shown excellent results, with 5-year recurrence-free survival rates of 65–70% in patients with unresectable tumours. The risks for disease progression and recurrence have been identified, and this multimodal therapy has been successfully applied at many centres.

Diagnostic criteria include: (i) positive or strongly suspicious intraluminal brush or biopsy; (ii) a radiographic malignant-appearing stricture plus either CA 19-9 of >100 U/ml in the absence of acute bacterial cholangitis or polysomy on FISH, and (iii) a well-defined mass on cross-sectional imaging. Patients with metastases, prior abdominal radiotherapy precluding additional therapy, a previous attempt at surgical resection with violation of the tumour plane, or any medical condition precluding transplantation were excluded. Vascular encasement and stricture/mass extension along the duct is not a contraindication, although a mass with a clear radial diameter of >3 cm is generally excluded (a longitudinal extension along the duct for >3 cm does not imply exclusion). Of note, there is no requirement for pathologic confirmation of a tissue diagnosis.

Neoadjuvant therapy includes external beam radiotherapy (EBRT) administered to a total dose of 4500 cGy (in 30 fractions of 150 cGy twice daily for 3 weeks) with a continuous infusion of 5-fluorouracil (5-FU) given for the duration of EBRT. An endoluminal brachytherapy boost is then delivered through transcatheter iridium-192 seeds. The strategy for delivery has changed from the administration of 2000 cGy over 24 h using low-dose brachytherapy to, most recently, high-dose brachytherapy of 1200–1600 cGy in two to four fractions. An EBRT boost of 1500 cGy in 10 fractions twice daily for 1 week is also acceptable. Patients remain on oral capecitabine at 2000 mg/m² of body surface area (BSA) in two divided doses
for 2 weeks in every 3-week period until transplantation. Operative exploration with routine biopsy of hepatic artery and pericholedochal lymph nodes plus any suspicious lesion is performed near the anticipated time of transplantation, and transplantation may involve either a deceased or living donor allograft. The indications and rationale for liver transplantation differ between patients with PSC and those with de novo hilar CC outside the setting of PSC, non-alcoholic steatohepatitis (NASH), or even occasionally hepatitis C viral infection. Patients with PSC are characterized by multifocal intrahepatic disease sites and extensive periductal fibrosis. The multifocality of the ductal lesions frequently precludes resection as a definitive option in patients with PSC. Outcomes following liver transplantation alone for incidentally diagnosed cholangiocarcinoma among patients with PSC are poor, with 3-year overall survival of <40%. When combined with a pre-transplant regimen of chemotherapy and radiation, 5-year survival from the start of therapy ranges from 55% to 65% among patients with cholangiocarcinoma arising in a background of PSC.51,52

In patients with unresectable de novo hilar CC, survival falls short of that seen in patients with PSC. From the start of therapy, 5-year patient survival ranges from 35% to 55% among these de novo patients.48,49 For these unresectable patients, neoadjuvant therapy followed by liver transplantation is the only potentially curative treatment option and should be considered despite the prolonged treatment course and high risk for recurrence.

The role of liver transplantation in patients with resectable de novo hilar CC is not well defined. As discussed, 5-year survival ranges for both margin-negative resection and neoadjuvant therapy combined with liver transplantation are similar. Barriers to resection include uncertainty regarding final margin status at the time of resection and the high rate of unresectability identified at the time of operative exploration. Barriers to liver transplantation include the significant dropout rate during pre-transplant induction therapy and the need for longterm immunosuppression. At this time, in light of the scarcity of donor resources and the absence of superior results with transplantation, resection should still be considered the standard of care for patients with de novo resectable hilar CC.

In summary, the standard therapy for hilar CC is resection, after which 5-year survival of 35–50% is possible in the setting of R0 resection, although many patients present with unresectable disease. In selected patients who are not eligible for resection, neoadjuvant chemoradiation followed by liver transplantation has facilitated excellent 5-year recurrence-free survival.

Consensus statements
- Resection of the involved intra- and extrahepatic bile ducts as well as the ipsilateral liver is the standard of care for suitable patients outside the setting of PSC.
- Portal vein embolization is a safe and effective strategy for increasing the FLR prior to resection and may be most useful in patients with an FLR of <30–40%.
- Preoperative biliary drainage in the setting of hyperbilirubinemia is indicated in patients with:
  - jaundice and the need for preoperative anti-neoplastic therapy
  - cholangitis
  - malnutrition, hepatic insufficiency or renal insufficiency possibly related to elevated serum bilirubin
  - preparation for PVE.
- Liver transplantation following a standardized protocol including external beam and transluminal radiation, as well as systemic chemotherapy, is the standard of care for both unresectable hilar CC, as well as hilar CC arising in the setting of PSC.

Traditional and novel adjuvant therapy and radiation approaches to hilar CC

Postoperative adjuvant therapy

The patterns of recurrence following resection of hilar CC play an important role in defining the appropriate strategy for adjuvant therapy. The initial site of failure following resection is more likely to be locoregional in patients with hilar CC (59%) than in patients with gallbladder cancer (15%). Based on this pattern of tumour recurrence and retrospective studies with limited numbers of patients, chemoradiation appears to offer a reduction in local recurrence for patients at high risk for recurrence. Several studies report improved overall survival in patients treated with postoperative adjuvant chemoradiation on multivariate analysis.54–57 In a recent non-randomized study from Japan, Todoroki et al. reported results in 63 patients with resected perihilar cholangiocarcinoma.57 Two thirds of patients received adjuvant radiation therapy with either intraoperative radiation therapy, external beam therapy, or both. The locoregional control rate was significantly better in the adjuvant therapy group than in the resection-alone group (80% versus 31%, respectively). The actuarial 5-year survival was also significantly better in the resection plus radiation group compared with the resection-alone group (39% versus 14%). In a retrospective study from the MD Anderson Cancer Center, patients with positive margins or positive nodes were referred for postoperative chemoradiation and showed similar locoregional recurrence rates (38% versus 37%) and overall 5-year survival (36% versus 42%) as patients without these high-risk features who did not receive radiation.58 Similar results were reported in a study from Korea conducted in patients treated with adjuvant radiotherapy, in which overall 5-year actuarial survival reached 31%.59 When patients were stratified by residual tumour, 5-year survival rates were 36% in patients with negative microscopic margins at the time of resection, 35% in patients with positive microscopic
Definitive therapy for patients with locally advanced, unresectable disease ineligible for transplant

For locally advanced inoperable tumours in patients who are not candidates for liver transplant, definitive chemoradiation with or without intraluminal brachytherapy has produced modest results with median survival ranging from 10.7 months to 14.6 months. Long-term survival has been reported after chemoradiation for resected cholangiocarcinoma and gallbladder tumours. Eighty patients were treated with four cycles (12 weeks) of gemcitabine and capecitabine followed by brachytherapy (54.0-59.4 Gy in 29-33 fractions).

Definitive therapy for locally recurrent or metastatic disease

The first cooperative group adjuvant trial has been completed and its results are pending. Southwest Oncology Group 0809 is a single-arm, Phase II trial of postoperative chemoradiation followed by brachytherapy selected patients treated with postoperative radiation, and irradiated patients were significantly more likely to have hepatic artery invasion.60,61

The initial evidence supporting the use of gemcitabine alone or in combination with other agents was derived from Phase II studies (Table 1).64-71 These studies identified a cohort of treated patients in whom treatment response to these agents was apparent and prompted the initiation of the Advanced Biliary Cancers (ABC)-01 trial, a Phase II study which subsequently transitioned into the Phase III ABC-02 trial based on encouraging initial results.72

In 2010, the ABC-02 trial published the results of a comparison of gemcitabine plus cisplatin with gemcitabine alone in patients with locally advanced or metastatic biliary tract cancers.73 This trial included 410 patients with intra- or extrahepatic cholangiocarcinoma, gallbladder cancer or ampullary cancer. Patients were randomized to either cisplatin (25 mg/m² BSA) or 5-FU/LV 21% 10%

<table>
<thead>
<tr>
<th>Study (year)</th>
<th>Trial design</th>
<th>Tumour types</th>
<th>Patients, n</th>
<th>Systemic agents</th>
<th>Response rate, %a</th>
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<td>Kubicka et al. (2001)</td>
<td>Phase II</td>
<td>CCA</td>
<td>23</td>
<td>GEM</td>
<td>30%</td>
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<td>Kuh et al. (2002)</td>
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<td>GEM + DOC</td>
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<td>30</td>
<td>GEM + 5-FU/LV</td>
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<td>Phase II</td>
<td>CCA, GBC, AMP</td>
<td>56</td>
<td>GEMOX</td>
<td>36%</td>
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<td>30</td>
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<td>51</td>
<td>MMC + GEM versus MMC + CAPE</td>
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<td>(ABC-01)</td>
<td>CCA, GBC</td>
<td>86</td>
<td>GEM versus GEM + CIS</td>
<td>23% versus 28%</td>
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| Table 1 | Summary of early results with gemcitabine-based systemic therapy for locally advanced or unresectable biliary tract cancers |

| aResponse rate: radiographic complete response or partial response. 5-FU, infusional 5-fluorouracil; 5-FU/LV, 5-fluorouracil followed by leucovorin; AMP, ampulla of Vater cancer; CAPE, capecitabine; CCA, cholangiocarcinoma; CIS, cisplatin; DOX, docetaxel; GBC, gallbladder cancer; GEM, gemcitabine; GEMOX, gemcitabine-oxaliplatin; MMC, mitomycin C; Retro, retrospective review; RT II, randomized Phase II trial. |
followed by gemcitabine (1000 mg/m² BSA) on days 1 and 8 every 3 weeks for eight cycles, or gemcitabine alone on days 1, 8 and 15 every 4 weeks for up to 24 weeks. Median survival in the cisplatin–gemcitabine group was greater than that in the gemcitabine-alone group (11.7 months versus 8.1 months; P < 0.001). In addition, progression-free survival and the rate of tumour control were superior in the cisplatin–gemcitabine arm.

The French Biliary Cancers: EGFR Inhibitor, Gemcitabine and Oxaliplatin (BINGO) trial randomized 101 patients with intra- or extrahepatic cholangiocarcinoma, gallbladder cancer or ampullary cancer to receive gemcitabine plus oxaliplatin with or without cetuximab. This study did not demonstrate any added benefit of the addition of an EGFR-inhibitor for these patients.

Despite the fact that the largest study of systemic chemotherapy for patients with advanced biliary malignancy included a disparate collection of histologies, the ABC-02 trial provides the best evidence for an effective chemotherapeutic strategy for these patients. The recommended treatment modality for patients with metastatic hilar CC is the combination of cisplatin and gemcitabine as defined in ABC-02.

Consensus statements

- After resection of margin-positive or node-positive hilar CC, chemoradiation should be offered to patients. The role of adjuvant chemotherapy is still not clearly defined, but may be considered based on clinical trial experience with advanced biliary cancers.
- For patients with unresectable tumours who are ineligible for liver transplantation, definitive chemoradiation with or without intraluminal brachytherapy should be considered.
- For patients with local recurrence, chemotherapy is the recommended palliative approach because there are inherent toxicity risks associated with radiation delivery to the jejunal anastomosis.
- For patients with advanced and metastatic hilar CC, the standard first-line chemotherapy is gemcitabine and cisplatin.

Overall summary

Hilar cholangiocarcinoma is an uncommon gastrointestinal malignancy which requires the collaboration of providers from multiple disciplines including hepatobiliary surgery, transplant surgery, medical oncology, radiation oncology, diagnostic radiology, interventional radiology, gastroenterology and pathology. This expert-level collaboration is necessary not only because practitioners from multiple medical fields are involved in each patient’s care, but also because the risk for disease recurrence is high even after attempts at curative therapy. Continued efforts to standardize best practices will need to involve all of these disciplines, as well as translational research efforts aimed at broadening the present treatment options and tailoring treatment choices.

Conflicts of interest

None declared.

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