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Perspective

Cancer Treatment and Considerations for the Biliary Tract

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DESCRIPTION

The following list of treatment options for biliary tract cancer includes the following:

- Surgery
- Adjuvant treatments
- Systemic treatments
- Single-agent approaches

Surgical resection

- Because surgery is the sole treatment option for biliary tract malignancies, care teams with specialised knowledge should determine whether the disease is surgically resectable.
- The absence of all of the following criteria, including extrahepatic adjacent organ invasion, disseminated disease, invasion of the portal vein or main hepatic artery, retropancreatic and paraceliac nodal metastases, or distant liver metastases, is required for resectability. However, some centres may offer vascular reconstruction.
- Depending on the location of the tumour, surgical resection typically entails cholecystectomy, en bloc hepatic resection, and lymphadenectomy with or without bile duct excision.
- Delayed open laparotomy is appropriate if cancer is discovered inadvertently during surgery for unrelated reasons, resectability is not clearly proven, or if the surgeon is untrained in the procedure. This is because there is no survival disadvantage when compared to prompt resection.

Neoadjuvant therapy

- For patients with biliary tract cancer, neoadjuvant chemoradiotherapy is not currently a common treatment option. Nine out of 91 patients who presented with more advanced illness got chemoradiotherapy in a small, carefully chosen case series, and they all achieved a R0 resection. However, a subsequent research looking at chemoradiotherapy with 5-FU failed to find a survival benefit.
- Kobayashi et al. performed a retrospective analysis and found that chemoradiation therapy, which consisted of three cycles of full-dose gemcitabine plus 50–60 Gy radiation, increased both recurrence-free survival and overall survival (P=0.0263, P= 0.00187). Compared to 79 individuals treated without neoadjuvant therapy, 27 patients who received neoadjuvant chemoradiation therapy experienced a 3-year recurrence-free rate of 78%.
- High-dose neoadjuvant radiation with chemosensitization, followed by liver transplantation, produces excellent results for patients with early-stage, unresectable hilar cholangiocarcinoma or cholangiocarcinoma occurring in the context of primary sclerosing cholangitis.

Following is the Mayo Clinic protocol:

- External beam radiation therapy followed by ongoing 5-FU for three weeks
- Two weeks of brachytherapy, followed by
- Capecitabine (kept perioperatively during staging) till transplantation, then
- Exploration of the abdomen for staging
- Transplanting the liver

Adjuvant therapy following curative-intent resection

Stage IB-III (T1-3, N0-1, M0):

- According to Spanish Society of Medical Oncology (SEOM) recommendations, adjuvant capecitabine medication should be given to all patients who have had curative resection of biliary tract cancer for a period of six months.
- In addition to encouraging clinical trial participation, the National Comprehensive Cancer Network (NCCN) guidelines state that only a small amount of clinical trial data are currently available to define a standard regimen or definite benefit. However, they do offer the options of fluoropyrimidine- or gemcitabine-based chemotherapy followed by fluoropyrimidine- or gemcitabine-based chemoradiation or fluoropyrimidine-based chemoradiation, which may be followed by fluoropyrimidine- or
- High rates of local failure following surgery lead to recommendations for radiation therapy in the adjuvant setting. A retrospective analysis of patients who received

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adjuvant radiotherapy reveals an initial survival benefit, but a longer-term follow-up series suggests that this benefit may be lost after more than 5 years.

Adjuvant chemoradiotherapy regimens for stage IB-III:

- 5-FU 225 mg/m^2 IV every day while receiving radiation,
- 5-FU 500 mg/m^2 IV bolus administered during radiotherapy on days 1-3 and 29–31;
- During radiation, capecitabine 825 mg/m^2 PO twice daily; after radiation, consider a further 4 months of therapy;
- Capecitabine 1000 mg/m^2 PO once every 14 days, or
- On radiation-days, capecitabine 800-900 mg/m^2 PO BID
- If you have several positive lymph nodes or aggressive or high-risk illness (positive margins), you might want to switch to a gemcitabine-based treatment.

Systemic therapy for nonresectable or metastatic disease

Selected stage III-IV (T3-4, Any N, M0-1):

- Front-line chemotherapy as a standard of care for patients with a satisfactory performance status (ECOG score 2)
- Cisplatin 25 mg/m^2 IV on days 1 and 8, as well as 1000 mg/m^2 IV of gemcitabine on those same days, followed by every 21d for up to 24 weeks or until the disease progresses.
- Other suitable regimens for patients with good performance status (gemcitabine regimens are preferred):
- Oxaliplatin 100 mg/m^2 IV on day 2, followed by 1000 mg/m^2 IV of gemcitabine every 14 days until progression or toxicity.
- Capecitabine 650 mg/m^2 PO on days 1 through 14 and 1000 mg/m^2 IV on days 1 and 8, followed by every 21 days until progression or toxicity.
- Oxaliplatin 130 mg/m^2 IV on day 1 and capecitabine 1000 mg/m^2 PO twice daily for days 1 through 14; then every 21 days until progression or toxicity.
- Leucovorin 400 mg/m^2 IV infused over 2 hours prior to 5-FU plus a 400 mg/m^2 IV bolus of 5-FU on day 1, then 2400 mg/m^2 IV infused over 46 hours plus 100 mg/m^2 IV of oxaliplatin on day 1; thereafter every 14d until progression or toxicity.
- Cisplatin 60 mg/m^2 IV on day 1 and capecitabine 1250 mg/m^2 PO twice daily for days 1–14; then every 21 days until progression or toxicity.
- Cisplatin 100 mg/m^2 IV on day 2, followed by 5-FU 1000 mg/m^2/day IV continuous infusion on days 1-5, then every 4 weeks until progression or toxicity.

For patients with a lower performance status (ECOG score > 2), single-agent regimens:

- Gemcitabine 1000 mg/m^2 IV every 21 days until progression or toxicity.
- Capecitabine 1000 mg/m^2 PO once every 21 days for the first 14 days, then as needed until progression or toxicity.
- 5-FU 425 mg/m^2 IV bolus plus 20 mg/m^2 IV folinic acid, followed by weekly administration until progression or toxicity.
- Docetaxel 100 mg/m^2, given intravenously, then every 21 days until progression or toxicity additional factors
- Chemotherapy should often only be administered to healthy patients.
- Patients with advanced, incurable biliary tract cancer frequently require palliative biliary drainage.
- Compared to endoscopic stenting, percutaneous biliary drainage often has a higher rate of success and fewer complications.
- Another therapy option for patients with unresectable intrahepatic cholangiocarcinoma is radioembolization using yttrium-90 microspheres.