Opinion

China's surgical expert consensus on the diagnosis and treatment of cholangiocarcinoma: an interpretation

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Cholangiocarcinoma is a medical term denoting the malignant tumors originated from the lining epithelium of bile duct system. It can be classified as intrahepatic cholangiocarcinoma (ICC) and extrahepatic cholangiocarcinoma. To further standardize the cholangiocarcinoma management, a Surgical Expert Consensus on the Diagnosis and Treatment of Cholangiocarcinoma has recently released in China.

The consensus proposed that the risk factors of cholangiocarcinoma include old age and bile duct stones.

Adenocarcinoma is the most common histological type among the intra- and extra-hepatic cholangiocarcinoma, whereas the morphologic types are more diverse. The bile duct epithelial neoplasia, intraductal papillary neoplasms, and bile ducts mesenchymal hamartoma are regarded as the precancerous lesions of cholangiocarcinoma.

The diagnosis of cholangiocarcinoma should be based on clinical manifestations, haematological examination results, and imaging findings. The common clinical symptoms (e.g., the upper right abdominal discomfort, abdominal pain, anorexia, and emaciation) of cholangiocarcinoma are often non-specific. Hilar or extrahepatic cholangiocarcinoma is often associated with obstructive jaundice. Cholangiocarcinoma has no specific tumor markers; however, serum tumor markers including CA19-9, CEA, and CA-125 have certain value for the diagnosis of cholangiocarcinoma. Proper imaging is helpful for the locating, qualitative diagnosis, and staging of cholangiocarcinoma. Ultrasound is the preferred method for the diagnosis of biliary obstruction. Endoscopic ultrasonography can better observe distal extrahepatic bile duct, local lymph nodes, and blood vessels. Also, it can be used to guide fine-needle aspiration biopsy of lesions and lymph nodes. High-resolution spiral CT can display the range of lymph node metastasis, whereas MRI is the best way to diagnose cholangiocarcinoma. Positron emission tomography-computed tomography (PET-CT) can be used for distinguishing the benign and malignant masses and evaluating the potential distant metastasis. Endoscopic retrograde cholangiopancreatography (ERCP), percutaneous transhepatic cholangiogram (PTC), duodenoscopy, and colonoscopy have certain values in the diagnosis of cholangiocarcinoma, and can be used for biopsy.

Pre-operative needle biopsy is not recommended in the Expert Consensus. During the pathological diagnosis, the histological type should be correctly identified. Any pathologic factor that may affect the prognosis should be described in the pathology report in details. If condition allows, molecular markers that are related with targeted drug therapy, biological behavior assessment, and prognosis should also be detected to provide useful information for clinical decision-making.

The staging of cholangiocarcinoma should be based on TNM system (American Joint Committee on Cancer, 2010). However, the staging of hilar cholangiocarcinoma can be based on Bismuth-Corlett classification system.

Surgery remains the treatment of choice for cholangiocarcinoma. Although surgical resection is the preferred treatment for *tumors in stage* I, II and III it is not recommended for stage IV cholangiocarcinoma; instead, only palliative care should be provided for these patients. The value of palliative resection has not been demonstrated. The range of surgical resection varies for lesions with different locations and TNM stages. For hilar cholangiocarcinoma, the range of hepatectomy can also be based on its Bismuth-Corlette

stage. The effectiveness of a surgery mainly depends on the tumor location, infiltration of tumor into bile duct, tumor-free resection margin, and lymph node metastasis, if any. Neoadjuvant chemotherapy can improve the effectiveness of surgical treatment. However, the prognosis tends to be poor in patients with a large tumor (>3 cm in diameter), distant metastasis, peritoneal tumor growth, and history of previous malignancy.

For unresectable or metastatic advanced cholangiocarcinoma, gemcitabine combined with platinum-based antitumor drugs and/or tegafur-gimeracil-oteracil potassium is recommended. Adding erlotinib to the protocol may improve the anti-tumor efficacy. The clinical efficacy of targeted drug treatment has yet to be confirmed in large prospective randomized clinical studies. Adjuvant radiotherapy or radiotherapy alone may be applied.

Preoperative conventional biliary drainage is not recommended. However, for patients with malnutrition, cholangitis, or preoperative serum bilirubin levels higher than 200 μmol/L and for whom extensive liver resection is required, preoperative biliary drainage should be performed. In patients who need to undergo extensive liver resection (removal of half or more than half of the liver) and the residual liver will not be able to compensate for the lost functions, portal vein embolization at the diseased side may be performed firstly, and then the safety of surgical resection can be re-assessed 2 or 3 weeks later.

According to the consensus, while no special treatment is needed after the radical resection (R0), the patients should receive regular examinations within the next two years. For patients who have received R1 or R2, radio-frequency ablation, microwave coagulation, chemotherapy (gemcitabine combined with platinum-based anti-tumor drugs), and/or radiochemotherapy should be provided. Imaging evaluation should be conducted every 2-3 months for 2 years.

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