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### Role of surgery in cholangiocarcinoma: From resection to transplantation



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#### A B S T R A C T

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The treatment of cholangiocarcinoma (CCA) represents a major challenge to modern medicine. Diagnostics and treatment modalities are complex and require close interdisciplinary work-up. However, surgical resection currently offers the only potentially curative treatment option. Improved peri-operative strategies as well as optimized surgical techniques have generated significantly increased survival chances for patients in recent years. Complete tumor resection is the key parameter to long-term survival. In spite of expanded surgical limits R0 resection cannot be achieved in some cases as parenchymal disease may limit the extent of resection. Although liver transplantation (LT) is not a standard therapy for CCA today, it may be an option in such selected cases. Protocols including neo-adjuvant radio-chemotherapy and staging-lymphadenectomy before LT have generated impressive results in the recent past. Since palliative options generate only short-term survival extension LT for CCA has lately been discussed more extensively after the procedure had been abandoned due to dismal survival data in the 1990-years. This review offers a comprehensive picture of the current surgical treatment option for cholangiocarcinoma.

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## Status quo

Complete surgical resection represents the only potentially curative option for patients suffering from intra- or extrahepatic cholangiocarcinoma (CCA). Despite extensive surgical approaches and perioperative chemotherapeutic treatment long-term survival of patients is limited. In many cases complete surgical resection of the tumor is impossible due to central vascular and biliary tract invasion or hepatic parenchymal disease. For these patients liver transplantation (LT) may represent a curative option if extrahepatic tumor dissemination can be ruled out.

Complete resection including microscopically tumor-free margins (R0) represents the key to curative treatment. Extended hepatic resection with or without vascular reconstruction and complete removal of the extrahepatic bile duct system is the current gold-standard offering 5-year survival rates of up to 50% in specialized centers [1,2]. Currently, liver transplantation is not regarded as a potential standard treatment for these patients. This attitude, however, is based on rather discouraging long-term results following LT for CCA in the 1990-years. Tumor recurrence rates under immunosuppression were unacceptably high, therefore ubiquitous organ shortage has prompted graft allocation to patients with potentially higher survival chances [3–6]. Only a small number of highly selected patients with small yet anatomically complicated tumors were furthermore considered candidates for LT.

Overall, the number of patients receiving LT for CCA in the past 15 years was extremely small and no prospective or randomized trials exist concerning the question of acceptable benefit by LT for these patients in the light of worldwide organ shortage [7]. Recently, however, some new data has become available demonstrating encouraging results for LT in CCA patients following meticulous individual evaluation and peri-operative treatment by radio-chemotherapy.

Here, we will provide an overview on the current surgical treatment options for CCA with respect to the individual therapeutic decision dependent on the diagnostic work-up.

In order to categorize the treatment modalities we will establish different groups of CCA based on the anatomical position:

1. Intrahepatic CCA
2. Hilar CCA
3. Extrahepatic CCA
4. Distal CCA

*Intrahepatic CCA* in the liver periphery should be approached by (extensive) surgical resection. Radical surgery is often possible for these patients as they do not suffer from parenchymal liver dysfunction such as patients with cirrhosis and hepatocellular carcinoma (HCC). Therefore, surgical resection can often be performed successfully; sometimes multimodular approaches such as preoperative portal venous embolization and percutaneous bile drainage may be necessary. Under the presence of anatomical limitations such as enormous tumor size or massive vascular invasion the tumor stage must be regarded too advanced for considering liver transplantation as a potential option. In many of these cases extrahepatic tumor spread can be detected in hilar or even retroperitoneal lymph nodes.

The surgical procedure must be preceded by a careful and conclusive diagnostic work-up: Adequate CT or MRI imaging is needed to evaluate exact tumor size and localization as well as exclusion of satellite nodules in the post-surgical liver remnant. The anatomy of the biliary tree should be visualized by MRCP or ERC. If significant cholestasis is present preoperative decompression is needed especially for the future remnant part of the liver in order to guarantee optimal functional capacity. If biliary decompression cannot be achieved by ERC percutaneous maneuvers may be necessary (PTCD).

Portal venous embolization of the tumor-bearing liver lobe serves to induce atrophy of the respective liver tissue with consecutive hypertrophy of the contra-lateral side [8–10].

Usually, two to three weeks of “waiting time” are needed for sufficient hypertrophy. Historically, arterial embolization was preferred to the portal venous approach due to less complexity of the procedure. Contra-lateral hypertrophy induction, however, was more often insufficient and the “waiting time” was increased considerably thereby conflicting with continuous tumor growth [11]. In the case of

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