Hilar En Bloc resection for hilar cholangiocarcinoma

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Bile duct carcinomas (cholangiocarcinomas) are a rare, but highly fatal disease. They are classified in intrahepatic, hilar and distal extrahepatic bile duct tumors according to their localization in the biliary system. The majority of cases are extrahepatic hilar cholangiocarcinomas originating from the hepatic bifurcation (Klatskin tumor). Cholangiocarcinomas are relatively uncommon and account for only 3% of all gastrointestinal cancers, but, the incidence of intrahepatic cholangiocarcinoma increased in many countries some years ago.

Surgery represents the only potentially curative treatment option for cholangiocarcinomas. The extent of the surgery depends on the site of the cancer within the liver and/or the biliary tract. For locally contained disease, resectability is primarily determined by the extent of biliary or vascular involvement. Almost half of the patients with resectable intra- or extrahepatic bile duct cancer have regional lymph node involvement at the time of diagnosis. However, this is not a contraindication for surgery unless para-aortal nodes are involved. The major goal of surgery is to achieve negative resection margins.

Intrahepatic cholangiocarcinoma

Surgical treatment of intrahepatic bile duct cancer does not significantly differ from the treatment of other primary or secondary liver tumors. Resection includes the involved segments together with a regional lymph node dissection. Due to the unspecific symptoms and the delayed diagnosis large tumors are often present and require an extended hemihepatectomy. Due to the large tumor size only relatively few functional liver tissue has to be removed in most cases. Therefore, postoperative liver failure or severe complications are relatively rare. Subsequently, more radical liver resections for cholangiocarcinoma have resulted in a increasing number of patients with negative resection margins and an improved 5-year survival within the last decades. 5-year survival rates vary from 10 % to 50%. The highest 5 year suvival of more than 50 % is achieved in patients with solitary tumors, negative lymph nodes and negative resection margins. But also in patients with advanced tumors 5 year survival rates of 20 to 40 % can be achieved after curative resection. The most relevant prognostic factors after resection are a R0 resection, nodal status, vascular invasion and tumor grading. Since early symptoms are lacking most tumors are relatively large at the time of diagnosis. Therefore radiofrequency ablation is not possible in inoperable cases. In few centers interstitial brachytherapy is used for irrescatable cases without distant metastases, since treatment of tumors up to 10 cm has been reported using this technique.

Hilar cholangiocarcinoma

Surgical management of hilar cholangiocarcinomas is complex. Curative treatment by radical surgical procedures with surgical preparation distant to the tumor region results in 5-year survival rates of 30-50%. This requires en-bloc liver resection and resection of the extrahepatic bile duct often together with vascular resections. Nevertheless, the ideal safety margin of 0.5 to 1 cm remote from the macroscopic tumor extensions can not be achieved in all cases. Based on hilar anatomy the probability of an adequate safety margin is higher using extended right hemihepatectomies together with portal vein resection compared to left hemihepatectomies. However, due to severe atrophy of the left liver lobe solely left sided hepatectomies are feasible in a part of patients. In case of eligibility for both procedures right hemihepatectomies are preferentially used due to its higher oncological radicality, sufficient liver function provided. Postoperative hepatic insufficiency and bile leaks after demanding biliary reconstructions -often with several small orifices- contribute to the postoperative complication rate of this complex surgical disease. The extent of resection is determined by the respective biliary or vascular involvement and potential atrophy of one liver lobe. Thereby a simultaneous partial hepatectomy is the most important surgical factor for improving the long term results in patients with hilar cholangiocarcinoma. Even after formally curative local excision of the extrahepatic biliary system more than 70% of patients suffer from locoregional recurrence.

Major problem of extensive liver surgery in hilar cholangiocarcinoma is an increased perioperative morbidity and the risk of postoperative liver dysfunction. Therefore an optimal preoperative conditioning of the future liver remnant is therefore mandatory.

After R0-resection patients with major liver resection reveal 5 year survival rates of 30 to 65%. In contrast, the 5-year survival rates after isolated resection of the extrahepatic bile ducts are 0 to 25%. In general, the most relevant prognostic factors are R0 resection, nodal status, lymphangiosis carcinomatosa and tumor grading.

In a very selected population of patients with small, irresectable hilar cholangiocarcinomas liver transplantation might be an option. These include PSC patients with hepatic dysfunction or locally unresectable tumors in an otherwise normal liver. Recent data using strict patient selection and adjuvant or neoadjuvant protocols have shown encouraging results. Using strict selection criteria including small tumor size (< 3 cm) and negative lymph nodes, the Mayo Clinic protocol of neoadjuvant chemoradiation, followed by liver transplantation has achieved a 5 year recurrence free survival of 65% in a recent multicenter analysis. At present liver transplantation does not represent a standard treatment for these patients, but it can be considered for carefully selected patients with cholangiocarcinomas.

Distal cholangiocarcinoma

Bile duct cancers distal to the cystic duct have a close proximity to the pancreatic head and are managed in parallel to ampullary cancers by partial pancreatoduodenectomy. In addition, the bile duct is resected up to the hepatic bifurcation or further. The most important prognostic factors are a margin-negative resection, followed by negative lymph nodes. In several patient series 5-year survival rates of 20-50% have been reported.

Palliative treatment

More than half of the patients with biliary cancers have irresectable disease, which implicates a median survival of less than 1 year. Mainstay of palliative treatment is endoscopic or percutaneous drainage of the biliary system. In patients with good performance status, palliative chemotherapy provides a survival benefit together with an improved quality of life. It has been recently shown in a randomized phase III tiral, that combination therapy using cisplatin plus gemcitabine improves the median overall survival (11.7 months) compared to gemcitabine alone (8.1 months). Since adverse events were comparable both groups gemcitabine plus cisplatin are used as standard first line treatment in most centres.

Photodynamic therapy has shown promising result and radiation might be helpful for localized disease. Preliminary data show that PDT is a promising palliative treatment for selected patients with cholangiocellular carcinoma, reaching a prolongation of survival and a reduction of cholestasis, but further studies are necessary. Especially the combination of photodynamic therapy with other treatment modalities like chemotherapy has not been investigated so far.