Surgical Resection of Metastatic Cancer to the Liver

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Summary: Background: Surgical resection is the only treatment modality that provides the chance of cure for patients with metastatic spread to the liver.

Methods: This report reviews the indication, technique and results of surgical resection of liver metastases.

Results: Most of the data on hepatic resection for metastatic disease relates to colorectal secondaries. Generally 5-year survival rates between 30 and 40% have been reported after surgical treatment of liver metastases originating from colorectal cancer. The operative mortality ranges between 0 and 5%. However these positive results are only obtained in patients with less than 4 metastases and without extrapleural spread. Consequently careful preoperative staging is mandatory to identify patients who are likely to benefit from operative treatment. The criteria for the indication for liver resection of non-colorectal liver metastases have not yet been defined clearly. For such tumors the prognosis after liver resection is significantly poorer compared to patients with colorectal malignancy.

Conclusions: Surgical resection of liver metastases from colorectal cancer may improve the prognosis in selected patients and even result in cure. In contrast liver resection in patients with non-colorectal metastases rarely improves in prognosis.

Operative Therapie von Lebermetastasen

Zusammenfassung: Die chirurgische Resektion von Lebermetastasen ist weiterhin die einzige Therapieoption, die eine kurative Therapie von Lebermetastasen ermöglicht.

Methodik: In dieser Arbeit stellen wir die Indikationen, Technik und Ergebnisse der operativen Therapie von Lebermetastasen anhand der eigenen Erfahrungen und Bewertung der Literatur dar.


Schlußfolgerungen: Die Resektion von Lebermetastasen führt bei definierten Patienten-Subgruppen mit kolorektalem Karzinom zu einer verbesserten Prognose und teilweise zur Heilung.

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Introduction

Although liver metastases may give the first evidence of cancer progression they almost always indicate general dissemination of malignancy. Treatment options for hepatic metastases include surgical resection, administration of regional chemotherapy, systemic chemotherapy, radiotherapy and various innovative strategies to achieve specific drug targeting. In spite of all advances presently surgery is the only therapy prolonging survival or even providing the chance of cure. In the meantime the technical ability is no longer a limiting factor to the application of hepatic resection for malignant disease. Although hepatic resection remains a major procedure current mortality rates of 0-6% justify widespread use of this operation (16, 20). Consequently it is even more important to establish accurate guidelines defining the indications of hepatic resection for malignant disease.

Due to the high incidence most of the available information regarding hepatic resection for metastatic disease relates to metastases arising from colorectal primaries. About 50% of the hepatic resections are performed for colorectal secondaries while 20% are undertaken for non-colorectal metastases (31). In spite of the poor prognosis of patients with liver metastases occasional success of surgical resection resulting in long term survival has been reported. This observation suggests the existence of a subset of patients who benefit of surgical therapy. After resection of non-colorectal metastases a 5-year survival rate of 20% has been demonstrated (68). More encouraging results have been obtained in patients with colorectal cancer. Hepatic resection of colorectal cancer may result in a 5-year survival rate of 30 to 40% if appropriate selection criteria are considered (16, 52).

Staging

In contrast to other gastrointestinal tumors a generally accepted classification for primary or secondary hepatic malignancy has not yet been developed. Currently a study is being performed by the UICC to elaborate a TNM-classification for liver metastases results of which are not available so far.

Nonetheless it is mandatory to consider a special strategy for accurate diagnostic evaluation of suspected hepatic metastases. The most important factor is to characterize the histology of the suspicious lesion. Once malignancy is established it is of major interest to elucidate the localization of the metastases and their relation to the major branches of the hepatic and the portal veins and the main bile duct in order to ascertain resectability. Furthermore, substantial diagnostic efforts must be provided to define the number and distribution of metastases and to exclude intra- and extrahepatic tumor spread. This enables assessment of curability and estimation of the prognosis of the patient which strongly influences the therapeutic strategy.

Diagnosis

The basic step in the diagnostic evaluation of liver lesions is to confirm the presence of malignancy which may be difficult without biopsy. While liver function tests provide no specific information, determination of the serum level of a panel of tumor markers can be helpful to establish the correct diagnosis (3, 39). If high levels of AFP (> 100 ng/l) are detected, presence of a primary hepatocellular carcinoma is very likely. Colorectal metastases may be associated with increased levels of CEA and CA19-9. An increased level of CEA (> 5 ng/ml) is found in about 90% of all patients with hepatic metastases of colorectal carcinoma. On the other hand only a low specificity and sensitivity (60 to 65%) is found for CA19-9 (25). Pathologic liver function tests and increased levels of CA15-3 are indicative of hepatic metastases of breast carcinoma (21).

Generally ultrasonography is the initial imaging method for detection of suspected liver metastases. The accuracy of this method is substantially influenced by the presence of independent hepatic pathology such as liver cirrhosis. Consequently sensitivity and specificity of sonography may be as low as 50% for the detection of hepatic tumors and similar results have been reported for conventional CT (67). Special techniques of combined tomography, e.g. angiographically enhanced CT and incremental dynamic bolus CT have been demonstrated to be more sensitive for the detection of small liver tumors (9, 54). Recently comparable results have been found for magnetic resonance imaging (MRI), and further development of contrast media such as Gadolinium-DPTA may improve imaging of hepatic tumors by this technique (44, 53).

Presently a reasonable degree of accuracy in the differentiation of benign and malignant liver tumors is only achieved by a combination of several imaging methods. Dynamic bolus CT is reasonably specific in the diagnosis of hemangioma. Characteristically hemangioma appear as a hypodense lesion followed by peripheral enhancement during infusion of a bolus of contrast and gradual filling of the lesion. However these criteria are typical in no more than 55% of the cases (18). Other radiologic investigations such as angiography, scintigraphy and single photon emission computed tomography (SPECT) can contribute significantly to increase the accuracy of the diagnosis. In a recent study on 83 patients with hepatic lesions, MRI allowed discrimination between hemangiomias and malignant lesions with a 97% accuracy (41). Promising results were also reported for MR imaging of focal nodular hyperplasia (FNH) and hepatic adenoma (13).

Immunoscintigraphy using monoclonal anti-CEA antibodies has proved valuable for the detection of liver metastases of colorectal carcinoma. A sensitivity ranging from 50% to 80% and a specificity of up to 85% has been obtained (24, 30). The results of this technique are dependent on the specificity of the antibodies as well as on the stability of the labelling and the imaging technique used (26).

Resectability

The assessment of resectability necessitates accurate evaluation of the local extent and distribution of metastases within the liver. Generally involvement of the porta hepatitis with infiltration of the central liver veins and the portal vein indicate non-resectable disease. On the other hand hemihepatectomy is still possible if the metastasis infiltrates only the left or the right branch of the portal vein and there is more than 1 cm distance to the main stem of the portal vein. Infiltration of the gall-bladder has no influence on resectability.

Besides MRI, CT arterial portography has proved to be the most sensitive imaging method for the evaluation of resectability. Generally correct assessment of resectability is warranted in 88% of the patients, while positive predictive values for non-resectable disease of 73% have been reported (63). The infiltration of major vascular structures and the number and distribution of liver metastases are important limiting factors to surgery. Generally a surgical procedure is abandoned if more than three metastases are detected in both lobes of the liver. However, preoperative transcutaneous ultrasound and computed tomography are not sensitive enough to determine the localization and the number of metastases (23). More recently, intraoperative tomography is capable to improve the situation. A study of various imaging methods on 189 patients with liver metastases revealed a significantly higher sensitivity for intraoperative sonography (93%) compared to preoperative ultrasound (41%), CT (47%) and surgical exploration (66%). Re-evaluation based on follow-up results ultimately decreased the sensitivity to 82% which is still considerably better than with other methods (40).

Curability

Indication for hepatic resection is limited to patients who are potentially curable by the operation. The presence of hepatic or celiac node involvement as well as other extrahepatic spread implies the impossibility of eradicating the disease completely by