Clinical and experimental studies on portal vein embolization / Diagnosis of hepatocellular adenoma and focal nodular hyperplasia
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Part 2

Summary, conclusions and future perspectives

Diagnosis of hepatocellular adenoma and focal nodular hyperplasia
Summary and conclusions

The second part of this thesis deals with two liver tumors, hepatocellular adenoma (HCA) and focal nodular hyperplasia (FNH), which are relatively rare, benign liver tumors. The main focus is on differentiation of these tumors using current imaging modalities.

Chapter 10 is a literature review of the studies that describe the typical features of HCA and FNH using several imaging modalities and of studies focussing on the accuracy of imaging modalities in differentiating HCA from FNH. Based on typical features, especially FNH can be diagnosed with high certainty by several imaging studies. However, there are atypical findings in both FNH and HCA that preclude a definitive diagnosis and may resemble other tumors. We found many case reports and studies which described the features of FNH and HCA. However, there is little evidence regarding the diagnostic performance of imaging modalities in the differentiation of FNH and HCA. In many studies the final diagnosis was often only based on imaging and follow-up, while the gold standard remains histopathological confirmation of the tumor. In addition, sample sizes were often small. Reliable evidence of the best way to differentiate FNH from HCA is therefore lacking.

The aim of Chapter 11 was to review all the case reports and case series of patients with HCA published from 1998 to 2008 in China and other parts of the world in order to compare clinical presentation and surgical management. A total of 356 patients were identified, including 191 patients from China, 104 from Europe, 46 from North America, and 15 from South-East Asia. The clinical presentation of HCA in China differed from other parts of the world regarding male predominance and a higher incidence of coexistent HCC in China. This might be the result of the birth control policy in China, limited oral contraceptive use, and the higher incidence of HBV. The management of HCA consisted of resection in most cases.

In Chapter 12, the additional value of the hepatobiliary phase in magnetic resonance (MR) imaging after administration of a hepatobiliary contrast agent (Gd-EOB-DTPA) was evaluated for differentiating HCA from FNH in a prospective study. Histological diagnosis revealed 24 HCA and 28 FNH. Standard MR showed 21 inconclusive cases, 11 HCA, and 10 FNH. Detection rate was 50% for HCA and 64% for FNH with a positive predictive value of 100 and 94%, respectively. The additional hepatobiliary phase resulted in a detection rate of 96% for HCA and 96% for FNH, with a positive predictive value of 100 and 96%, respectively. Features with significant predictive value for diagnosis in HCA included bleeding, fat, and glycogen content. The presence of a central scar was highly predictive for FNH. This study showed high accuracy of Gd-
EOB-DTPA MR imaging when the standard series are combined with the hepatobiliary phase for differentiation of FNH and HCA in lesions larger than 2 cm.

The aim of Chapter 13 was to evaluate the use of PET/CT with the tracer \(^{18}\)F-fluorocholine in the differentiation of HCA from FNH. Twenty one patients with liver lesions larger than 2 cm suspicious for HCA or FNH were prospectively included. All patients underwent PET/CT with \(^{18}\)F-fluorocholine and histopathological diagnosis was obtained by either liver biopsy or after resection. An SUV ratio cut-off value between 1.12 and 1.22 differentiated patients with FNH from those with HCA with 100% sensitivity and 100% specificity. This pilot study showed that PET/CT with \(^{18}\)F-fluorocholine can differentiate HCA from FNH. A drawback of the use of PET/CT using non-contrast enhanced low-dose CT is that the tumours might be difficult to localize. In such cases image fusion with a contrast enhanced CT or MRI scan is advised to locate the lesions.

**Future perspectives**

Because of the lack of reliable evidence, we started a prospective trial, the DiFA trial, to assess the accuracy of several imaging studies for the differentiation of FNH and HCA. The DiFA trial, which is the acronym for ‘differentiation of focal nodular hyperplasia and hepatocellular adenoma’. The aim of the DiFA trial is to compare the accuracy of a multiphase CT scan, MRI with Gd-EOB-DTPA (Primovist), PET/CT scan with \(^{18}\)F-fluorocholine and contrast-enhanced US for the differentiation of FNH and HCA. The diagnosis based on the different imaging studies is compared with histological outcome (core biopsy and/or resection specimen). The final aim is to develop a diagnostic algorithm for patients with suspicion of either FNH or HCA in order to obtain a correct diagnosis and provide proper treatment. A French research group has discovered a variant of HCA (\(\beta\)-catenin positive with histopathological staining) which carries a high risk of transforming into a hepatocellular carcinoma. It would be interesting to be able to select those lesions with a high risk of malignant transformation with imaging studies. Further research on this subject is needed.