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Selective internal radiation therapy for cholangiocarcinoma

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1. Epidemiology and risk factors

Cholangiocarcinoma is a relatively rare primary malignant neoplasia of the gallbladder (intra- and extrahepatic bile ducts) with an incidence of 2–6 cases per 100,000 in western countries. Over the last 20 years, an increase in the incidence of intrahepatic and a decline in the incidence of extrahepatic bile duct cancers has been observed. Roughly, 10% of bile duct cancers are located intrahepatically, 60% perihilar and 30% distal extrahepatically. The main risk factors for bile duct cancers include: primary sclerosing cholangitis, fibropolycystic liver disease, cholelithiasis and, in some areas of the world, parasitic infections.

2. Therapeutic options

Surgical resection is the only option for curative therapy. However, the majority of patients present with advanced disease at time of diagnosis. Other established therapeutic options include: photodynamic endoscopic therapy for extrahepatic bile duct cancer, external beam radiation therapy for selected cases, and systemic chemotherapy. Combination chemotherapy with gemcitabine and cisplatin has recently been compared to gemcitabine alone in locally advanced and metastatic cholangiocarcinoma in a large phase III clinical trial.[1] Overall survival was 11.7 months in the combination therapy arm compared to 8.1 months with monotherapy.[1] Local transarterial therapies including selective internal radiation therapy (SIRT) and transarterial chemoembolisation (TACE) have so far only been evaluated in small studies.

3. Evidence for SIRT

The evidence for SIRT in cholangiocarcinoma is based on retrospective studies. Ibrahim *et al.* (2008)[2] treated 24 cholangiocarcinoma patients with yttrium-90 glass microspheres; 29% of patients had previously received chemotherapy, 80% had bilobar disease and 92% were ECOG '0' or '1'. Median survival was 9.3 months. Saxena *et al.* (2010)[3] included 25 patients with cholangiocarcinoma in a retrospective study with yttrium-90 resin microspheres; 72% of patients had previously received chemotherapy, 67% had bilobar disease, and 88% were

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ECOG '0' or '1'. Median survival was 14.9 months. Hoffmann *et al.* (2012) [4] have recently published the largest series of SIRT, so far, in patients with cholangiocarcinoma. Thirty-three patients were treated with yttrium-90 resin microspheres and included in this analysis: 79% with previous chemotherapy, 64% with bilobar disease, and 83% ECOG '0' or '1'. Overall, 36.4% of patients had partial remission, 51.5% had stable disease as best response, resulting in a disease control rate of 85%. Time to progression was 9.8 months, and median overall survival was 22 months. Subgroup analysis revealed that overall survival was best in patients with ECOG '0' (29.4 months; 95% CI 17.7–44), those without previous chemotherapy (22.7 months; 95% CI 5.1–22.7), those with prior surgery for cholangiocarcinoma (26.7 months; 95% CI 5–44), and patients with a tumour burden $\leqslant$25% of the total liver volume (26.7 months; 95% CI 17.7–35.3). Finally, Haug *et al.* (2011) [5] analysed the role of positron emission tomography (PET) as an indicator for response in a subgroup of patients from the Hoffmann study. The analysis found that 18F-FDG PET independently predicted survival in patients with cholangiocarcinoma treated with SIRT.

4. Conclusions

Current evidence supports surgery, systemic chemotherapy, and photodynamic therapy as treatment options for patients with cholangiocarcinoma. SIRT has so far only been studied retrospectively. Especially patients in a very good general condition, those with limited disease, failure of prior surgery, and patients without prior chemotherapy appear to benefit best from SIRT. Prospective clinical trials are needed to determine the place of SIRT in the treatment algorithm for patients with cholangiocarcinoma, either as a first-line or as a salvage therapy.

Conflict of interest statement

The author has received honoraria for scientific presentations from Sirtex Medical. The author has served as a member of advisory boards for Bayer.

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