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Orthotopic liver transplantation after extended bile duct resection as treatment of hilar cholangiocarcinoma

First long-terms results

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Abstract Although the surgical treatment of hilar cholangiocarcinoma represents the only potentially curative option, survival figures remain low over the long term. After hilar and partial hepatic resections for hilar cholangiocarcinoma, locoregional tumor recurrence appears as the primary site of failure. From April 1992 to April 1996, 14 patients underwent extended bile duct resections. Extended bile duct resections combine total hepatectomy, partial pancreatoduodenectomy, and liver transplantation in an attempt to eradicate the entire biliary tract without dissecting the hepatoduodenal ligament. The postoperative 60-day mortality rate was 14% ($n = 2$).The rate of curative resections was 93% (13 of 14 extended bile duct resections). One- and 4-year survival rates after curative resections were 56% and 30%, respectively. The rate of curative resections increased by combining total hepatectomy, partial pancreatoduodenectomy, and liver transplantation, i.e., extended bile duct resection. However, survival figures have not improved accordingly. Therefore, this extended surgical procedure has to be implemented with caution and possibly not without modifications (e.g., multimodal treatment).

Key words Hilar cholangiocarcinoma · Extended bile duct resection · Liver transplantation

Introduction

Surgical resection as well as total hepatectomy and liver transplantation have failed to produce favorable results in the treatment of hilar cholangiocarcinoma over the long term. Even after formally curative resections, locoregional tumor recurrences developed in a high percentage within the resection line and in regional lymph nodes [6]. In contrast, distant metastases have been described in most patients who exhibit a locoregional recurrence, but were the site of first failure in only 24%. Total hepatectomy and liver transplantation did not substantially improve survival figures, partly due to a considerable rate of recurrence at the pancreatic head [1–3, 8, 12]. In 1992, we proposed the 'extended bile duct resection', a procedure combining total hepatectomy, partial pancreatoduodenectomy, and liver transplantation in an attempt to eradicate the entire biliary tract without dissecting the hepatoduodenal ligament [7]. The rationale of this surgical approach was to comply with principles of surgical oncology which prove to be worthwhile in the resective treatment of other solid organ tumors, wide resection margins, no dissection within tumorous tissue, and a selection of less advanced tumor stages.

Patients and methods

From April 1992 to April 1996, extended bile duct resections were performed in 14 patients, while a total of 80 patients underwent various resective procedures of hilar cholangiocarcinomas from 1989 to 1996. The mean age of patients undergoing extended bile duct resections was 50.4 ± 9.3 years; 9 patients were male, and 5 patients female. The preoperative evaluation comprised tumor

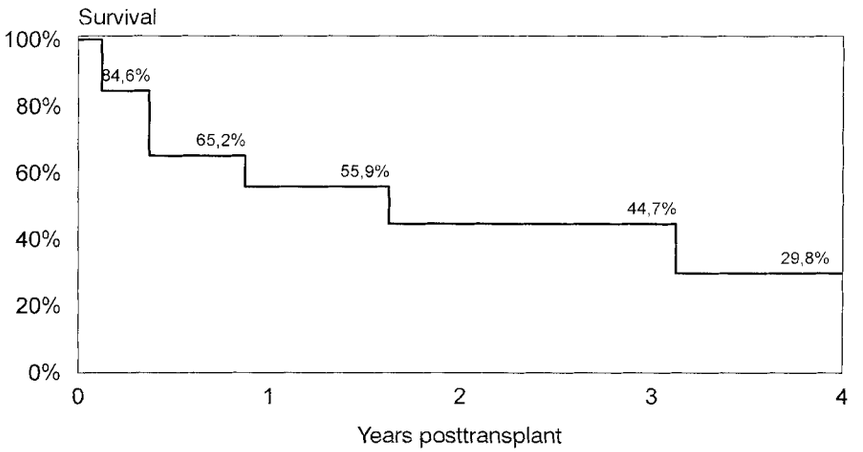

Fig. 1 Actuarial patient survival after formally curative extended bile duct resections of hilar cholangiocarcinomas ($n = 13$)

markers, ultrasound, ERC and brush cytology, angiography, CT (later also MRT), and laparoscopy.

The resection line of extended bile duct resections included liver, hepatoduodenal ligament, pancreatic head, distal stomach, duodenum, vena cava, and all lymph nodes at the lesser curvature and at the right side of the aorta down to the renal vessels. The retroperitoneal layer was incised from Gerota's fascia of the right kidney to the abdominal wall and the entire connective tissue including lymphatics, perirenal fat, and suprarenal vena cava inferior was dissected en bloc together with the organ cluster, thereby leaving the biliary system and hilar cholangiocarcinoma completely untouched. In addition, the right upper quadrant was deperitonealized. Liver transplantation was performed using a venovenous bypass. The pancreatic tail and bile duct were anastomosed in an end-to-side technique to a single Roux-en-Y jejunal loop.

Immunosuppression followed a standard quadruple induction protocol with CsA, steroids, azathioprine, and ATG; the concomitant treatment has been described previously [4]. The patients did not undergo a pre- or postoperative multimodal therapy.

Results

Most hilar cholangiocarcinomas ($n = 9$) were node positive and locally advanced UICC IVa lesions (UICC I/II: $n = 4$). In 1 patient, a distant intrapelvic metastasis had not been detected until the operation was too advanced and this had also to be resected. The histopathological differentiation of the tumors was classified as moderate ($n = 9$) or poor ($n = 5$). Formally curative resections were achieved in 13 of the 14 patients (93%) undergoing extended bile duct resections. The postoperative 60-day mortality rate after extended bile duct resection was 14% ($n = 2$); 1 patient each from multiorgan failure and bleeding from a late erosion of the hepatic artery. An uncomplicated course was observed in only 1 patient. The main complications arose from the pancreatic remnant, pancreatitis ($n = 6$; resulting in total pancreatectomy in 4 patients) and pancreatic fistula ($n = 6$). Others were bleeding ($n = 3$), cholangitis ($n = 3$), wound infection ($n = 2$), CMV infection ($n = 1$), and cellular rejection ($n = 3$). All cellular rejections could be associated with low levels of CsA and were successfully treated by conversion to oral tacrolimus. The 1- and 4-year survival figures after formally curative extended bile duct resections were 56% and 30%, respectively (Fig. 1). A tumor recurrence was detected in 8 of the 14 patients after extended bile duct resections as peritoneal carcinomatosis ($n = 4$), as implantation metastases after percutaneous draining ($n = 2$), and after seeding at the terminal ileum ($n = 1$) and the Roux-en-Y jejunojejunostomy ($n = 1$).

Discussion

An attempted selection of earlier tumor stages for extended bile duct resections could not be achieved, which points to the fact that the current state of diagnostic imaging fails as yet not only to discriminate reliably between benign and malignant lesions of the hepatic confluence but also with respect to preoperative staging [10, 11]. However, the rate of curative resections increased by combining total hepatectomy, partial pancreatoduodenectomy, and liver transplantation. In our experience, the rates of formally curative resections after hilar or partial hepatic resections approximate 30% and 70%, respectively [5].

A comparably favorable effect with respect to survival figures was not evident. Survival was mainly impaired by tumor recurrences which also included implantation metastases. At least one metastasis could be attributed to a preoperative percutaneous biliary drainage and corroborates previous reports of this implantation pathway in cholangiocarcinoma [9]. A promoting impact of immunosuppressive therapy on tumor cell kinetics and recurrence rates has been reported after resection of hepatocellular carcinoma and may represent

a specific problem after extended bile duct resections for cholangiocarcinoma as well [13]. Though the true potential of this procedure remains to be established, extended bile duct resections have to be implented only with caution and possibly not without modifications, such as a multimodal therapeutic concept.

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