Surgical strategies in the management of hilar cholangiocarcinoma
Gerhards, M.F.

Citation for published version (APA):

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.
Prevention of implantation metastases after resection of proximal bile duct tumors with preoperative low dose radiation therapy

M.F. Gerhards, M.D., D. Gonzalez Gonzalez, M.D., H. ten Hoopen-Neumann, M.D., T.M. van Gulik, M.D., L.Th. de Wit, M.D., D.J. Gouma, M.D.

Departments of Surgery and Radiation Oncology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands.

European Journal of Surgical Oncology; Accepted for Publication
Abstract

**Background:** Preoperative ERCP with biliary drainage is associated with a greater risk of implantation metastases after resection of proximal bile duct tumors. In a previous study among patients who had undergone biliary drainage before resection, 8 patients (20%) developed implantation metastases, within one year after resection. The aim of this analysis was to evaluate the results of preoperative irradiation with regard to a possible reduction of implantation metastases.

**Methods:** Twenty-one patients with a proximal bile duct tumor who had undergone resection following preoperative irradiation were retrospectively analyzed. Preoperative radiation therapy consisted of three fractions of 3.5 Gy external beam irradiation of the hilar area.

**Results:** Preoperative biliary drainage was performed in 19 patients (90%). All patients received preoperative radiotherapy. No complications were noted during preoperative radiotherapy. None of the patients developed implantation metastases within a follow-up time of 2 to 79 months.

**Conclusion:** The results of this study suggest that preoperative radiotherapy in patients with a resectable proximal bile duct tumor who have undergone preoperative drainage, decreases the risk of implantation metastases. To be certain about the role of preoperative radiotherapy, a randomized study is required. Until then, we advocate standard low dose radiotherapy preceding resection, in all patients with lesions suspicious of a proximal bile duct tumor who have undergone biliary drainage.
Introduction

Bile duct carcinoma is an uncommon malignancy associated with a poor prognosis. Most series report an overall 5-year survival after resection between 5 and 30%. Of all extrahepatic bile duct carcinomas 28% occur at the hepatic duct confluence.

There are surgical limitations in performing a radical resection because of the location of the tumor, which is usually in strong relation with the portal vein and the hepatic artery. Also the proximal extension of the tumor with possible bilateral invasion of the secondary branches of the hepatic ducts and liver parenchyma, makes curative surgery only possible in 15 to 55% of all these tumors. Therefore assessment of the tumor and its extension into the intra- and extrahepatic bile ducts is crucial in forming a treatment strategy in particular for patients who are candidates for resection.

More than 90% of the patients with hilar bile duct carcinoma will present with obstructive jaundice due to the tumor. Endoscopic retrograde cholangiopancreatography (ERCP) is the most common diagnostic procedure for these patients. To relief the obstruction, the biliary tract can be drained by passing one or more stents across the obstruction, during this procedure.

However, stent placement has several disadvantages. During placement of an endoprosthesis, microorganisms are introduced into the bile ducts frequently leading to cholangitis when the biliary system is not completely drained. Furthermore, in case of cholangiocarcinoma, the bile potentially contains tumor cells exfoliated from the primary tumor. Endoscopic drainage may increase the risk of contaminating the bile with tumor cells by detaching more cells when the stent is forced through the obstruction. Spill of contaminated bile into the abdominal cavity will occur during resection of the tumor and in particular during the construction of the hepato-jejunostomies. In a previous study from our department, implantation metastases were found in 8 out of 41 patients (20%) who had undergone resection for a proximal bile duct tumor after endoscopic biliary drainage. These implantation metastases were apparent in drain tract scar or laparotomy scar.
Buskirk et al. suggested low-dose preoperative irradiation before surgery of extra hepatic bile duct carcinoma, to diminish the implant ability of spilled tumor cells during the operative procedure. No other reports about the use of preoperative radiotherapy for bile duct tumors have been published. Starting in 1990, preoperative radiotherapy was introduced in our institution in patients with resectable hilar bile duct carcinoma who had undergone preoperative stent placement during ERCP, in an attempt to prevent the occurrence of implantation metastases. The aim of this study was to evaluate the results of preoperative irradiation with respect to reduction of implantation metastases after resection of hilar bile duct carcinoma.
Material and methods

Patients
Twenty-three patients with proximal bile duct carcinoma who had undergone resection following preoperative irradiation between 1990 and 1996, were retrospectively analyzed. Because in a previous study, all implantation metastasis were found to occur within one year after surgery, only patients operated before 1997 were included. Two patients died early in the postoperative period due to either massive gastro-intestinal bleeding or persistent liver failure with cholestasis (hospital mortality: 9%). They were excluded from this analysis. The remaining group of patients consisted of 12 men and 9 women with a mean age of 59 years (median age: 60 years, range 37-73 years).

Pre-operative work-up
In all patients, preoperative imaging consisted of ultrasonography combined with Doppler and ERCP. Since January 1993 diagnostic laparoscopy with laparoscopic ultrasonography is performed, to more accurately determine resectability of the tumor and to differentiate a hilar bile duct tumor from an infiltrating gallbladder carcinoma. Bile duct tumors were classified according to the modified Bismuth-Corlette classification.

Although all patients underwent ERCP, preoperative stent placement in one or two bile ducts was achieved in only 18 patients (86%). In one patient the bile duct was drained by PTC (percutaneous transhepatic cholangiography) because it was not possible to pass the stricture at ERCP. In the remaining two patients, biliary drainage failed during ERCP for reasons that could not be retrieved.

Preoperative radiation therapy
Preoperative radiation therapy consisted of external beam irradiation of the hilar area, which was identified using the ERCP images and the radiographic position of the stent(s). Irradiation fields were generally 10 x 10 cm. and two opposite fields (anterior-posterior and posterior-anterior) were used. Irradiation was given with megavoltage energy. Three
fractions of 3.5 Gy in three consecutive days were given (total dose: 10.5 Gy). The radiation dose was specified at midplane. In all patients surgery took place within one week after the last fraction.

**Surgical procedures**

Surgical procedures consisted of local resection of the hilar region, including part of segment IV and/or the caudate lobe for Bismuth type I and type II tumors, and in some type III tumors if a macroscopically non-radical resection was carried out as a palliative, biliary drainage procedure. For the remaining type III tumors a local resection was combined with hemi-hepatectomy. All right sided hemi-hepatectomies were extended including resection of segment IV, and in most cases, also with resection of the caudate lobe.

**Pathology**

The diagnosis of cholangiocarcinoma was confirmed histologically in all resected specimens. The resection margins are defined as the surgical resection planes of the distal and proximal bile ducts or the liver. The dissection margins constitute the surgical cleavage planes with adjacent hilar structures, such as the portal vein. In 6 patients (29%), a bile sample was taken during the operation for assessment of tumor cells.

**Postoperative radiotherapy**

Standard postoperative radiotherapy was given in addition to preoperative irradiation. Postoperative radiotherapy consisted of a basis dose of 35 Gy directed to an area encompassing the liver hilus and the site of the hepatico-jejunostomies. The target area was defined by referring to the report of the operative procedure, the postoperative computed tomography (CT) scan in treatment position and the original ERCP. We did not aim to include all the lymphatic nodes in the vicinity of the hepatic hilus within the radiation fields. Initial field sizes were not larger than 8 x 8 cm. A more-field technique was used to avoid excessive radiation doses to the liver, kidneys and stomach. A boost of 10 Gy was given to a small area around the anastomosis either by using brachytherapy or
external beam irradiation. For brachytherapy endoscopical access to the biliary anastomoses was obtained via the end of the Roux-Y loop, brought out for this purpose as terminal jejunostomy during the resection.\textsuperscript{23} Mean total dose to the hilum in all patients was 45 Gy, excluding the 10.5 Gy already administered preoperatively. None of the patients were treated with adjuvant chemotherapy.

**Follow-up**

During the first postoperative year, all patients were checked once every 3 months. After one year this frequency was reduced to twice a year. At the end of this study six patients (29\%) were still alive and had visited the outpatient clinic between October and December 1997.
Results

In 8 patients (38%), preoperative radiotherapy was given on an out-patient basis. In all other patients, the complete preoperative irradiation schedule was given after admission. The longest time interval between the last radiation fraction and the surgical procedure was 7 days. One patient had the last irradiation at the day of operation. The mean duration between the last fraction and the operation was 2.9 (±2.0) days. No complications were noted during preoperative radiotherapy and the days preceding surgery. The mean time interval from admission to surgery was 7.9 (±1.7) days, which was 1.2 days longer than the mean interval in the period before preoperative irradiation was instituted.

Local resections were carried out in 16 patients (76%). Three patients (14%) underwent local resection combined with a left hemi-hepatectomy and two patients (10%), combined with an extended right hemi-hepatectomy (table 1). In all patients one or more cholangio-jejunostomies were constructed to restore biliary continuity. In no patients adverse effects of preoperative irradiation were experienced during surgery.

In 2 of 6 patients (33%), bile samples obtained during the operation revealed tumor cells. One sample showed atypical cells and in the remaining 3 samples (50%), no viable tumor cells were found.

Resection and dissection margins were microscopically tumor free in 5 patients (24%), (R0 resections). Two patients had a type IIIa tumor, one of them underwent a local resection including a central part of the liver parenchyma, and the other a local resection in combination with an extended right hemi-hepatectomy. The other three patients had undergone a local resection for type I or II tumors. In all remaining patients, the surgical margins showed residual tumor on microscopical examination (table 1).

As mentioned above, all patients were treated with preoperative radiotherapy. Two patients died within 2 months after discharge from the hospital and did not receive postoperative radiotherapy. In the remaining 19 patients (90%) postoperative external irradiation was given. An extra boost by using brachytherapy was given in 14 patients, and in 5 patients the complete dose was given by external beam irradiation alone.
<table>
<thead>
<tr>
<th>Gender</th>
<th>Age (Years)</th>
<th>Type</th>
<th>Preoper. Drainage</th>
<th>Resection</th>
<th>Curative</th>
<th>Postoper. Irradiat.</th>
<th>Local Recurr.</th>
<th>Distant Metastas</th>
<th>Alive(^1)</th>
<th>Survival Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>69</td>
<td>II</td>
<td>Yes</td>
<td>HR</td>
<td>No</td>
<td>Brach/Ext</td>
<td>No</td>
<td>Liver</td>
<td>No</td>
<td>13</td>
</tr>
<tr>
<td>Male</td>
<td>45</td>
<td>I</td>
<td>Yes</td>
<td>HR</td>
<td>No</td>
<td>Brach/Ext</td>
<td>No</td>
<td>Lymphnode</td>
<td>No</td>
<td>39</td>
</tr>
<tr>
<td>Male</td>
<td>69</td>
<td>I</td>
<td>Yes</td>
<td>HR</td>
<td>Yes</td>
<td>Brach/Ext</td>
<td>No</td>
<td>No</td>
<td>No(^*)</td>
<td>18</td>
</tr>
<tr>
<td>Female</td>
<td>70</td>
<td>II</td>
<td>Yes</td>
<td>HR</td>
<td>No</td>
<td>Brach/Ext</td>
<td>No</td>
<td>Pleural</td>
<td>No</td>
<td>19</td>
</tr>
<tr>
<td>Male</td>
<td>48</td>
<td>IIIa</td>
<td>Yes</td>
<td>HR</td>
<td>No</td>
<td>External</td>
<td>Yes</td>
<td>Skeletal</td>
<td>No</td>
<td>19</td>
</tr>
<tr>
<td>Male</td>
<td>60</td>
<td>IIIa</td>
<td>Yes</td>
<td>HR</td>
<td>Yes</td>
<td>Brach/Ext</td>
<td>No</td>
<td>No</td>
<td>No(^**)</td>
<td>8</td>
</tr>
<tr>
<td>Female</td>
<td>65</td>
<td>II</td>
<td>Yes</td>
<td>HR</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Mesenteric</td>
<td>No</td>
<td>2</td>
</tr>
<tr>
<td>Female</td>
<td>68</td>
<td>II</td>
<td>Yes</td>
<td>HR</td>
<td>Yes</td>
<td>External</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>79</td>
</tr>
<tr>
<td>Female</td>
<td>59</td>
<td>II</td>
<td>Yes</td>
<td>HR/HHL</td>
<td>No</td>
<td>External</td>
<td>No</td>
<td>No</td>
<td>No(^**)</td>
<td>15</td>
</tr>
<tr>
<td>Male</td>
<td>43</td>
<td>IIIb</td>
<td>Yes</td>
<td>HR/HHL</td>
<td>No</td>
<td>External</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>27</td>
</tr>
<tr>
<td>Female</td>
<td>61</td>
<td>IIIa</td>
<td>Yes</td>
<td>HR</td>
<td>No</td>
<td>Brach/Ext</td>
<td>Yes</td>
<td>Liver</td>
<td>No</td>
<td>15</td>
</tr>
<tr>
<td>Male</td>
<td>71</td>
<td>II</td>
<td>Yes</td>
<td>HR</td>
<td>No</td>
<td>Brach/Ext</td>
<td>No</td>
<td>No</td>
<td>No(^**)</td>
<td>40</td>
</tr>
<tr>
<td>Male</td>
<td>46</td>
<td>II</td>
<td>Yes</td>
<td>HR</td>
<td>No</td>
<td>Brach/Ext</td>
<td>No</td>
<td>Liver</td>
<td>No</td>
<td>18</td>
</tr>
<tr>
<td>Female</td>
<td>63</td>
<td>IIIa</td>
<td>Yes</td>
<td>HR</td>
<td>No</td>
<td>Brach/Ext</td>
<td>No</td>
<td>No</td>
<td>No(^**)</td>
<td>19</td>
</tr>
<tr>
<td>Male</td>
<td>48</td>
<td>IIIa</td>
<td>No</td>
<td>HR</td>
<td>No</td>
<td>Brach/Ext</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>51</td>
</tr>
<tr>
<td>Male</td>
<td>71</td>
<td>II</td>
<td>Yes</td>
<td>HR</td>
<td>Yes</td>
<td>Brach/Ext</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>41</td>
</tr>
<tr>
<td>Female</td>
<td>73</td>
<td>IIIa</td>
<td>Yes</td>
<td>HR/HHRe</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No(^**)</td>
<td>3</td>
</tr>
<tr>
<td>Male</td>
<td>59</td>
<td>IIIb</td>
<td>Yes</td>
<td>HR/HHL</td>
<td>No</td>
<td>External</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>30</td>
</tr>
<tr>
<td>Female</td>
<td>55</td>
<td>IIIb</td>
<td>Yes</td>
<td>HR/HHL</td>
<td>No</td>
<td>Brach/Ext</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>26</td>
</tr>
<tr>
<td>Female</td>
<td>37</td>
<td>IIIa</td>
<td>Yes</td>
<td>HR/HHRe</td>
<td>No</td>
<td>External</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>18</td>
</tr>
</tbody>
</table>

\(^1\) Resection: HR=Hilus (Local) resection; HHRe=Extended Right Hemi-hepatectomy; HHL=Left Hemi-hepatectomy

\(^2\) Postoperative irradiation: Brach.=Brachytherapy; Ext.=External irradiation

\(^3\) Alive at the end date of this analysis:

\(^*\): Died due to irresectable esophagus carcinoma

\(^**\): Died without proven local recurrences or metastases (US and/or CT was done at least twice a year)
Morbidity and mortality

Hospital morbidity in this series of patients was 57% (n=12). The most frequently recorded late complications (after discharge from the hospital) were cholangitis (n=10, 48%), jaundice (n=7, 33%), abdominal pain (n=6, 29%), ileus (n=4, 19%), ascites (n=4, 19%) and upper gastrointestinal ulcers and/or bleeding (n=4, 19%). Only 3 patients (14%) did not have any late complications.

Two patients died within 3 months after discharge from the hospital. One patient with histologically proven mesenteric metastases, who had undergone local resection and had no postoperative complications, died within 2 months at home of recurrent disease. The other patient died 3 months after the resection in another hospital. She had undergone a radical, extended hemi-hepatectomy with as late complications, liver abscesses and gastro-intestinal bleeding.

Follow-up, local recurrence and/or metastases

In contrast to the previous period in which preoperative radiotherapy was not given, implantation metastases were now not seen in one patient (table 2). In 9 patients (43%), distant metastases and local recurrences were recorded during follow-up (table 2). All metastases and local recurrences were confirmed by US and/or CT. In the 2 patients with pleural metastases or supraclavicular lymphnode metastases, malignancy was proven by biopsy and histological examination. One of the patients with liver metastases was also treated for a prostate carcinoma in the past. Because no liver biopsies were taken, the primary tumor causing these metastases was not identified. None of the radically resected patients developed distant metastases or a local recurrence during follow-up.

Six patients died without evidence of a local recurrence or distant metastases on US and/or CT. As mentioned above, one of them died within 3 months after discharge from the hospital due to late postoperative complications. Another patient died due to an irresectable esophagus carcinoma, diagnosed one year after the local bile duct resection. The remaining 4 patients were conservatively treated for recurrent episodes of cholangitis.
or other late complications and eventually died at home. At the end of 1997, 6 patients (29%) were alive. None had evidence of local recurrence or distant metastases.

Median survival of all patients with a resected proximal bile duct tumor and pre- and postoperative radiotherapy was 19 months (range: 2-79 months). The actuarial survival rate was calculated for all patients (fig. 1, Kaplan-Meier curve). A second, disease specific actuarial survival rate was calculated for patients with proven local recurrences or distant metastases (n=9, all dead, median survival: 19 months) and for the remaining group (n=12, 6 alive, median survival: 40 months) (fig. 2, Kaplan-Meier curve).

### TABLE 2. INCIDENCE OF IMPLANTATION METASTASES, IN PATIENTS WHO HAVE UNDERGONE A RESECTION OF A PROXIMAL BILE DUCT TUMOR

<table>
<thead>
<tr>
<th></th>
<th>Group I (n=41)</th>
<th>Group II (n=11)</th>
<th>Group III (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>27m/14f</td>
<td>5m/ 6f</td>
<td>12m/ 9f</td>
</tr>
<tr>
<td>Age (median)</td>
<td>58 (21-74)</td>
<td>52 (18-70)</td>
<td>60 (37-73)</td>
</tr>
<tr>
<td>Preoperative drainage</td>
<td>100% (n=41)</td>
<td>None</td>
<td>90% (n=19)</td>
</tr>
<tr>
<td>Local resection</td>
<td>78% (n=32)</td>
<td>73% (n=8)</td>
<td>76% (n=16)</td>
</tr>
<tr>
<td>-with hemihepatectomy</td>
<td>22% (n=9)</td>
<td>27% (n=3)</td>
<td>24% (n=5)</td>
</tr>
<tr>
<td>Radical resections</td>
<td>2% (n=1)</td>
<td>18% (n=2)</td>
<td>24% (n=5)</td>
</tr>
<tr>
<td>Preoperative Rth.</td>
<td>None</td>
<td>None</td>
<td>100% (n=21)</td>
</tr>
<tr>
<td>Postoperative Rth.</td>
<td>63% (n=26)</td>
<td>73% (n=8)</td>
<td>90% (n=19)</td>
</tr>
<tr>
<td>Implantation metastases</td>
<td>20% (n=8)</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

Group I: patients after biliary drainage, without preoperative radiotherapy

Group II: patients without preoperative drainage and without preoperative radiotherapy

(Group I and II are analyzed in an earlier study)

Group III: patients after both preoperative biliary drainage and preoperative radiation therapy

(Group III is analyzed in this study)
FIGURE 1. (KAPLAN MEIER CURVE) ACTUARIAL SURVIVAL RATE OF ALL 21 PATIENTS WHO UNDERWENT RESECTION FOR A PROXIMAL BILE DUCT TUMOR AFTER PREOPERATIVE RADIOTHERAPY

Survival, months

Survival rate %

FIGURE 2. (KAPLAN MEIER CURVE) DISEASE SPECIFIC ACTUARIAL SURVIVAL RATE OF 9 PATIENTS WHO DIED OF RADIOLOGICALLY AND/OR PATHOLOGICALLY PROVEN LOCAL RECURRENCES AND/OR DISTANT METASTASES (----------), AND THE REMAINING 12 PATIENTS WITHOUT RECURRENT DISEASE OR METASTASES (--------)

Survival, months

Survival rate %
Tumor cells from bile duct tumors can exfoliate and contaminate the bile, as has been shown previously in bile samples taken during surgery. During resection of bile duct tumors, these malignant cells spill with the bile into the operative field at the time of transection and construction of the biliary-digestive anastomoses. Also some bile leakage from the anastomoses may occur postoperatively. Both events can lead to contamination of the peritoneal cavity, the operative wound and even drain tracts with tumor cells.

Some studies in the literature have shown that bile contaminated with tumor cells can cause drain tract metastases after PTC with biliary drainage (PTBD). We previously reported in patients with proximal bile duct tumors, who were drained preoperatively by ERCP or PTC, 8 patients (20%) who developed implantation metastases in the drain tract scar or laparotomy scar, within one year after resection (table 2). Patients without preoperative drainage did not show any implantation metastases. In bile samples of both groups, malignant or atypical cells were demonstrated in similar percentages. This previous study strongly suggested a correlation between an ERCP procedure with biliary drainage preoperatively and the development of implantation metastases postoperatively.

The concept of preoperative radiotherapy was devised to alter the implant ability of free-floating malignant cells in the bile. In the present study no implantation metastases were found after preoperative irradiation therapy and resection of hilar bile duct tumors. Although patient characteristics in this series and in the above-mentioned study without preoperative radiotherapy are not completely comparable in terms of tumor classification, radical resection and postoperative radiotherapy, the outcome seems to be in favor of preoperative radiotherapy. Preoperative radiotherapy already proved to be effective in preventing scar implants after surgical treatment of bladder cancer by decreasing viability of cells shedded by the tumor.

In a recently published analysis from our institution, regarding usefulness of cytology of peritoneal lavage performed during staging laparoscopy for gastrointestinal malignancies, 11/72 (15%) patients with a hilar cholangiocarcinoma had tumor cells in
Based on their lavage fluid, metastases were also found during laparoscopy in almost all cases, eventually none of these patients were included in the current analysis. This is an important fact, because when malignant cells had been present in the peritoneum, local radiation should have had no effect on the frequency of implantation metastases.

Some authors have claimed that preoperative drainage is effective in preventing postoperative complications after major resections for proximal bile duct tumors and provided a better outcome, especially in jaundiced patients. In our previous study, we concluded that the advantage of biliary drainage has to be weighed against the greater risk of implantation metastases. Because preoperative radiotherapy now has proven to be effective in prevention of implantation metastases, ERCP with biliary drainage should not necessarily be avoided in patients with a proximal bile duct tumor. Because the majority of patients with an obstruction at the proximal bile duct are treated with an endoprosthesis during ERCP, preoperative radiotherapy is now adapted as standard therapy in our department in every patient with a resectable proximal cholangiocarcinoma. However, because the definitive histological diagnosis is established only after resection, we cannot prevent that also patients with benign strictures, resected for presumed hilar bile duct carcinoma, are irradiated before resection.

In this analysis, preoperative radiotherapy did not seem to improve survival time. When we compare the survival time in patients analyzed in this series with results of other studies, it also ranged between 19 and 25 months.

Adverse effects of preoperative radiotherapy were not seen both during operation and in the postoperative period. We recently assessed hospital morbidity and mortality among 112 patients with a hilar cholangiocarcinoma after resection. There was no significant difference in hospital morbidity or mortality between the groups with preoperative radiotherapy (n=33, morbidity: 66% and mortality: 12%), or without preoperative radiotherapy (n=79, morbidity: 65% and mortality: 20%).

Although in our previous study, postoperative radiation therapy was administered in nearly all cases, still 8 of 41 patients developed an implantation metastasis. Thus, postoperative irradiation does not seem to have any influence on the development of
implantation metastases. We have to consider in this respect, that a healing wound is a favorable environment for malignant cells particularly during the first few days.\textsuperscript{32,33}

Patients in our protocol usually undergo postoperative radiotherapy several weeks after surgery. It is therefore unlikely that postoperative radiotherapy has any impact on the viability of peri-operatively spilled tumor cells.

In conclusion, the results of this study suggest that preoperative radiotherapy in patients with a resectable proximal bile duct carcinoma decreases the risk of implantation metastases. Adverse effects of this treatment modality were not encountered. To be certain about the role of preoperative radiotherapy however, a randomized study is needed. Until then, in our institution, all patients with lesions suspicious of a proximal bile duct tumor, who have undergone biliary drainage, are treated with radiotherapy before resection.
Reference List


