Local resection of biliopancreatic cancer

T.M. van Gulik, M. Gerhards, J. de Vries, R. van Geenen, L.T. de Wit, H. Obertop & D.J. Gouma
Dept. of Surgery, Academic Medical Center, Amsterdam, The Netherlands

Summary

Biliopancreatic tumors that are potentially amenable to local resection include proximal bile duct tumors (Klatskin tumors), mid-choledochal duct tumors and tumors arising from the papilla of Vater. This paper reviews our experience in the AMC, with local resection of these conditions. From 1983-1997, 112 patients underwent surgical resection of a carcinoma of the hepatic duct confluence (Klatskin tumor). Local resection was undertaken in 80 patients (52 patients with type I and II tumors, and 28 patients with type III tumors) whereas in 32 patients with type III tumors, hilar resection was performed with liver resection. Negative surgical margins were achieved in 10 patients after local resection of type I and II tumors (19.2%), in 1 patient after local resection of a type III tumor (3.6%), and in 5 patients after hilar resection and liver resection (15.6%). Middle-third carcinomas of the extra-hepatic biliary tract are less common than proximal or distal bile duct tumors. From 1993-1998, 12 patients underwent resection of a mid-choledochal duct carcinoma. In 8 patients, local resection was performed and in 4 patients, subtotal pancreaticoduodenectomy (PPPD) because of the close relationship of the tumor and the pancreas. Four patients had negative surgical margins, 2 after local resection (25%) and 2 after PPPD (50%). Although accepted for villous adenomas located in the ampulla, local resection for ampullary carcinoma is controversial. Nine patients underwent local resection of a presumed adenoma that proved to be an ampullary carcinoma. In 4 patients with T1 tumors, resection of the carcinoma was locally complete (44%). Additional PPPD was performed in 6 patients, including the 4 patients with complete local resections, showing no residual tumor at the previous site of excision, but lymphnode metastases in two resection specimens (both of patients with presumed T1 tumors). Hence, local resection of a T1 ampullary carcinoma might result in tumor free margins, but does not deal with (usually retropancreatic) lymphnode metastases. In conclusion, local resection is applicable to Klatskin type I and II tumors. Local resection may be considered in the proximally located, mid-choledochal duct carcinomas but, when located closer to the pancreas, PPPD is the preferred treatment. For ampullary adenomas, local resection is feasible unless frozen section examination raises suspicion on a malignancy. Local resection of even limited ampullary carcinomas is not advisable because of lymphatic dissemination of the tumor and consequently, inadequate clearance.

Key words: bile duct carcinoma, Klatskin tumor, local resection, papilla of Vater tumor

Introduction

Tumors of the extrahepatic biliary ducts comprise, apart from gall bladder tumors, proximal bile duct tumors located in the liver hilum and distal bile duct tumors arising in the retropancreatic portion of the bile duct. At the far end of the bile duct in the duodenal wall, tumors occurring at the papilla of Vater are termed ampullary tumors. Although less frequent, tumors may also arise intrabetween the proximal and distal bile duct, in the middle-third of the hepato-choledochal duct. All these biliopancreatic tumors have in common that they are closely related to the liver on the one side, and the pancreas on the other side.

Like in any malignancy of the gastrointestinal tract, treatment of biliopancreatic tumors requires local and regional control of the disease and radical, surgical excision of the tumor has classically been the mainstay of therapy. Even extended procedures have been devised to achieve a better loco-regional control, however, if this translates into improved survival needs further assessment. In light of this paradigm, local resection has been exclusively reserved for the more limited tumors, the stage I or T1 tumors. However, because reliable preoperative staging is often difficult in these types of tumors, surgeons tend to prefer wider excisions. There is no doubt that distal bile duct tumors because of their intimate relation with the duodenum and pancreatic head, require subtotal pancreaticoduodenectomy to achieve local and regional control (1). Likewise, proximal bile duct tumors that extend as far as the biliary radicals of the right or left liver lobe, the Klatskin type IIIa/b tumors, are resected in combination with (extended) right or left liver resection. However, bile duct tumors confined to the hepatic duct confluence, typically the type I and type II Klatskin tumors, are amenable to local resection (2). Gall bladder carcinomas limited to the mucosa, are adequately removed by cholecystectomy which can be regarded local therapy. Local resection of mid-choledochal duct tumors and ampullary tumors, however, is controversial. Ampullary adenomas are resected locally, but, the preoperative or intraoperative distinction of an ampullary adenoma or carcinoma is difficult, and even for the limited ampullary carcinomas, the effectiveness of local resection is questionable (3).

The advantage of local excision obviously is the lesser procedure compared to the more complex, radical resections which are associated with higher operative morbidity and mortality rates. Whether the lesser procedure results in complete tumor clearance, on the other hand, is a major concern. In view of the present controversy regarding local resection vs. radical resection, this study was undertaken to assess the effectiveness of local resection in the management of proximal bile duct tumors, mid-choledochal duct tumors.
and ampullary tumors. Although these tumors each have their specific, diagnostic and management problems, experience with local resections has accumulated in our institution and it therefore seemed worth while to evaluate the results of local resection with regard to the whole extrahepatic biliary tract.

Patients and methods

**Proximal bile duct tumors (Klatskin tumors)**

From 1983-1997, 112 patients (69 male; 43 female; age range 18-74 years) underwent surgical resection of a carcinoma of the hepatic duct confluence (Klatskin tumor). Klatskin tumors are classified according to the system devised by Bismuth and Corlette (4), which takes into account the proximal extension of the tumor. Patients with Bismuth type I and II Klatskin tumors undergo local resection. Although in recent years, type IIIa/b tumors are preferably treated with hilar resection in combination with hepatic lobectomy, at one time (1988-1992), a number of type III tumors were treated with local resection only. In case of involvement of the caudate lobe or segment IV, an additional caudate lobe resection or resection of a portion of segment IV was performed. The technique of local resection has been described elsewhere (5) and basically consists of division of the common bile duct at its entry of the pancreas and posterior dissection of the bile duct in cephalad direction up to the hilum. At this point, the dissection is continued intrapancreatically proximal of the confluence and the bile ducts are cut above the tumor. The resection margins are checked for residual tumor by frozen section examinations. For biliary reconstruction, two or more hepaticojejunal anastomoses are created using a Roux-en-Y jejunal limb.

Local resection was undertaken in 80 patients (52 patients with type I and II tumors, and 28 patients with type III tumors) whereas in 32 patients with type III tumors, hilar resection was performed with liver resection. Additional radiotherapy was given in 53/68 (78%) of patients after local resection and in 17/23 (74%) of patients after combined hilar and liver resection.

**Mid-choledochal duct tumors**

From 1993-1998, 13 patients (5 male; 8 female; age range 35-79 years) with mid-choledochal duct tumors were managed surgically. A mid-choledochal duct tumor was defined as a lesion proximal of, or at the level of the cystic duct junction, but, >2cm distal of the confluence of the hepatic ducts. The level of the tumor was assessed by ultrasound investigations and ERCP. During surgical exploration all patients were confirmed to have a mid-choledochal duct tumor. 8/13 patients underwent local resection of the hepatopancreatic duct, with the proximal resection plane at (2 patients) or proximal (5 patients) of the confluence. In 5/13 patients, a PPPD was performed because of the close relation of the tumor to the pancreas. In 4 patients, all in patients undergoing local resection, the right hepatic artery was resected with the specimen. Local resection of the hepatopancreatic duct consisted of dissecting the distal common bile duct for 1 cm into the pancreas, thus dividing the duct in its intrapancreatic portion. After posterior dissection towards the hilum, the confluence and main hepatic ducts were exposed. Frozen section samples of the proximal and distal resection margins were obtained. Bilateral hepaticojejunal anastomoses were constructed using a Roux-en-Y jejunal limb.

**Ampullary tumors**

From 1983-1997, 141 patients underwent resection of an ampullary carcinoma. PPPD was performed in 132 patients and local resection was undertaken as the initial treatment in 9 patients (male 4; female 5; age range 67-76 years). In these 9 patients, the preoperative diagnosis was ampullary adenoma with varying degrees of dysplasia, as based on endoscopic biopsies. Final histopathological examination of the specimen, however, revealed an ampullary carcinoma.

The technique of local resection for ampullary tumors consisted of wide excision of the papilla of Vater including part of the posterior duodenal wall, thus exposing the distal ends of the common bile duct and pancreatic duct. After division, both ducts are reimplanted in the duodenal wall using interrupted sutures (6,7).

**Results**

**Klatskin tumors**

Negative surgical margins were achieved in 10/52 patients after local resection of type I and II tumors (19.2%), in 1/28 patient after local resection of a type III tumor (3.6%), and in 5/32 patients after hilar resection and liver resection for type III tumors (15.6%). Lymph node involvement was found in 26/64 (41%) patients after local resection and in 7/18 (39%) patients after hilar resection and liver resection. Morbidity (overall) and mortality was 66% and 14%, respectively, after local resection, and 65% and 16%, respectively, after hilar resection combined with liver resection. Median survival was 17 months after local resection and 15 months after hilar resection combined with liver resection. These survival results are broken down for each type of Klatskin tumor in table 1.

**Mid-choledochal duct tumors**

Histopathology showed a carcinoma of the bile duct in 13 patients, invading into the pancreas in 2 patients (these patients had undergone a PPPD). Microscopically, only 5 resections were radical (local resection 2/8, PPPD 3/5). The 8 nonradical resections (local resection 6/8, PPPD 2/5) showed residual tumor at the dissection margins and in 3 also in the resection margins (1 only in the proximal resection margin, and 2 in proximal and distal dissection margins, all after local resections). 7/13 (54%) patients had tumor positive lymphnodes in the specimen (local resections 4/8, PPPD 3/5). There was no postoperative mortality and 6 patients had a postoperative complication, managed nonoperatively. Three patients died (all with irradical resections) after 3-13 months (mean: 8 months). Ten patients are still alive after 2-50 months (mean survival: 17 months) of which 2 have developed distant metastases.

**Table 1. Survival (median) after resection of Klatskin tumors, in relation with tumor type (Bismuth classification) and type of resection (local resection or combined hilar resection and liver resection).**

<table>
<thead>
<tr>
<th>Median survival</th>
<th>All types resections combined</th>
<th>Local resection</th>
<th>Hilar resection + liver resection</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMC '83-'97</td>
<td>n=112</td>
<td>n=80</td>
<td>n=32</td>
</tr>
<tr>
<td>Overall</td>
<td>15.5 mths</td>
<td>17 mths</td>
<td>15 mths</td>
</tr>
<tr>
<td>Type I</td>
<td>39 mths</td>
<td>n=14</td>
<td></td>
</tr>
<tr>
<td>Type II</td>
<td>18 mths</td>
<td>n=38</td>
<td></td>
</tr>
<tr>
<td>Type III</td>
<td>15 mths</td>
<td>n=17</td>
<td>5 mths</td>
</tr>
<tr>
<td>Type Iib</td>
<td>17 mths</td>
<td>n=11</td>
<td>28 mths</td>
</tr>
<tr>
<td>Overall mortality (30-days)</td>
<td>14.6%</td>
<td>14%</td>
<td>16%</td>
</tr>
</tbody>
</table>
Ampullary tumors

In 132 patients who had undergone PPPD for an ampullary carcinoma, the radicality rate was 82%. Lymph node involvement was found in 67 (51%) of the resection specimens of these patients. Of 9 patients undergoing local resection, 4 patients with a T1 carcinoma had a locally complete resection (44%). Additional PPPD was performed in 6 patients, including the 4 patients with complete local resections, showing no residual tumor at the previous site of excision, but, lymph node metastases in two resection specimens (both of patients preoperatively staged as T1 tumors). Hence, local resection of a T1 ampullary carcinoma did result in tumor free margins, but failed to deal with (usually retropancreatic) lymph node metastases. Three patients had died at the time of this study. The remaining 6 patients are alive without signs of recurrence.

Discussion

It was already the pathologist Virchow (1820-1902) who described the centrifugal spread of tumors. Surgeons like Halsted and Whipple in pioneering the concept of radical resections (8), took account of this centrifugal spread and devised wide local-regional excisions to achieve tumor control. In contrast, local resections have been reserved for small, localized tumors or for elderly patients not fit to undergo major surgery. Local resections as compared to radical resections are associated with less operative morbidity and mortality.

It may be evident that local resection is not appropriate for tumors manifesting lymphatic invasion. However, the absence of lymphatic involvement is difficult to exclude with conventional imaging techniques or during surgery. The lymphatics of the extrahepatic biliary ducts drain in the lymphatics of the hepatoduodenal ligament and can spread to the retropancreatic lymphatic basin and the celiac trunk (9). In a previous study in 63 patients who had undergone resection of a Klatskin tumor, we found positive lymph nodes in 23 (37%) of the specimens (10). The presence of lymph node metastases, however, did not preclude long term survival in this study. Also in the literature, data concerning the prognostic significance of lymph node involvement for survival in Klatskin tumors, is conflicting (2,11-13). Hence, the importance of lymph node clearance during resection of Klatskin tumors is uncertain with regard to survival.

The lymphatics of the ampullary region terminate in the lymph nodes of the retropancreatic area (14). In a series of 104 patients who underwent radical resection for an ampullary carcinoma, 51% had microscopic evidence of lymphatic invasion and 31% had involved regional lymph nodes (15). In the presence of positive lymph nodes, median survival was significantly reduced from 3.3 years without positive lymph nodes to 1.4 years with lymph node metastases. Lymphatic involvement, therefore, appears to be a strong prognostic factor in ampullary tumors.

Klatskin tumors in many ways seem to exhibit a different biological behavior than their counterparts elsewhere in the biliary tree. Despite the high incidence of incomplete resections and lymph node metastases, patients after local resections do quite well. In a recent report from our department, analysing long-term survival among 64 patients who underwent resection of a Klatskin tumor, 51 patients had undergone local resection whereas 13 had hilar resection combined with liver resection (10). In the whole group, there were 12 patients (19%) who survived for more than 5 years, all of whom were preoperatively classified as Bismuth type I or type II Klatskin tumors. Of these patients, 9 underwent local resection and 3 hilar resection combined with liver resection. Mortality after local resection and after the combination of hilar resection and liver resection was 14% and 16%, respectively. Survival was not significantly different for patients after local resection or after the combination of hilar resection and liver resection (median survival of 17 months and 15 months, respectively). These results are in line with data reported by Nakeeb et al. who in 109 patients, found a median survival of 19 months after local resection and of 18 months after the combination of hilar resection and liver resection (16). Cheng et al. (12) reported a median survival of 15 months after local resection and of 9.3 months after combined hilar resection and liver resection (table 2). Remarkable in our series is, that overall survival in the subset of patients with type III tumors undergoing local resection (n=28) or combined hilar resection and liver resection (n=32), were not significantly different (table 1). Hilar resections combined with major liver resections are associated with an increased mortality. Boerma in a large review of the literature found that hilar resections in combination with liver resections were associated with higher postoperative mortality than local resections, but that ultimately, patients had a better chance for longer survival (17). In the present series, mortality was highest in patients undergoing hilar resection with extended right hemihepatectomy and consequently, median survival was shorter than in patients undergoing hilar resection with left hemihepatectomy (5mths and 28mths, respectively; table 1). Now that the results of hilar resections combined with major liver resections have improved in several series, the benefit of these extended procedures are becoming apparent (18). The choice of performing local resection vs. resections with partial liver resections, is however, in the first place dictated by the proximal extension of the tumor. Klatskin tumors confined to the confluence, can be appropriately treated by local resection, including the caudate lobe when there is posterior infiltration of the tumor into this segment. Mid-choledochal duct tumors are less frequent than proximal or distal bile duct tumors. In a survey of the French Surgical Association (AFC) comprising 572 patients with tumors of the extrahepatic bile ducts, the middle-third tumors comprised 12.6% of all tumors (19). The relation of the tumor to the duodenum and pancreas determines if local resection is feasible. Since this is difficult to ascertain on preoperative imaging studies, the decision to undertake local resection or PPPD, usually depends on assessment of the tumor during laparotomy. In view of the potential involvement of lymph nodes -more than half (7/13 patients) in this series- and drainage of the periductal lymphatics into the retropancreatic lymphatic basin, PPPD is probably the more effective resection in terms of wider tumor and lymph node clearance. The small series included in the present study with involved dissection margins in 8/13 (62%)
patients, however, suggests that achieving free dissection margins of mid-choledochal duct tumors is a far greater problem determining outcome of the resection. This is in part due to the tumor infiltrating in the free, middle section of the hepatoduodenal ligament.

Although accepted for villous adenomas located in the ampulla, local resection for ampullary carcinoma is controversial (3,7). The high incidence of lymph node metastases justifies radical resection by performing PPPD for even small ampullary carcinomas. As villous adenomas are commonly resected by local resection, an additional problem is the poor accuracy of preoperative diagnosis and staging. In the present series, local resection was carried out in ampullary tumors misdiagnosed as adenomas. Subsequent radical resection, as carried out in 6/9 (66%) of the patients that underwent PPPD, teaches us that even if no residual tumor was found after local resection in the pancreatoduodenectomy specimen, lymph node metastases existed in the retropancreatic area. This experience has led us to the policy that after local excision of an ampullary adenoma, intra-operative frozen section examinations are performed and when these are suspicious of malignancy, we proceed with PPPD.

In conclusion, local resection is applicable to Klatskin type I and II tumors. In mid-choledochal duct carcinomas, the choice of local resection or PPPD depends on the relation of the tumor to the pancreas. The high incidence of lymphnode metastases favors total excision of the hepatopancreatic duct in combination with PPPD. However, tumor free dissection margins at the level of the hepatoduodenal ligament are difficult to achieve. For ampullary adenomas, local resection is feasible unless frozen section examination raises suspicion on a malignancy. Local resection of even small ampullary carcinomas is not advisable because of lymphatic dissemination of the tumor and consequently, inadequate clearance.

**References**


**Correspondence to:**

T.M. van Gulik, M.D.  
Dept. of Surgery  
Academic Medical Center  
9 Meibergdreef  
1105 AZ Amsterdam  
The Netherlands  
E-mail: t.m.vangulik@amc.uva.nl