Strategies to improve outcome after partial liver resection

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Chapter 4

The importance of complete excision of the caudate lobe in the surgical treatment of hilar cholangiocarcinoma

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Abstract

Background. The number of margin negative resections and survival time have greatly improved because of a more aggressive surgical approach of resectable hilar cholangiocarcinoma (Klatskin tumor). It has been shown initially by Japanese authors, that complete resection of the caudate lobe together with partial hepatectomy leads to more margin negative (R0) resections. However, this concept has not been unanimously taken up by the Western world. The aim of this study was to examine the role of complete caudate lobe resection in our series of resected hilar cholangiocarcinoma.

Methods. From January 1993 to January 2003, 54 patients had undergone resection for Klatskin tumors. These patients were divided into two groups, according to the two 5 year periods in which they had been operated. In the first period, patients did not routinely undergo complete excision of the caudate lobe, whereas in the second period, partial liver resection was combined with complete excision of the caudate lobe in 15 patients. These two patient groups were evaluated in respect with postoperative morbidity and mortality, microscopic tumor margins and survival time.

Results. Postoperative complications occurred in 59% of patients in total, while overall mortality was 11%. No difference was found in postoperative morbidity or mortality between the two periods. The number of margin negative resections increased significantly from 32% in the first to 59% in the second 5 year period (p<0.05). A significantly higher number of margin negative resections were found in the second 5 year period, together with improved survival.

Conclusion. In conclusion, concomitant complete excision of the caudate lobe for patients with hilar cholangiocarcinoma did not lead to increased morbidity or mortality. The addition of complete excision of the caudate lobe therefore, is a safe procedure contributing to a higher rate of R0 resections and improved survival.
Introduction

Due to the central anatomical position of Klatskin tumors within the liver hilum, it has been difficult to perform curative resections for this type of tumor. During the last 15 years, a shift took place towards a more aggressive approach in the treatment of hilar cholangiocarcinoma. Many authors have emphasized the importance of negative surgical margins to improve survival. In patients with Bismuth-Corlette type II, III and IV tumors, this can only be achieved by combining the hilar resection with a partial liver resection. Because of frequent anterior and posterior infiltration, partial hepatectomy is advocated in combination with resection of segment 4 and complete excision of the caudate lobe. Japanese surgeons in particular, convincingly demonstrated a survival benefit of a more aggressive approach including extended liver resection and concomitant complete excision of the caudate lobe. Despite these results, complete excision of the caudate lobe has not been implemented in the surgical treatment of hilar cholangiocarcinoma by all Western surgeons.

Also in our institution, as of the early 90's, an increasing number of patients with type III or incidentally IV hilar cholangiocarcinoma underwent hilar resection in combination with partial liver resection, occasionally including part of the caudate lobe. From 1998, more partial liver resections were performed in conjunction with Klatskin tumors and these were routinely combined with complete excision of the caudate lobe. The aim of this study was to assess the outcome of patients who underwent hilar resection and partial hepatectomy with or without concomitant complete caudate lobe resection in regard with postoperative morbidity and mortality, microscopical tumor clearance and patient survival.

Patients and methods

From January 1993 to January 2003, 54 patients underwent resection for hilar cholangiocarcinoma in our institution. A total of 123 patients were evaluated for resection resulting in a resectability rate of 44%. Criteria for resectability were the absence of 1) peritoneal or liver metastases, 2) vascular in growth of the contralateral portal vein or hepatic artery, 3) atrophy of the contralateral liver lobe, 4) lymph node involvement outside the hepatic hilar region and 5) ingrowth into the biliary radicals of the contralateral liver lobe, leaving no space for biliary anastomosis. Starting in 1998, a more aggressive policy consisting of more extensive, partial liver resections was adopted and these were combined with total excision of segment one in a total of 15 patients. Resections were performed in 31 men and 23 women with a mean age of 59.5 ± 1.5 years (range: 29 -79 years). There was no statistical difference in gender or mean age of patients who had undergone surgery before and after 1998.

Preoperative staging

Preoperative assessment of patients with hilar cholangiocarcinoma showed little changes during the whole study period. The usual imaging techniques in the two time periods included endoscopic retrograde cholangiopancreatography (ERCP), ultrasound with Doppler
imaging and computed tomography (CT). Diagnostic laparoscopy was used routinely to detect small liver or peritoneal metastases in both study groups. Percutaneous transhepatic cholangiography (PTC) was used in 1 patient in the first period and in 5 patients in the second period. After 1998, thin sliced (3 mm), spiral CT scan became more valuable and was used more often. It was used in 12 patients before 1998 (48%), while it was used in 22 patients after 1998 (76%). As of the end of 2000, MRCP was performed to assess vascular ingrowth in 6 patients in total.

**Tumor classification**

The Bismuth-Corlette classification was used to describe proximal tumor extension, preoperatively and intraoperatively in all patients (Table 1). Pathologic evaluation during and after surgery revealed an accurate preoperative diagnosis in 45 patients (83%). These patients were equally distributed among the 2 time periods.

**Preoperative biliary drainage**

To relieve jaundice and to optimize future remnant liver function, preoperative biliary drainage was performed in 48 patients (89%). In these patients, ERCP was used in 46 (96%) patients and PTC was used in 6 patients (13%). Both techniques were used in 4 patients (8%). The percentage of patients who had undergone preoperative biliary drainage was 96% before 1998 and 83% after 1998.

**Additional therapy**

Low dose preoperative radiotherapy (3 x 3.5 Gy) was given to all patients to prevent implantation metastases. Patients routinely underwent postoperative radiotherapy (55 Gy) in both periods.

**Statistical analysis**

To assess the significance of differences between groups, the chi-square test and the Fisher's exact test were used. Numeric data were evaluated using independent-samples T-test and were expressed as mean ± standard error of the mean (SEM). The Kaplan-Meier method was used to construct survival curves and the log-rank significance test was used for comparison of survival between groups. SPSS 10.0.7 for Windows (SPSS Inc, Chicago, Ill) was used as statistical software and a P value of less than 0.05 was considered significant.

**Results**

**Bismuth classification**

Definitive Bismuth classification is shown in table 1. There were no statistically significant differences in Bismuth type between patients of the two study groups. Most partial liver resections were performed in patients with type III tumors (67%).
Table 1. Bismuth-Corlette classification, types of resection and outcome of patients who had undergone resection for Klatskin tumors, divided into two five year periods

<table>
<thead>
<tr>
<th>Type of resection</th>
<th>1993-1998</th>
<th>1998-2003</th>
<th>P-value</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>25</td>
<td>29</td>
<td></td>
<td>54</td>
</tr>
<tr>
<td>Bismuth type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type I</td>
<td>4 (16%)</td>
<td>2 (7%)</td>
<td>NS</td>
<td>6 (11%)</td>
</tr>
<tr>
<td>Type II</td>
<td>5 (20%)</td>
<td>5 (17%)</td>
<td></td>
<td>10 (19%)</td>
</tr>
<tr>
<td>Type IIIa</td>
<td>9 (36%)</td>
<td>12 (41%)</td>
<td></td>
<td>21 (39%)</td>
</tr>
<tr>
<td>Type IIIb</td>
<td>7 (28%)</td>
<td>8 (28%)</td>
<td></td>
<td>15 (28%)</td>
</tr>
<tr>
<td>Type IV</td>
<td>0 (0%)</td>
<td>2 (7%)</td>
<td></td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Type of resection</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local resection</td>
<td>12 (48%)</td>
<td>8 (28%)</td>
<td>NS</td>
<td>20 (37%)</td>
</tr>
<tr>
<td>Hilar resection + partial liver resection</td>
<td>13 (52%)</td>
<td>21 (72%)</td>
<td></td>
<td>34 (63%)</td>
</tr>
<tr>
<td>(extended) right hemihepatectomy</td>
<td>7(6) (54%)</td>
<td>11(7) (52%)</td>
<td></td>
<td>18 (53%)</td>
</tr>
<tr>
<td>left hemihepatectomy</td>
<td>6 (46%)</td>
<td>10 (48%)</td>
<td></td>
<td>16 (47%)</td>
</tr>
<tr>
<td>Complete caudate lobe resection</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local resection</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>NS</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Hilar resection + partial liver resection</td>
<td>0 (0%)</td>
<td>15 (52%)</td>
<td></td>
<td>15 (28%)</td>
</tr>
<tr>
<td>Portal vein reconstruction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1 (4%)</td>
<td>6 (21%)</td>
<td></td>
<td>7 (13%)</td>
</tr>
<tr>
<td>No</td>
<td>24 (96%)</td>
<td>23 (79%)</td>
<td></td>
<td>47 (87%)</td>
</tr>
<tr>
<td>In hospital morbidity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>13 (52%)</td>
<td>19 (66%)</td>
<td>NS</td>
<td>32 (59%)</td>
</tr>
<tr>
<td>No</td>
<td>12 (48%)</td>
<td>10 (34%)</td>
<td></td>
<td>21 (41%)</td>
</tr>
<tr>
<td>In hospital mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>3 (12%)</td>
<td>3 (10%)</td>
<td>NS</td>
<td>6 (11%)</td>
</tr>
<tr>
<td>No</td>
<td>22 (88%)</td>
<td>26 (90%)</td>
<td></td>
<td>48 (89%)</td>
</tr>
<tr>
<td>Margin negative resections (R0)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local resection</td>
<td>8 (32%)</td>
<td>17 (59%)</td>
<td>P &gt; 0.05</td>
<td>25 (46%)</td>
</tr>
<tr>
<td>Hilar resection + partial liver resection</td>
<td>3 (38%)</td>
<td>5 (29%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete caudate lobe resection</td>
<td>0/0 (0%)</td>
<td>10/15 (67%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NS: not significant  NA: not applicable

Types of resection

The types of resection that were performed, were local resection for type I tumors, local resection with partial excision of the caudate lobe and/or segment 4 for type II tumors and hilar resections in combination with (extended) right or left hemihepatectomy for type IIIa and IIIb tumors, respectively. Extended right hemihepatectomy was performed in 13 patients. The 2 type IV tumors were treated with hilar resection and left hemihepatectomy and in 1 of these patients a portal vein reconstruction was performed. Portal vein reconstruction was performed in 7 patients (13%) in total. As of 1998, complete excision of the caudate lobe was performed in combination with hilar resection and partial hepatectomy in 15 patients (52%). Apart from concomitant caudate lobe excision, no statistical differences were found in the various types of resection among the two study periods.
**Morbidity and mortality**

Overall, postoperative complications, including minor and major, procedure related complications occurred in 59% of the patients (Table 1). No significant differences were found in the rate of postoperative complications in the two study periods. The most frequently occurring complications were liver failure, bile leakage and liver abscess or intra-abdominal abscesses (data not shown). The hospital mortality was 12% in the first and 10% in the second period (Table 1). All 6 patients ultimately died due to multi-organ failure. In 5/6 patients, multi-organ failure was preceded by liver failure, whereas in 1 patient, sepsis was the main cause of multi-organ failure and subsequent death.

**Histopathological examination**

The microscopic resection and dissection margins were analyzed, along with tumor differentiation, invasion into perineural tissue and lymph node involvement. Significantly more patients had undergone a margin negative (R0) resection in the second period, compared to the first period (59% versus 32%, respectively, P < 0.05). There were no differences in tumor differentiation, invasion into perineural tissue or lymph node involvement between the two study groups (data not shown).

**Survival**

The mean overall survival of the two patient groups was 4.8 years with a 95% confidence interval (CI) of 3.4 - 6.1 years. The overall 1, 2 and 5 year survival rates were 78%, 54% and 38%, respectively. Figure 1 shows the survival curves of the two periods. The mean survival

![Survival curves of all patients, divided into two five year periods](image)

<table>
<thead>
<tr>
<th>Number at risk</th>
<th>Time (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25 19</td>
<td>29 25</td>
</tr>
<tr>
<td>22 12</td>
<td>20 17</td>
</tr>
<tr>
<td>17</td>
<td>17</td>
</tr>
</tbody>
</table>

The straight line represents the period 1993-1998 while the dotted line represents the period 1998-2003. * A significantly better survival was found in the period 1998-2003 (P < 0.05).
time in group 1 and 2 was 3.6 years (CI 2.1-5.2) and 3.7 years (CI 3.0-4.5), respectively. Survival was significantly longer in the second period (P < 0.05). A total of 21 patients were still alive at the completion of the study, of which 4 in the first and 17 in the second period. As more than 50% of patients in the second period are still alive, the median survival times were not assessed.

Discussion

The outcome of surgical treatment for hilar cholangiocarcinoma has improved during the last decade. This is mostly due to the fact that more resections are combined with partial hepatectomy, leading to more R0 resections. In addition, Japanese authors in the late eighties and early nineties, reported that combining hilar resection and partial hepatectomy with complete caudate lobe resection further increased the rate of margin negative resections. Tsao and colleagues stated that this procedure can be performed safely, when performed by experienced surgeons who are familiar with caudate lobe anatomy. These findings resulted in implementation of this concept by other Japanese and some Western surgeons.

As of 1998, we also applied the concept of complete excision of the caudate lobe along with partial hepatectomy in our institution. In this study, patients who had undergone resection for hilar cholangiocarcinoma were analyzed retrospectively during a 10 year period and were divided into two 5-year periods, the second starting in 1998. No significant differences were found in tumor types according to the Bismuth-Corlette classification or types of resection between these groups, although more hilar resections in combination with partial liver resections were performed in the last period (72% vs. 52% in the first period). There were also no differences in accuracy of preoperative imaging or other general characteristics of patients, such as age and gender. The surgical team remained the same in both periods.

The overall postoperative morbidity rate of 59% in this study is comparable to what can be found in recent series, in which postoperative morbidity varies from 37% to 85%. When recent literature is compared to earlier reports, a slight increase in postoperative morbidity has occurred, which could be explained by a generally adopted, more aggressive surgical approach in the treatment of Klatskin tumors. The addition of complete excision of the caudate lobe in the second period, did not lead to an increase in postoperative complications or mortality in this study, even though also more portal vein resections were performed in this period.

In recent literature, overall mortality rates vary from 0% to 10%. In the first five-year period, mortality in this series was 12% whereas in the second five-year period, mortality was 10%. Liver failure was the most important cause of multi-organ failure and subsequent death in this study, underscoring the need for methods to accurately predict and to optimize future remnant liver function.

Significantly more margin negative resections were performed in the second five-year period. Apart from the addition of complete caudate lobe resection, increased surgical experience and the tendency to perform more extended resections, i.e. hilar resections in combination with partial liver resection, may have contributed to this improved outcome. Despite the short follow-up of patients in the second period, a significantly increased survival was found.
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compared to the first period. The increased rate of margin negative resections obviously is
the most significant factor to determine improved survival, as has repeatedly been shown
in literature \textsuperscript{1-6,9}. Because of the small number of patients in this study, univariate and
multivariate analysis was not performed.

The caudate lobe, designated as segment 1 in Couinaud's segmental classification of the
liver, constitutes 5-10 percent of the entire liver mass. The caudate lobe is composed of three
portions, i.e. the Spiegel lobe located dorsally to the inferior vena cava, the paracaval portion
lying anteriorly to the inferior caval vein and the caudate process traversing between the
inferior vena cava and the portal vein, from the paracaval portion to segment 7 of the right
liver \textsuperscript{15}. The blood supply to the caudate lobe is independent and originates mainly from the
left portal vein and left hepatic artery. Bile ducts from the caudate lobe may drain into any
part of the hepatic duct confluence but, most frequently enter the left hepatic duct near the
hepatic duct confluence. Because of the proximity of the caudate lobe posterior to the hepatic
duct confluence, the caudate lobe biliary ducts are frequently involved in Klatskin tumors,
necessitating en bloc removal of the entire lobe along with the hepatic duct confluence in
curative resections (figure 2). Total excision of the caudate lobe was advocated, since the
incidence of caudate bile duct invasion by hilar cholangiocarcinoma was found in 31%-98%
of cases \textsuperscript{3,4,9}. Incomplete removal, usually of the caudate process alone, does not suffice for
radical excision of all tumor. In the present series, all caudate lobe excisions were performed
in conjunction with partial liver resection in the second 5-year period of the study. Although
local excision, along the same lines, may require en bloc removal of the caudate lobe, most
local excisions in the second period of this series were performed for Bismuth type I or II
tumors, in which tumor infiltration into the caudate lobe bile ducts is less frequent. The
type III and IV tumors which were treated by local excision, were intentionally palliative
resections. In case of type II Klatskin tumors, we now choose to undertake local resection
in combination with excision of the caudate lobe, or preferably in combination with partial
liver resection.

In conclusion, concomitant complete excision of the caudate lobe for patients with hilar
cholangiocarcinoma did not lead to increased morbidity or mortality. The addition of
complete excision of the caudate lobe therefore, is a safe procedure that can lead to a higher
rate of R0 resections and increased survival.

Reference list


Complete excision of the caudate lobe


