Strategies to improve outcome after partial liver resection

Dinant, S.

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: https://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.
Chapter 3

Klatskin tumor: new surgical approaches

Thomas M. van Gulik¹, Sander Dinant¹, Olivier R.C. Busch¹, Erik A.J. Rauws², Hugo Obertop¹, Dirk J. Gouma¹

¹ Dept. of Surgery, Academic Medical Center, Amsterdam, The Netherlands
² Dept. of Gastroenterology, Academic Medical Center, Amsterdam, The Netherlands

Presented at the Highlights of Gastroenterology 2005, April 7-10, Pafos, Cyprus
Abstract

Background. Surgical treatment of hilar cholangiocarcinoma (Klatskin tumors) is difficult due to its central location in the liver hilum. Recent developments in surgical techniques have improved the outcome after resection. This paper deals with the surgical approaches currently applied in our center and the impact of these strategies on outcome and criteria for resection.

Methods. From 1988-2003, 99 consecutive patients underwent resection for hilar cholangiocarcinoma. Patients were analyzed for rate of R0 resections in relation with Bismuth classification. Morbidity, mortality and survival were assessed.

Results. The rate of hilar resections in combination with (extended) liver resections for type III and IV tumors increased from 24% to 95% in the last 5 years of the study period. 8 patients (8%) had Bismuth type IV tumors. Four of these patients underwent palliative local excisions of the hepatic duct confluence whereas the other 4 patients underwent hilar resection in combination with partial liver resection, resulting in microscopically radical resections. There was no mortality in this group. Overall postoperative morbidity and mortality were 68% and 10%, respectively.

Conclusion. An aggressive surgical approach consisting of hilar resections combined with partial liver resections including segments 1 and 4, resulted in a higher rate of R0 resections. Even Bismuth type IV tumors may be resectable depending on biliary anatomy of the hepatic duct confluence.
Klatskin tumor: new surgical approaches

Introduction

Cholangiocarcinoma may arise in any part of the intrahepatic and extrahepatic biliary tree. Most frequently, however, the hepatic duct confluence is affected. These hilar cholangiocarcinomas are called Klatskin tumors, after the American pathologist who first described this tumor in 1965. The management of Klatskin tumors is notoriously difficult, for several reasons. Firstly, patients present late when the bile duct is occluded and jaundice has developed, usually without pain. Secondly, diagnosis is cumbersome despite advanced imaging techniques, taking into account that inflammatory processes may mimic malignant strictures. Reliable tissue or cytological diagnosis is difficult to obtain. Thirdly, complete surgical excision is difficult to achieve because of its central location in the liver hilum and its proximal extension into the intrahepatic biliary segmental ducts. Notwithstanding these facts, considerable progress has been made in the management of Klatskin tumors in the past decade. New, more aggressive surgical strategies have significantly changed treatment policy of patients with Klatskin tumors. This presentation will focus on new approaches for surgical treatment of Klatskin tumors and its impact on the criteria used for resectability of this difficult tumor. The current status of diagnostic imaging and classification is reviewed as well, because of its importance in determining a surgical strategy.

Diagnostic work-up and imaging modalities

The first issue when visualizing a biliary stricture is whether the stricture is based on a malignant tumor or is benign, usually of inflammatory origin such as primary sclerosing cholangitis. There are no imaging modalities that can reliably differentiate between a benign or malignant hilar stricture. PET scan leads to false positive results because of enhanced glucose metabolism in inflammatory lesions. Tumor serum markers and brush cytology also have low sensitivity. When we adhere to strict guidelines for resection of Klatskin tumors, we have to accept that in 15-18% of cases, a tumor is resected which on histopathological examination turns out to be a benign lesion. Resection of Klatskin tumors is based on proximal extent of tumor into the intrahepatic biliary tree, as laid down in the Bismuth-Corlette classification system (type I-IV). Assessment of bile duct invasion is therefore essential to select patients with potentially resectable tumors. Whereas ultrasound and ERCP are frequently used to depict the biliary tree, technology of MRI has improved and now offers a noninvasive alternative with high image quality. ERCP has been abandoned as diagnostic modality and is now primarily used for therapeutic purposes, i.e. drainage of the biliary system. The Bismuth classification system does not take into account liver parenchymal invasion, vascular invasion into the portal venous system or hepatic arteries and lobar atrophy, criteria which all are important when assessing resectability of Klatskin tumors. Cross-sectional imaging modalities such as CT and MRI are of value to examine the latter features. Innovative techniques are intraductal ultrasound and contrast-enhanced MR angiography to assess vascular involvement. Although controversial in distal bile duct and pancreatic tumors, staging laparoscopy is useful in Klatskin tumors, avoiding laparotomy in 25-40% of patients. Another controversy relates to the need of preoperative biliary drainage. Most centers agree that especially in Klatskin tumors requiring extensive liver resection, complete biliary drainage of at least the
future remnant liver is mandatory for adequate postoperative liver function. Complete preoperative biliary drainage on the side of the future remnant liver, is essential for adequate postoperative liver function and liver regeneration. CT volumetry is used to determine volume of the future remnant liver and this may be increased by preoperative portal vein embolization.

**Classification**

Surgical excision is the only option for curative treatment of Klatskin tumors. The Bismuth classification (Fig. 1), based on proximal extension of the tumor into the intrahepatic biliary system:

**Figure 1. Bismuth classification of Klatskin tumors (hilar cholangiocarcinoma)**

Type I and II tumors are confined to the confluence of right and left hepatic ducts. Type III tumors extend proximally into the right (IIIa) or left (IIIb) intrahepatic, segmental biliary ducts. Type IV tumors extend into both intrahepatic, biliary systems. All type III and IV tumors, and most of type II tumors, require hilar resection in combination with (extended) hemihepatectomy, *en bloc* with excision of segment 1.
Klatskin tumor: new surgical approaches

system, is used to select patients for surgical exploration. Other criteria that preclude curative resection are intra- or extrahepatic metastases, including lymph node metastases along the common hepatic artery or around the celiac axis. Regional lymph node metastases in the hilar area do not contradict curative resection whereas resectability in the presence of lymph node metastases distally in the hepatoduodenal ligament is a matter of debate. Some surgeons contend that in the latter case, resection with extensive lymph node resection will improve survival compared to non-surgical therapy. Klatskin tumors, along with progression into the biliary tree, tend to infiltrate into the ipsilateral portal venous trunk and/or hepatic artery. Since these vessels are removed with hemihepatectomy, this does not preclude radical resection. Involvement of the portal bifurcation requires portal venous reconstruction whereas infiltration into the common hepatic artery is considered a sign of unresectability.

**Surgical approach**

In previous years, Klatskin type III a/b tumors which extend into the first segmental biliary ducts of one side of the liver were treated by hilar excision in combination with hemihepatectomy, whereas Type IV tumors, with tumor extension to both sides were considered unresectable. Nowadays, while extended liver resections are undertaken, type IV tumors may be curatively resected depending on bile duct anatomy at the liver hilum. Also, whereas type I and II tumors (confined to the major hepatic ducts) were considered for local excision of the hilar bile ducts, type II tumors now tend to be resected in combination with hemihepatectomy to achieve R0 resection. The Bismuth classification takes into account tumor extension into the right and left biliary system, but, tumor extension anteriorly to the quadrate lobe (segment 4) and posteriorly to the caudate lobe (segment 1) is equally important. Surgical treatment, therefore, should include resection of segments 4 and 1, which in case of right sided tumors (type IIIa) comes down to extended right hemihepatectomy *en bloc* with segment 1. In conjunction with any resection, complete lymphadenectomy of the hepatoduodenal ligament is carried out.

The portal vein bifurcation lies in direct posterior position of the hepatic duct confluence and is therefore, frequently involved in the tumor. Curative surgery therefore requires concomitant excision of the portal vein bifurcation. During a right sided resection, the portal vein bifurcation is resected *en bloc* with the hilar tumor and the right hemi-liver including segments 4 and 1, after which the left portal vein branch is reconstructed by end-to-end anastomosis to the main trunk of the portal vein. From the left side, the portal vein bifurcation is taken with the left hemi-liver and segment 1. An interposition graft is usually not required.

**Results**

The experience in the AMC with surgical management of Klatskin tumors comprises 99 patients resected over a 15 year period (1988-2003). Over this period, the rate of (extended) liver resections for type III and IV tumors increased from 24% to 95%. Of these 99 patients, 8 patients (8%) were classified as Bismuth type IV tumors. Four patients in which during
The left biliary system shows extensive infiltration into the segmental branches (B2, B3 and B4) (Fig 2a). On the right side, only the anterior segmental biliary ducts (B5, B8) are visualized (arrow). Two stents were placed for biliary drainage. The posterior segmental biliary ducts (B6, B7) drain directly into the hepatic duct confluence and are occluded by the hilar tumor. These posterior segmental ducts are seen on the CT scan as dilated ducts in the hilar area (Fig 2b, arrow).

### Figure 3. Depiction of tumor and hilar anatomy of the patient whose imaging studies are shown in Fig. 2

This patient underwent a left hemihepatectomy which in the hilar region was extended to the right to include the complete right side of the confluence, resulting in a microscopically radical resection.

exploration, advanced tumor infiltration was found into both the right and left biliary systems, underwent palliative local excision of the hepatic duct confluence. Usually, the distal bile duct was already cut to allow accurate assessment of the hepatic hilum, precluding access for palliative treatment using biliary stents. The other 4 patients underwent hilar resection in combination with partial liver resection, resulting in microscopically radical resections. Three of these patients had tumor extending into the left segmental bile ducts and to the right, into a short right hepatic duct or into the right anterior and right posterior sectorial ducts, draining directly into the confluence (Figs 2a/b). These patients underwent a left hemihepatectomy which in the hilar region was extended to the right to include the complete right side of the confluence (Fig 3). In one patient, the portal vein bifurcation was partially resected along with the tumor. Biliary reconstruction
was performed by creating anastomoses on the segmental ducts (B5/8 and B6/7) using a Roux-Y jejunal loop. The fourth patient was deemed unresectable because of type IV tumor with tumor infiltrating into the segmental branches of the right liver and to the left, into the left hepatic duct including a segment 4 bile duct draining close to the confluence (Fig 4). An extended right hemihepatectomy (which includes segment 4) was performed which resulted in a R0 resection (Fig 5). A biliary anastomosis was constructed on the B2/3 segmental ducts. There was no mortality or major morbidity in this group and all resected patients were alive at the conclusion of this study (18, 23, 61 and 70 months, respectively). In the group of patients with palliative resections, all patients had died with a median survival of 15.7 months.

Overall, the rate of R0 resections increased from 13% to 59%, with significantly improved survival (from 33% to 60% for R0/1 resections at two years) (8). The extended type of resections, however, carry a high risk of complications, although overall morbidity and mortality (66% and 10%, respectively) did not increase over the years.

Discussion

Several studies have shown that the single most important prognostic factor for long-term survival is complete (R0) resection of the hilar tumor. Margin negative resections are however difficult to achieve due to the central location of the tumor at the liver hilum and its intimate relationships with adjacent liver parenchyma and blood vessels. Resection of the portal vein bifurcation is mandatory when the tumor invades into the portal vein, in order to achieve R0 resection.
Assessment of vascular ingrowth during exploration is however difficult without disrupting the tumor, because of the small area involved at the hepatic hilum. Considering these close anatomical relationships, the surgical group in Berlin advocate a no-touch technique to resect Klatskin tumors in conjunction with extended liver resection, in accordance with principal oncological guidelines (9). The surgical strategy consists of performing hilar resection \textit{en bloc} with extended right-sided liver resection and resection of the portal vein bifurcation. Dissection of structures in the vicinity of the tumor is hence avoided. During resection, the left portal vein branch is reconstructed by end-to-end anastomosis to the main trunk of the portal vein. The 5-year survival rate of patients operated according to these principals who indeed had a R0 resection was 72%, which is a remarkable outcome. Mortality after these extensive resections however, was considerable (10-13\%).

Bismuth type IV Klatskin tumors are generally considered unresectable even using extensive liver resections, because of inability of obtaining tumor free margins at the cut bile ducts of the remnant liver. The anatomy of the biliary ducts at the hepatic duct confluence, however, determines whether a radical resection can be obtained despite proximal infiltration of the tumor into the first segmental bile ducts of both the right and left biliary systems. The hepatic duct confluence often consists of the right anterior (B5/8) and right posterior (B6/7) sectorial ducts draining together with the left hepatic duct into the common hepatic duct. A tumor at this site infiltrates into the right segmental ducts and when extending into the left segmental ducts (B2/3/4), will be classified as a type IV tumor. Hilar resection in combination with a left hemihepatectomy potentially clears all tumor, as has been shown in our series. Likewise, on the left side, the place of drainage of the segmental duct coming from segment 4 varies, and when located close to the confluence, is readily infiltrated by tumor. When a tumor also extends into the right segmental ducts, the tumor is diagnosed as a type IV tumor. When performing extended right hemihepatectomy (which includes segment 4), the segment 4 bile duct is completely removed, leaving a tumor free resection margin on the bile ducts of segments 2 and 3. Hence, not every Klatskin type IV tumor is by definition unresectable and each case should be assessed by a multidisciplinary team consisting of experienced surgeons, endoscopists and (interventional) radiologists.

The down-side of these extensive surgical procedures obviously is substantial morbidity and mortality. In the present series, overall morbidity and mortality was 66% and 10%, respectively, although these rates had not increased over the years while adopting a more aggressive surgical approach. Comparable mortality rates (10-13\%) are reported in other series (9, 10). An increased postoperative risk after extensive liver resection appears justified when considering the long-term results of curative resection, also in the light of the limited survival after non-operative treatment. Mortality in most patients after hilar resection and extensive liver resection is due to liver failure. Accurate risk assessment and determination of liver functional reserve, therefore, is of paramount importance in selecting patients for surgical treatment.

In conclusion, recent more aggressive surgical approaches have contributed significantly to an increased rate of R0 resections and improved outcome in patients with Klatskin tumors. Patients with Klatskin type IV tumors may undergo curative resection depending on biliary anatomy of the hepatic duct confluence, and should be considered by a multidisciplinary team in a specialized center.
Reference list


