



Radical Resection and Liver Grafting as the Two Main Components of Surgical Strategy in the Treatment of Proximal Bile Duct Cancer

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In the treatment of adenocarcinoma of the proximal bile duct, our current strategy is to resect the tumor radically and to offer patients with unresectable tumors the chance of hepatic transplantation, if extrahepatic tumor growth is excluded. Tumor resection is performed by resection of the hilum alone or combined with partial hepatectomy. The latter procedure enables radical treatment of more advanced tumor stages and, eventually, a higher degree of radicality is achieved, and is recommended. This concept is based on our experience with 108 patients with proximal bile duct carcinoma operated on between February, 1975 and October, 1986.

In 10 patients, no therapeutic or palliative surgical procedure could be performed during laparotomy because of advanced tumor stage. In 30 patients, various drainage procedures were performed. Fifty-two patients underwent resection: 25 underwent resection of the hilum only, and 27 underwent resection of the hilum combined with partial liver resection. Twenty-eight of these resections were classified as curative and 24 as palliative. Sixteen patients with unresectable tumors had hepatic transplantation. In 7 of these patients, extrahepatic tumor growth was already present at the time of liver transplantation.

Median survival times were: laparotomy only, 1 month; drainage procedures, 5 months; total resection, 15 months; curative resection, 23 months; palliative resection, 7 months; liver grafting, 16 months. Seven patients are alive up to 21 months posttransplantation. On the basis of favorable results in our more recent group of patients, liver grafting as the ultimate chance for tumor removal in patients otherwise treatable only by palliative drainage procedures may be justified.

In the last decade, progress has been made in the palliative treatment of carcinoma of the bile duct system of the hilar region and especially in the so-called Klatskin tumors [1] through endoscopic and transhepatic means [2]. Similarly, the surgical approach in the treatment of these tumors, aimed at resection, has been developed, offering at least some chance for cure or superior palliation compared to endoprosthetic and drainage procedures [3]. In unresectable situations, liver transplantation has been carried out as the ultimate means of surgically removing the tumor [4]. Results of liver grafting have not been very successful in these tumors in the last years due to early tumor recurrence [5]. Nevertheless, we continue to per-

form liver transplantation in selected cases of proximal bile duct carcinoma with the aim of elaborating more clearly the use of this procedure in a larger number of patients than previously experienced [6].

This study was based on a very wide indication for resectional therapy, so that liver grafting was offered only to truly unresectable patients. Thus, of course, tumor staging and other conditions were different in both groups. In this article, our own data are analyzed and the results of the combined approach—radical resection, if possible, and liver grafting, in unresectable cases—are presented.

Material and Methods

Between February, 1975 and October, 1986, a total of 108 patients with proximal bile duct carcinoma were selected for surgery at our institution. The patients consisted of 65 males and 43 females. Age ranged from 29 to 81 years with a median of 55 years (Fig. 1).

The combination of diagnostic procedures usually applied (Table 1)—localizing and classifying these tumors according to Bismuth and Corlette [7]—was used and yielded criteria for the surgical approach (drainage, resection, transplantation) (Table 2). Percutaneous transhepatic cholangiography, usually followed by drainage (PTCD), in combination with endoscopic retrograde cholangiography provided important information about the intraductal extent of the lesion, the situation at the confluence of both main hepatic ducts, and the type of tumor according to the classification proposed by Todoroki et al. [8]. Computed tomography usually did not show gross tumor; if it did, resectability was highly unlikely, and most cases proved to be unresectable. Angiography provided normal findings of the hepatic artery and portal vein branches and did not rule out tumor infiltration of the vessels, but compression, deviation, and thrombosis could be demonstrated. If, from the clinical situation or from unequivocal diagnostic findings of unresectability (Table 2), a surgical procedure could not offer a therapeutic chance, the patient was not operated on (these patients were not included in this series). Otherwise, the decision about therapeutic possibilities was made by laparotomy. The different surgical steps for making the decision are described in detail

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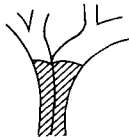

Classification [7]		Patients n, (%)
Type I		7 (6)
Type II		6 (6)
Type III		95 (88)
Total		108 (100)

Fig. 1. Localization of carcinoma at the bile duct bifurcation in 108 patients (Medizinische Hochschule Hannover, February, 1975–October, 1986).

Table 1. Main diagnostic findings and parameters in proximal bile duct carcinoma.

Diagnostic method	Finding
Clinically	Painless jaundice
Biochemically	Pattern of extrahepatic obstruction
Ultrasonography	Dilated intrahepatic bile ducts
Endoscopic retrograde cholangiography	Break off in the proximal part of the common bile duct
Percutaneous transhepatic cholangiography followed by drainage	Localization of the upper margin of the lesion, one or both sides affected, situation at the confluence: preserved communication or discontinuation of right and left bile duct system, subtype of the tumor [8]
Computed tomographic scan (angiography)	No gross tumor
Angiography	Type of arterial blood supply of the liver: gross infiltration, compression, deviation or thrombosis of main arterial or portal vein branches
Main differential diagnoses	Benign stenosis (primary or secondary sclerosing cholangitis) Other tumors (e.g., carcinoma, papillomatosis)

below. Several patients had been operated before elsewhere because of obstructive jaundice with a variety of procedures performed (not listed here), and have been referred for further surgical treatment including liver transplantation. A liver graft

Table 2. Criteria for surgical approach in proximal bile duct carcinoma according to preoperative findings.

Finding	Approach
A. Upper margin of infiltration below or within the confluence of both main hepatic ducts (Bismuth type I and II), polypoid or nodular type [8], no other signs of findings listed below	Potentially resectable by resection of the hilum alone or combined with partial liver resection
B. Upper margin of infiltration at one side within the main hepatic duct or further branches (Bismuth type III), with or without discontinuation of both ductal systems, with or without lesions of the ipsilateral blood vessels	Potentially resectable by combined resection of the hilum and part of the liver
C. Upper margin of infiltration at both sides at the level of the second bifurcation of the bile ducts, lesion of the artery of both sides or contralateral to one side, tumor location according to B (above), gross hilar tumor mass	Unresectable, potential transplant candidate
D. Signs of broad infiltration distally and proximally, diffuse or infiltrating type [8], lymph node enlargement, intra- or extrahepatic metastases	Incurable, not a transplant candidate

Table 3. Operative procedures for carcinoma of the bile duct bifurcation in 108 patients.

Procedure	No. of patients, (%)
	108 (100)
Laparotomy alone	10 (9)
Drainage procedures	30 (28)
Resection	52 (48)
Resection of the hilum alone	25 (23)
Resection of the hilum + partial hepatectomy	27 (25)
With right hemihepatectomy	3 (3)
With left hemihepatectomy	10 (9)
With extended right hemihepatectomy	7 (6)
With extended left hepatectomy	7 (6)
Liver transplantation	16 (15)

was only planned if unresectability was proven by laparotomy at our institution or by a previous operation elsewhere.

The surgical procedures performed are listed in Table 3. In 10 patients, exploratory laparotomy disclosed far advanced tumor stages, e.g., infiltration of adjacent organs, so that no further treatment was performed. Included is 1 patient who bled after an attempt at placing a PTC, and who underwent laparotomy with the aim of achieving hemostasis. Diagnostic laparotomies followed by liver transplantation are not included in this group. In 30 patients, drainage procedures have been performed (retrograde drainage via choledochotomy, U-tube drainage combined with choledochojejunostomy mainly for endoluminal irradiation procedures and PTC, or endoscopic stenting preceding or following exploratory laparotomy). Overall survival

Table 4. Liver transplantation (LTX) in 16 patients with carcinoma of the proximal bile duct (Medizinische Hochschule Hannover, February, 1980–November, 1986).

LTX no.	Date of LTX	Sex	Age (yr)	Previous history and indication for LTX	Extrahepatic tumor spread	Potentially curative	Survival (mo)	Outcome	Remarks
16	2/11/80	M	50	Res 7/78, drain, rad, expl 2/80 ^a : Persistent tumor, no left-sided intrahepatic bile duct found	Pancreatic lymph node	No	10	Died	Chronic rejection, sepsis, no recurrence
23	12/26/80	F	40	Res 4/79: Tumor progress, no free proximal margin	None	Yes	36 days	Died	Hemorrhagic shock
24	1/2/81	M	29	Expl 12/80, 1/81 ^a : Unresectable tumor, high intrahepatic infiltration	None	Yes	27	Died	Recurrence
45	11/10/81	M	50	Cholecystectomy 1/80: Unresectable adenocarcinomas of the whole bile duct	Regional lymph node	No	44 days	Died	Rejection, infection, multiorgan failure
81	2/13/83	M	27	Multiple drain: Suspected PSC	Unknown	No	4	Died	Recurrence
92	5/31/83	M	29	Cholecystectomy 12/82, expl 12/82, expl 5/83 ^a : Local tumor infiltration of hepatoduodenal ligament	Hepatoduodenal ligament	No	7	Died	Recurrence
119	3/1/84	M	53	Suspected PSC + SBC, expl 2/84 ^a	Extrahepatic bile duct	No	1 day	Died	Septic shock
133	7/1/84	M	39	Expl 8/82, drain, rad, chem: Unresectable tumor extending high above the bile duct bifurcation	Pancreas, stomach regional, lymph node ^b	No	17	Died	Recurrence
151	2/16/85	F	46	Expl 6/84, drain, rad, chem: Local tumor infiltration of hilar structures	None	Yes	21	Alive	No recurrence
155	4/20/85	F	43	Expl 10/84: Suspected PSC + SBC	Common bile duct ^c	Yes	18	Alive	No recurrence
160	5/25/85	F	36	Res 10/84: Persistent tumor after noncurative resection	None	Yes	17	Alive	No recurrence
166	8/12/85	F	26	Expl 8/85: Locally unresectable tumor	None	Yes	14	Alive	No recurrence
167	8/26/85	M	59	Expl 7/85, drain: tumor invasion of the hepatic artery	None	Yes	14	Alive	Recurrence 12 mo after LTX
205	3/9/86	M	45	Multiple drain: Suspected PSC + SBC	Portal vein, vena cava, celiac axis lymph node	No	6 days	Died	Liver failure due to inadequate portal perfusion
247	8/31/86	M	39	Expl 5/86: Unresectable tumor due to high intrahepatic infiltration	None	Yes	3	Alive	No recurrence
260	11/6/86	M	46	Expl 9/86: Unresectable tumor, local extent	None	Yes	14 days	Alive	No recurrence

Res = palliative resection of bile duct bifurcation; drain = biliary drainage procedures, e.g., stenting; rad = intraluminal tumor irradiation; expl = exploratory laparotomy; chem = chemotherapy; PSC = primary sclerosing cholangitis; SBC = secondary biliary cirrhosis.

^aExploratory laparotomy in view of conventional resectional or reconstructive procedures, but with potential liver donor available.

^bLTX + total pancreatectomy, gastrectomy, splenectomy.

^cResection of remaining bile duct, 7/85.

time for both of these groups is reported below. Two patients from the drainage group were lost to follow-up.

In resected patients, 2 types of procedures have been employed: (a) the hilar resection, i.e., resection of the hepatic bifurcation with surrounding tissue and eventually the adjacent liver parenchyma (parts of segment IV); and (b) the combined hilar resection and anatomical liver resection, either left or right hemihepatectomy (anatomical or extended).

The extent of resection of the main hepatic ducts and further smaller intrahepatic ducts of the right and left lobe can be classified into different degrees: (I) resection below or within the next intrahepatic bile duct confluence thus resulting in only 1 proximal bile duct lumen, and (II) resection beyond the next intrahepatic bile duct confluence resulting in at least 3, and

usually 5, branches (sometimes as many as 10 branches) on the right side, and 2–3 bile duct lumina on the left.

Bile ducts from the caudate lobe, sometimes branching near the confluence of the main hepatic ducts, are not considered in this gradation. Extent II resection has been performed routinely, except in a few Bismuth type I cases where, on the left side, extent I resection seemed to be sufficient.

Resection was performed in a total of 52 patients: 25 patients underwent hilar resection alone, 27 underwent resection combined with partial hepatectomy (Table 3). In all hemihepatectomies, right- or left-sided, at least the caudal part of the caudate lobe behind the portal vein was also removed. Of 52 resections, 28 have been defined as curative, and 24 as palliative. Curative means that there are tumor-free margins of resection, and

macroscopically, there is no residual tumor, and there are no lymph node metastases. The operation was thought to be only palliative if 1 or more of these criteria were fulfilled. (Note: The assessment of lymph node status in this way may be criticized; it has been used because extensive lymph node dissection had not always been performed in the past and, thus, no precise statement can be made about residual lymph nodes in cases where resected lymph nodes had been found to be infiltrated.) Sixteen patients underwent liver grafting. Previous medical history and surgical interventions are summarized in Table 4.

Sometimes, especially in the earlier patients, there was a considerable interval between the definite diagnosis of adenocarcinoma of the proximal bile duct and performance of hepatic transplantation (up to 1.5 years in 1 case), whereas recently, liver transplantation has become the first therapeutic choice after an exploratory laparotomy had disclosed an unresectable tumor.

In 13 of the 16 patients, liver grafting was the first therapeutic operation. The other 3 had had a previous hilar resection, which, retrospectively, had to be regarded as noncurative. Two of the latter 3 developed local tumor recurrence or progress with obstructive jaundice (LTX no. 16, 23). One had been transplanted before manifestation of a clinical recurrence (LTX no. 160), and after transplantation, the removed liver showed histologically distinct tumor infiltration around the hepaticojunostomy. Another patient (LTX no. 133) was accepted for transplantation since, during the previous operation, done at an institution with substantial experience, no extrahepatic tumor spread could be detected. During transplantation, massive scar formation proved histologically to be tumor infiltration. Liver grafting, which was underway, was performed in combination with a total gastrectomy and a total pancreatectomy because of infiltration of the celiac axis.

It should also be emphasized that 4 patients with a rather long history were transplanted with a suspected diagnosis of primary sclerosing cholangitis, 2 of these with secondary biliary cirrhosis. All of them had undergone previous surgical explorations, sometimes multiple explorations, however, tumor was not detected until the time of liver transplantation. In 1 case, tumor was only disclosed in the pathological work-up of the explanted liver and was not suspected during surgery (LTX no. 155). Due to better criteria for indication of liver transplantation, almost all patients (since 1985) can be regarded as potentially curatively transplanted with only 1 exception (LTX no. 205: diagnosis of primary sclerosing cholangitis, palliative transplantation because the patient would not have survived exploratory laparotomy after extensive dissection, severely reduced general state, advanced secondary biliary cirrhosis, marginal liver function).

Liver grafting was always performed in the typical orthotopic manner. Reconstruction of the biliary system has always been carried out by an anastomosis of the common bile duct of the donor liver to a Roux-en-Y loop of jejunum in order to resect the recipient bile duct far distally. Immunosuppression was performed according to the current protocols: up to 1981, mainly azathioprin and prednisolone and, since then, mainly cyclosporin and prednisolone; antilymphocyte serum was sometimes added.

Histology of the removed liver confirmed the diagnosis of adenocarcinoma of the bile duct system. The differentiation

between an adenocarcinoma originating from the proximal bile duct and a true intrahepatic cholangiocarcinoma (also adenocarcinoma) was unclear in at least 1 patient (LTX no. 205) because of the wide expansion of the tumor within the liver parenchyma. In 7 patients, extrahepatic tumor growth in lymph nodes or adjacent tissues had been found during transplantation or by histological examination of the removed liver and tissues.

Surgical Steps

Whenever the chance for resection or transplantation was not clearly excluded by the preceding diagnostic procedures or the general status of the patient, a laparotomy was performed. The following steps were taken to differentiate between unresectability, local resectability, and potential tumor removal only by total hepatectomy.

1. General assessment of the peritoneal cavity and dissection of the hilar structures with lymph node biopsy: Extrahepatic tumor growth extending to the hilar structures and lymph node metastases rule out liver transplantation. A resection which will only be of palliative value may be regarded.

2. Further centrally directed dissection of the fibrous tissue around the upper part of the common bile duct and to both sides of the bile duct confluence: Location of the tumor and the depth of the tumor spread into the liver parenchyma (of 1 or both liver lobes) can be determined. It has to be decided at this stage if at least part of the liver (1 lobe or at least 2 segments) can be preserved, and if the tumor is to be resected radically, regarding parenchymal as well as bile duct infiltration. If a curative resection cannot be expected, a palliative resection may be performed in individual cases—perhaps to facilitate intraluminal irradiation.

On the other hand, in this particular situation of local unresectability, tumor removal by total hepatectomy and subsequent liver replacement may be discussed. At this stage, and particularly if a decision for liver transplantation is considered, it has to be decided whether the diagnosis of malignant tumor is unequivocal or should be verified histologically. In performing a biopsy, one has to consider the well-known difficulties of obtaining representative specimens in this particular type of tumor and perhaps also the speculative danger of propagation of tumor spread by the incision of a previously well delineated tumor.

3. Careful dissection of the hepatic artery, its bifurcation, the left and right hepatic artery, and eventually of further branches: This step sometimes has to be combined with step 2 in order to elucidate the anatomy of the arterial blood supply and to avoid lesions of arterial branches in this early phase of dissection, when a final decision about the kind of operation that can be performed has not yet been made.

The determination whether essential arterial branches are infiltrated is regarded to be a further important—if not the most important—step in determining resectability. There is no question that the trunk of the right or left hepatic artery can be reconstructed, but the risk of subsequent arterial thrombosis and ensuing liver failure is considerable; and in the case of tumor infiltration, invasion may extend further into the arterial branches. Thus, from our point of view, tumor infiltration into both hepatic arteries or contralaterally to the planned resection is taken as a sign of unresectability. True tumor invasion will

sometimes be difficult to differentiate from inflammatory adhesions. Frozen sections may clarify the situation, but the very close connection between tumor and vessels will always bear the risk of tumor infiltration. An infiltration of the portal vein or its branches seems to be less problematic: reconstruction can be performed more easily and successfully; in the case of extended resections, particularly in extended right hepatectomy together with hilar resection, the residual left portal vein often has to be resected and shortened in order to avoid kinking. A potentially tumor-infiltrated segment can also be removed. Thus, the decision about the therapeutic approach can be made: bilateral deep parenchymal or high ductal infiltration as well as bilateral arterial infiltration exclude curative resectability, leaving open the discussion about palliative procedures or liver grafting. In the case of tumor-free lymph nodes, and absence of other extrahepatic tumor spread in a patient younger than 55–60 years of age, in an acceptable general condition, we would choose the option of liver transplantation. If this approach is chosen, which, of course, has to be discussed with the patient as one possible decision before operation, the intervention is stopped and the abdomen closed. Biliary decompression is usually performed by PTCD until transplantation, which should be performed within the next few weeks.

Definitive PTCD is also the favored procedure in unresectable situations not permitting liver grafting; other surgical palliative methods such as hepatojejunostomy or surgical insertion of a bile duct prosthesis are rarely performed. Postoperative intraluminal irradiation by iridium [9, 10] can usually be performed via PTCD, eventually a U-tube is inserted during surgery from a choledochotomy, usually followed by a choledochojejunostomy.

In the case of potential resectability, the following further steps are performed.

4. Division of the common bile duct far distally at the level of the head of the pancreas and dissection together with lymphatic and surrounding tissue away from the artery and portal vein.

5. Further centrally directed dissection of the proximal bile duct particularly of the right and left hepatic ducts with further isolation away from the arterial and portal vein branches.

6. In the case of hilar resection alone, the hepatic ducts are divided at a level that appears tumor-free and distant enough from the tumor margin (extent I and extent II as described above). In the case of combined hilar and liver resection, the preferred technique is the procedure that starts with the anatomical liver resection: division of the arterial and portal branches and all corresponding liver veins is followed by dissection of the liver parenchyma; the isolation and division of the bile ducts of the remaining liver is performed as the last step, thus enabling optimal access to this ductal system and the highest degree of surgical radicality. Different types and degrees of liver resections will be indicated according to the site and the extent of the tumor (Fig. 2). During or after this step, resection and reconstruction of the portal vein or hepatic artery can eventually be performed.

7. Reconstruction of the biliary system starts with isolation of a Roux-en-Y loop of jejunum followed by anastomoses of all essential ducts; as an exception, in resection of extent II (above the second confluence resulting in several duct stumps), 1 or 2 particularly small branches may be ligated. Closely situated intrahepatic bile ducts may be joined together by some stitches

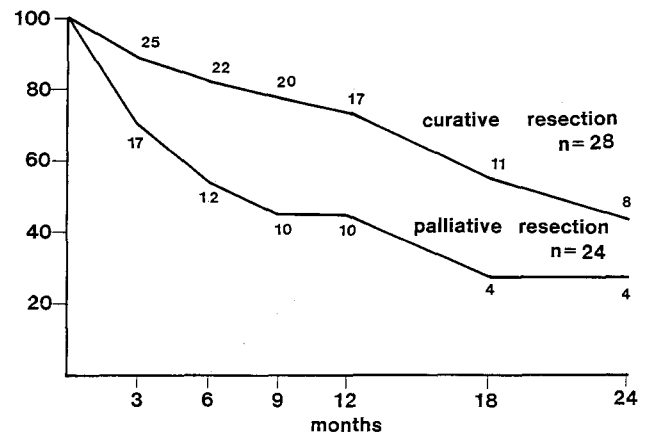


Fig. 2. Survival rates after resection of the hilum alone or in combination with partial hepatectomy in 52 patients with carcinoma of the bile duct bifurcation, according to curative and palliative resections.

to facilitate the anastomosis. A careful mucosa-to-mucosa adapting suture technique is performed. Transhepatic stenting of the lumina (at least of the main trunks) is used for about 2–3 weeks.

Results

In patients with unresectable tumors, if the operation had to be confined to laparotomy or to a surgical drainage procedure, usually the far advanced tumor stages and reduced general state of the patient resulted in a high operative mortality rate (50% and 29%, respectively), and a short median survival time (1 month and 5 months, respectively). Survival was assumed to be prolonged in a few patients treated by endoluminal irradiation (these results have not been evaluated any further.)

Hilar and Combined Liver Resection

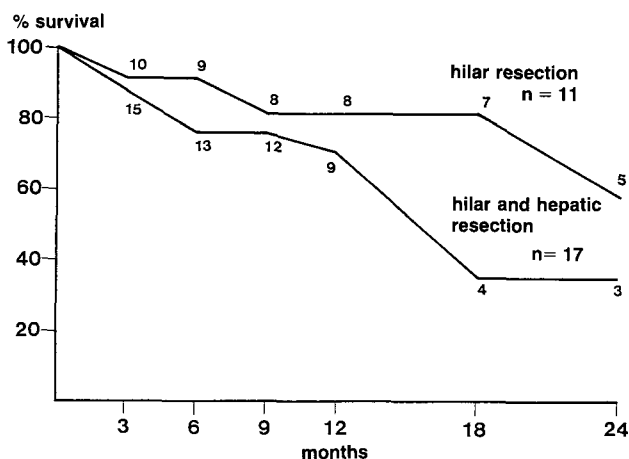
Overall mortality rate (60 days) of all resected patients was 17%. Resection of the hilum combined with partial hepatectomy did not show a significantly higher mortality than resection of the hilum alone (Table 5). The main causes of early mortality were bile leakage with prolonged complications and hepatic failure, some of them presumably because of complications of hepatic artery reconstruction. The median survival time of the hilar resected patients and hilar/hepatic resected patients was 22 months and 14 months, respectively. Curatively resected patients evidently had a better prognosis than palliatively resected patients: the 2-year survival rates were 44% versus 28% (Fig. 2).

Stratification of the curatively treated patients into subgroups according to the extent of resection resulted in a median survival of 35 months of hilar resection alone versus 16 months for resection with partial hepatectomy (Fig. 3). Two patients who had pre- or intraoperatively suspected adenocarcinomas proved to have carcinoid tumors of the bile duct after postoperative histological examination. These patients are not included in the results: one of them is still alive and tumor free 7 years after resection of the hilum (extent II, both sides), and the other is alive 6 months after extended left hepatectomy and

Table 5. Operative mortality (60 days) and median survival time in 108 patients with proximal bile duct carcinoma.

	No. of patients	60-day mortality (%)	Median survival time (mo)
Laparotomy only	10	50	1
Drainage procedures ^a	28	29	5
Resection	—	17	—
Of the hilum only	25	16	22
Of the hilum combined with partial hepatectomy	27	18	14
Curative resections	28	7	23
Palliative resections	24	29	7
Transplantation	16	25	16
Total	108	24	9

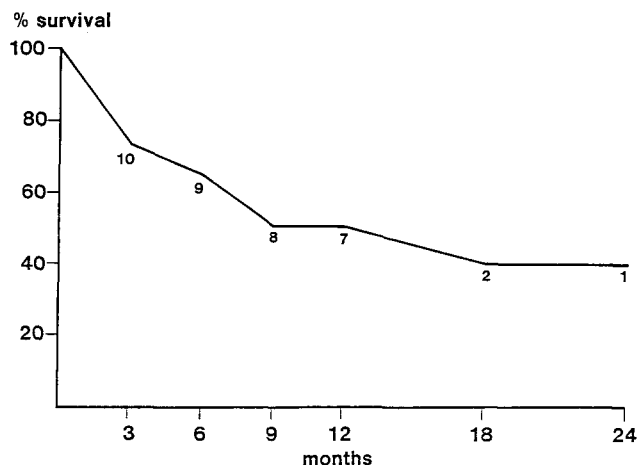
^aNo follow-up was obtainable for 2 patients with drainage procedures, including exploratory laparotomy plus PTCD.

**Fig. 3.** Survival rates of 28 patients with curatively resected proximal bile duct carcinomas, according to procedures performed.

resection of the hilum (extent II, right side, combined with partial duodenopancreatectomy because of lymph node metastases around the head of the pancreas, and portal vein reconstruction).

Transplantation

Previous history, tumor stage, and outcome of liver-grafted patients are summarized in Table 4. The causes of early posttransplant mortality in 4 of 16 patients were hemorrhagic shock, rejection, septic shock, and acute graft failure. In the long-term follow-up, 4 patients died, due to tumor recurrence, between 4 and 27 months postoperatively. Only 1 patient died 10 months after transplantation because of chronic rejection (LTX no. 16). Tumor recurrence developed either within the liver itself or intraperitoneally. One patient was found to have peritoneal metastasis leading to intestinal obstruction 1 year after transplantation. He is still alive and free of symptoms at 14 months (LTX no. 167). In 15 of 16 liver recipients with a follow-up of more than 3 months, the median survival time was 16 months. The actuarial 1- and 2-year survival rates are 51%, and 40%, respectively (Fig. 4). At the moment, 7 patients are

**Fig. 4.** Survival rates in 15 liver transplantation patients with carcinoma of the bile duct bifurcation (minimum follow-up: 3 mo).

still alive and well, survival ranging from 2 weeks to 22 months, 6 of them without signs of tumor recurrence. In spite of tumor recurrence, general rehabilitation can be declared as good or excellent in the majority of patients.

Discussion

In the past, most proximal bile duct carcinomas, especially tumors located in the central hilar area, have been considered to be technically unresectable, and attempts at resection appeared to be highly dangerous. Advances in liver surgery during the last 2 decades opened the field for resection of hilar structures. Thus, recently, even bile duct tumors located in the region of the hepatic duct confluence turned out not to be technically unresectable in principle. The fundamental descriptions and publications by Klatskin [1], Longmire et al. [3], Bismuth and Corlette [7], Iwasaki et al. [11], Launois et al. [12], Todoroki et al. [8], Evander et al. [13], and Blumgart et al. [14] should be mentioned. The arguments against resectional therapy are listed below.

1. The distances, which can be obtained between tumor and resection lines, are inadequate for surgical radicality.
2. Palliative, particularly nonsurgical drainage procedures, eventually combined with external or internal irradiation have been shown to offer good palliation and even prolongation of life with a lower mortality rate in comparison with surgery in a considerable number of patients [15, 16]. On the other hand, resectional therapy seems to be justified by the fact that some of these tumors, which are characterized by the richness of fibrous tissue, apparently do not infiltrate adjacent structures aggressively and are sharply delineated. Resection, in contrast to the aforementioned drainage procedures, may give the chance for cure. Perhaps, more realistically, an asymptomatic period with good rehabilitation and without external tubes can be obtained in the majority of patients.

Apart from the fact that each method has its specific limitations, it seems impossible at present to compare the results and benefits of the different approaches, unless they would be applied under equal conditions, particularly in comparable






Classification [7]	Surgical approach
Type I 	Resection of the hilum, extent II, both sides Evtl. extent I, left side (?)
Type II 	Resection of the hilum, extent II, both sides Alternative (preferred): Left hemihepatectomy combined with resection of the hilum, extent II, right side Alternative: segment IV resection combined with resection of the hilum, extent II, both sides
Type III Left side 	Left hemihepatectomy (evt. extended left hemihepatectomy) combined with resection of the hilum, extent II, right side
Type III Right side 	Right hemihepatectomy (evt. extended right hemihepatectomy) combined with resection of the hilum, extent II, left side
Type III Both sides 	Irresectability Evtl. indication for liver grafting

Fig. 5. Types of resection in patients with proximal bile duct carcinoma.

tumor stages. Thus, superior results by resectional treatment over those by palliative drainage procedures—as shown in our experience—are, of course, strongly influenced by differences in tumor stages or tumor characteristics which, in the case of palliative drainage, did not permit any kind of resectional therapy at all. Randomized trials in patients suitable for both kinds of therapy are, to our knowledge, lacking, and might be disputable. Although there are no controlled studies, resectional therapy may prove to be the treatment of choice, particularly if more long-term survivors and presumably cured patients will be observed. But these data are not sufficient at the moment to be entirely conclusive. The relatively short history of resectional treatment and the limited experience of all groups engaged in this field [17–24] and of our own [25] have to be considered here. For further clarification, it seems reasonable to promote resectional therapy because of the potential advantages mentioned above (Fig. 5).

Recurrence after curative resection may demonstrate that the individual tumor cannot be cured by radical surgery in every case. This will be true, in fact, for a large number of adenocar-

cinomas of the hilar bile duct system already advanced at the time of diagnosis. This will also be true in the majority of patients with lymph node metastasis or in the diffuse, infiltrating tumor types according to Todoroki et al. [8]. But local recurrence may also indicate that local surgical radicality was insufficient. It is our impression that during the period of growing experience, the degree of radicality could be enhanced. This is particularly true for the combined resectional approach, i.e., hemihepatectomy and contralateral hilar resection of extent II. We now strongly advocate this combined resectional treatment at least in all tumors of Bismuth type III, but also in Bismuth type II cases. Frequently, in this type of tumor, the spread shows some accentuation to one side, which would then be the preferred side for liver resection. If no predominance on either side is obvious, a left hemihepatectomy might be indicated. The loss of liver tissue is, in most cases, tolerable, and the access to the hilar structures on the right side is facilitated. Division of bile ducts on the right side can be performed easily above the second bifurcation, liver parenchyma of the right side adjacent to the bile ducts can be included into the resection area, and the access for the proper performance of the cholangiojejunostomy is much better than in a resection of the hilum alone. From the point of view of radicality as well as from the point of view of technical performance, the resection of the caudate lobe, at least of its caudal part, is also included in the resection. In advocating this wide indication for combined resectional therapy, we are in agreement with others, particularly the recent publication of Iwasaki et al. [23].

Both advantages, higher degree of radicality and better access, may also be obtained, to some extent, by resection of segment IV; but technically, this type of resection will be more difficult and the gain in radicality will perhaps be somewhat less than that by left hepatectomy including segment IV. Thus, we favor the combined resection procedures summarized in Fig. 1.

The second critical region regarding radicality is the connective tissue around the bile duct system including the essential hepatic vessels. Again, here the combined resectional procedure will add to radicality if the lesion is predominant on one side, which then will be resected. Lymphatic vessels, nerve tissue, and connecting tissue always have to be dissected away from the vessels carefully. Although peritumoral adhesions and scar formation may simply be inflammatory, those and even some true tumorous adhesions can be dissected free, and radicality always remains questionable in these situations. In other situations, deep infiltration of blood vessels makes their separation almost impossible. If, in these situations, a tumor-free segment of blood vessels can be isolated proximally (within the liver), a resection of the infiltrated vascular area with reconstruction (direct anastomosis or autologous graft) may be indicated [26]. As mentioned above, this can be easily performed with portal vein branches, but may be critical with the smaller arterial branches. These are situations in which radicality will hardly be obtained by any extension of the operation or in which the tumor is totally unresectable. Deep infiltration into both liver lobes and tumor invasion of the vessels of both lobes are the main situations that limit resection. Total hepatectomy and subsequent liver transplantation can be considered as the only possibility of radical tumor removal [4]. Under these prerequisites, namely unresectability of the tumor even by aggressive conventional liver surgery, hepatic transplantation

was performed in the series presented here. A variety of conditions caused unresectability: in most cases it was the extent of tumor growth found during laparotomy, but in some patients local recurrence or lack of radicality by previous resectional surgery was the rationale for liver grafting. Although extrahepatic tumor growth and lymph node metastases had been excluded before the decision for transplantation was taken, several of the patients showed advanced tumor stages and metastases during transplantation. The failure to diagnose these metastases before transplantation is partly related to the fact that, in some patients, an exploratory laparotomy had been done shortly before liver transplantation, particularly in those who had already undergone resection.

With the above described aggressive surgical concept of liver transplantation in only truly unresectable cases, it is obvious that, in this particular group of patients, far advanced tumor stages are found. Therefore, tumor recurrence will be the usual fate after liver grafting in bile duct tumors that already have metastasized locally, even if, macroscopically, tumor removal has been achieved radically by transplantation. This became true in almost all of our patients in such a tumor stage. In these patients, death due to tumor recurrence occurred between 4 and 17 months. Palliation—and perhaps some prolongation of life—by liver grafting might have been valuable for those patients, but there is agreement that these tumor stages should be excluded from transplantation. A question remains: whether a solitary positive lymph node within the liver hilum should exclude liver transplantation.

More relevant in the judgment of liver grafting in bile duct carcinomas is the course of patients with unresectable tumors, who did not have metastasis at the time of liver transplantation. Nine of our patients can be classified into this group. Nevertheless, 2 of them have developed tumor recurrence so far (the longest survivor died after 27 months). The other 7 do not show clinical signs of tumor recurrence at present—with the maximum follow-up of 21 months after transplantation. Certainly, this observation period is too short and the number of patients too small to draw any final conclusions about the value of liver grafting in these unresectable patients as compared to palliative procedures. The particularly disappointing results with liver grafting in this disease during the first period of our experience as well as in the experience of Starzl et al. [5] and Calne [27] led to the opinion that patients with bile duct carcinomas should perhaps not be transplanted [28, 29]. In view of our recent experience, this might not be regarded as the final answer.

Moreover, there might also be justification for a different approach to resection or transplantation: the fact that even curatively resected bile duct carcinomas are frequently followed by local recurrence could lead to a more liberal indication for liver grafting including or favoring even potentially resectable cases. Possibly, recurrence could be prevented by total hepatectomy and transplantation in some of these patients. A randomized study between resection and transplantation in patients suitable for both procedures could clarify the question and might be justifiable, but one may doubt if such a study can be performed at present due to: the shortage of grafts; the difficulties of tumor staging, even intraoperatively; and the suspected prevalence of the patients to be treated—if possible—with conventional resection therapy. We suppose that one should at least gain some more experience and precise infor-

Table 6. Present criteria for indication of hepatic transplantation in the treatment of proximal bile duct carcinoma.

Tumor type	Criteria
Unresectable	Deep tumor spread into both liver lobes and respective bile ducts Invasion of essential hepatic blood vessels (not reconstructable or not safely reconstructable)
Residual (histologically or macroscopically)	After a proper resection (without chance of removal of residual tumor by further resection)
Recurrent	After resection, and only if locally confined

Prerequisites: Any extrahepatic/extrahilar tumor growth and lymph node metastases excluded by best possible means—as a rule, by laparotomy (a solitary positive hilar lymph node accepted); no severe systemic infection; acceptable general status for liver grafting (age approximately 55–60 years).

mation with both methods, with extended combined resectional therapy in all potentially resectable patients and with liver grafting in truly unresectable, but potentially curatively treatable patients. At present, we will continue with this restricted indication for liver grafting (Table 6). For these patients, liver grafting is the only chance to become free of tumor, which may justify this procedure as an alternative to purely palliative methods, particularly in the light of improving overall results in liver transplantation reflected in our more recent group of patients.

Résumé

Pour traiter le cancer de la partie supérieure de l'arbre biliaire la stratégie actuelle des auteurs est de procéder à l'exérèse radicale de la tumeur ou de pratiquer une transplantation lorsque la tumeur ne peut être réséquée dès lors qu'il n'y a pas d'extension extra-hépatique du processus tumoral. L'exérèse de la tumeur est effectuée par résection isolée du hile biliaire ou résection associée de la lésion et d'un segment du foie; cette dernière méthode qui s'applique aux cancers plus étendus est recommandée car plus radicale. Leur conception repose sur leur expérience concernant 108 cas opérés de février 1975 à octobre 1986.

Chez 10 malades aucune intervention radicale ou palliative ne put être pratiquée en raison du stade avancé de la tumeur. Chez 30 patients: différentes opérations de drainage furent pratiquées. En revanche, 52 sujets subirent une exérèse: 25 une résection biliaire, 27 une résection du hile associée à une hépatectomie partielle; 28 de ces résections étant considérées comme opération palliative, 24 comme palliative. Seize malades qui présentaient une lésion inaccessible à l'exérèse ont été traités par une transplantation hépatique mais 7 d'entre eux accusèrent ultérieurement une extension extra-hépatique du processus tumoral.

Les temps de survie furent de 1 mois après laparotomie, 5 mois après intervention de drainage, 15 mois après résection, 23 mois après opération dite curative, 7 mois après opération dite palliative, 21 mois après transplantation chez 7 malades. En raison des résultats favorables chez les derniers malades, la transplantation hépatique constitue pour les auteurs l'ultime

chance de traitement radical des patients qui relèveraient autrement d'une opération palliative de drainage du fait de l'importance de la tumeur.

Resumen

Nuestra estrategia actual en el tratamiento del adenocarcinoma de la porción proximal del canal biliar es la resección radical del tumor y, para los pacientes con tumores no resecables, la posibilidad de trasplante hepático si se ha demostrado que no hay crecimiento tumoral extrahepático. La resección tumoral es realizada mediante la resección del hilio solamente o combinada con hepatectomía parcial. Este último procedimiento, que hace posible el tratamiento radical de los estados tumorales más avanzados y que eventualmente logra un mayor grado de radicalidad, es el recomendado. El concepto se fundamenta en la experiencia con 108 pacientes con carcinoma del canal biliar proximal operados entre febrero de 1975 y octubre de 1986.

En 10 pacientes no fue posible realizar procedimiento alguno de tipo terapéutico o paliativo durante la laparotomía debido al avanzado estado del tumor. Diversos procedimientos de drenaje fueron ejecutados en 30 pacientes. Cincuenta y dos pacientes fueron sometidos a resección, 25 con resección del hilio solamente, 27 con resección combinada con resección parcial del hígado; 28 de las resecciones fueron clasificadas como curativas y 24 como paliativas; 16 pacientes con tumores no resecables recibieron trasplante hepático, y en 7 de ellos había crecimiento tumoral extrahepático en el momento del trasplante hepático.

Las supervivencias medias fueron: laparotomía, 1 mes; procedimientos de drenaje, 5 meses; resección total, 15 meses; resección curativa, 23 meses; resección paliativa, 7 meses; trasplante hepático, 16 meses. Siete pacientes se hallan vivos a los 21 meses posttrasplante. Con base en los resultados favorables en el grupo más reciente de nuestros pacientes, el trasplante de hígado como la última posibilidad de remoción del tumor en pacientes que no podrían ser tratados sino mediante procedimientos paliativos de drenaje, puede estar justificado.

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Note added in proof: Since completion of this manuscript, the total number of patients with hepatic transplantation for central hilar carcinoma has been increased from 16 to 20, with a follow-up at present (November, 1987) of at least 3 mo. In dividing these patients into 2 groups, one with (9 patients) and one without (11 patients) infiltrated lymph nodes at the time of transplantation, the following results can be summarized: In the first group, the longest survival was 10 mo, and 4 patients died

due to or with tumor recurrence. There have been 4 early and 1 late death due to other reasons. In the second group, consisting mainly of patients operated on more recently, the postoperative mortality was 1 of 11 patients; 2 patients died due to tumor recurrence 17 and 27 mo, respectively, after surgery; and 8 patients are presently alive, 1 with tumor recurrence 14 mo postoperatively, and 7 without evidence of tumor recurrence 3,

11, 11, 26, 29, 30, and 32 mo postoperatively. Thus, we continue with the protocol of liver grafting in unresectable proximal bile duct carcinoma, but we try to restrict this therapy to lymph node negative tumor stages. Before a final decision on the relevance of liver grafting in the tumor type can be made, it will be necessary to study a larger number of patients for a longer time.