Coll. Antropol. **28** (2004) 1: 317–323
UCD 616.367-006:616-089.168
Original scientific paper

Klatskin Tumor – Results of Surgical Therapy

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A B S T R A C T

Between January 1st 1990 and December 31st 1999, 24 patients affected by Klatskin tumor underwent operation in our department of surgery. According to Bismuth's classification, there were 0 (0%) type I, 5 (21%) type II, 6 (25%) type IIIa, 4 (17%) type IIIb and 9 (37%) type IV tumors. Five patients (21%) were treated by curative resection (group I) while in 14 patients (58%) palliative surgical procedure was performed (group II). In 5 cases (21%) the extension of malignancy did not allowed any procedure (group III). Curative resection for malignant tumors of the hepatic duct bifurcation included wide tumor excision and bile duct resection at the liver hilum (with »wedge« hepatic resection in one patient) and creation of biliary-enteric anastomosis. Palliative surgical procedure included stent insertion. Jaundice was completely relieved in all patients undergoing resection, since 3 patients (21%) after stenting hadn't satisfactory biliary drainage. There was 1 (20%) perioperative death in the group 1, while in group 2, 5 patients (36%) died postoperatively. In this series, the mean postoperative survival of all patients was 16 months. The mean postoperative survival of patients undergoing localized tumor resection with curative intent was 38 months, in contrast to 10 months for those undergoing operative stent insertion. In addition, only 1 patient from group III, in whom only exploratory surgery were performed survived 7 months, while other 4 patients died in the hospital. This retrospective review suggests that aggressive surgical treatment could improve survival and quality of life in patients suffering from Klatskin tumor.

Key words: *Klatskin tumor, cholangiocarcinoma, ERCP (endoscopic retrograde cholangiopancreatography)*

Received for publication April 3, 2003

Introduction

Cholangiocarcinoma is rare tumor with an incidence of 2–4/100,000 per year[1], accounting for less than 2% of all human malignancies[2]. Although this disease can occur at any site in the biliary tree, tumors involving the biliary confluence or the right or left hepatic ducts (Klatskin tumor) are most common and account for 40%–60% of all cases[3,4]. Although the exact cause of Klatskin tumor is unknown, it is believed that gallstones by repeated trauma and chronic inflammation might increase the risk of this disease[5]. In the absence of specific clinical symptoms, early diagnosis is delayed. Usually symptoms like jaundice, pain, and weight loss that are caused by tumor progression, direct the diagnosis towards perihilar tumor[6]. This long asymptomatic course of Klatskin tumor is cause for only 20% resectable patients at the time of diagnosis[1]. On the other hand, surgery offers the only chance for cure and long-term survival because neither chemotherapy nor radiation therapy improves the length or quality of survival[7]. The remaining 80% of patients with advanced unresectable carcinoma have a dismal prognosis with an overall survival rate of only 6–8 months[1]. The main symptom requiring treatment in these patients is jaundice due to extrahepatic biliary obstruction and it can be achieved by palliative procedures like endoscopic, percutaneous and surgical stenting or by surgical biliodigestive anastomosis. The aim of this study is to report the results of 24 patients that were surgically treated for carcinoma at the hepatic duct bifurcation, and by analysis of the literature, to emphasize the progress of the surgical treatment in hilar tumor.

TABLE 1
PRESENTATION OF PATIENTS AT THE TIME OF DIAGNOSIS

Symptoms	% of patients (N=24)
Jaundice	88
Right subcostal pain	36
Pruritus	28
Fever	12
Vomiting	8
Weight loss	8
Steatorhea	8

Material and Methods

We retrospectively reviewed the clinical courses of 24 consecutive patients with the tumor of the hepatic duct bifurcation treated between 1990 and 2000 at the Department of Surgery, University hospital »Sestre milosrdnice«, Zagreb, Croatia. Patients ranged in age from 52 to 84 years (mean: 69 years of age), with 11 women (46%) and 13 men (54%). Clinical presentation was typically that of obstructive jaundice (Table 1). Duration of symptoms before surgery ranged from 5 to 120 days (mean: 28 days). Initial patient assessment included a complete history and physical examination, assessment of general health, and review of imaging studies. Most patients (92%) were referred to us from Department of Internal Medicine with usual radiographic evaluation consisting of a computed tomographic scan in 13 (54%) patients, ultrasound in 19 (79%) and endoscopic retrograde cholangiopancreatography (ERCP) in 12 (50%) patients. Two patients were emergency operated after only abdominal ultrasound examination because of high suspicion on acute calculos cholecystitis and choledocholithiasis. Usual ultrasound and tomographic findings were obstruction of the extrahepatic biliary tract with a decompressed common bile duct and gallbladder, while ERCP revealed cut-off or high grade stenosis of the common hepatic duct at the

level of the hepatic duct bifurcation. In no of these 22 patients there was no evidence of tumor extension within the biliary tree, vascular and nodal involvement or metastatic disease on radiography's images. Therefore all patients in our study underwent exploratory surgery with curative intent. Before surgery, preoperative evaluation with a chest radiograph, routine laboratory studies, and assessment by an anesthesiologist were done in all the patients. At operation full abdominal exploration was firstly performed to exclude disseminated disease. Location of the tumor at the hilum of the liver was identified by palpation. In 5 cases (21%) no procedure could be performed because of disseminated or locally advanced malignancy. Palliative surgical procedure that included insertion of the stent in the left or right hepatic duct was performed in 14 patients (58%). Remaining five patients (21%) underwent curative surgical procedure. In this operation, cholecystectomy was initially performed to expose the hilum. The common bile duct distal to the tumor after dissection from the hepatic artery and portal vein was divided and oversewn following by resection of the entire extrahepatic biliary apparatus together with the tumor, and clearance of all lymph nodes within the hepatoduodenal ligament to the level of the common hepatic artery. Finally, continuity was established by creation of Roux-en-Y biliary-enteric anastomosis to a segment of jejunum. In one patient from this group »wedge« resection of liver metastasis were performed in addition to resection of extrahepatic billiary apparatus. Data were collected from admission record, surgeon's and anesthesiologist's reports, ICU patient's status sheets, blood tests and pathohystologycal examination of the removed specimens. Differences were analyzed by using the student t-test. Values of $p<0.05$ were chosen to identify statistical significance.

Results

The median duration of surgery was 110 minutes. It was longer in the group of patients treated by curative resection (group 1) and this difference was statistically significant ($p<0.001$). 50 % of patients required transfusion of blood products during the surgery and the median blood replacement was 230 (460 to 2030) ml. Although the use of blood products was greater in the resection group than in the patients who did undergo only palliative stenting (group 2), difference was not statistically significant ($p<0.05$). The median hospital stay was 14 days (range 1 to 56 days) and although longer in the resection group, different between the two groups was not significant ($p>0.05$) (Table 2).

According to the Bismuth-Corlette classification of tumor location and extent within the biliary tree, there were total of 0 (0%) BI, 5 (21%) BII, 6 (25%) BIIIa, 4 (17%) BIIIb and 9 (37%) BIV tumors. With regard to surgical procedure, there were 1 (20%) of BI+BII and 4 (80%)

TABLE 2
DIFFERENCES BETWEEN TWO GROUP IN DURATION OF SURGERY, BLOOD REPLACEMENT AND HOSPITAL STAY

	Group 1 (N=5)	Group 2 (N=14)	p
Median duration of surgery (minutes)	260 (170–350)	110 (60–150)	<0.001
Median blood replacement (ml)	920 (460–2030)	780 (570–1320)	>0.05
Median hospital stay (days)	21 (7–30)	14 (4–56)	>0.05

of BIII+BIV tumors in the resection group while in palliative group there were 4 (29%) BI+BII and 10 (71%) BIII+BIV tumors (Table 3).

Fourteen patients had metastatic disease: 4 to the liver, 5 to N2 level lymph nodes, 4 to the liver and N2 lymph nodes, and 1 to the peritoneum, liver and N2 lymph nodes (Table 4). The overall frequency of nodal metastases was 14 (58%).

In the group of patients treated by palliative stenting, complications occurred in 6 (43%) patients: hepatic failure in 4, cerebrovascular infarction (CVI) in 1 and cardio-respiratory failure in 1. Operative mortality was 5 (36%) (hepatic failure due to stent afunction was the underlying cause of death in 3 patients, massive CVI in one patient and multi-organ system failure in one).

In the resection group, postoperative complications occurred in 1 (20%) patient who died because of sepsis and multi-organ system failure. Thus operative mortality in this group was 20%.

Mean survival for all patients was 16 months (range: 2 to 51 months; median: 10 months). Mean survival in the resection group (n=5) was 38 months (range: 18 to 51 months; median: 45 months). For patients treated by palliative procedure (n=14) mean survival was 10 months (range: 2 to 30 months; median: 5 months). In addition, only one patient who underwent only exploration (n=5) survived 7 months after discharging from hospital, while other four patients died in the hospital immediately after surgical exploration.

TABLE 3
BISMUTH-CORLETTE CLASSIFICATION OF TUMOR LOCATION AND IT'S EXTENSION WITHIN THE BILIARY TREE

	Group 1 N=5 (%)	Group 2 N=14 (%)	Group 3 N=5 (%)
B I	0 (0)	0 (0)	0 (0)
B II	1 (20)	4 (28.6)	0 (0)
B IIIa	1 (20)	5 (35.7)	0 (0)
B IIIb	1 (20)	3 (21.4)	0 (0)
B IV	2 (40)	2 (14.3)	5 (100)

Discussion

Klatskin tumor has been recognized as one of the most incurable lesions and most difficult management problems faced by surgeons because of its anatomic location close to vital structures[8]. It is slow-growing tumor that is localized, sclerotic, hypocellular, and intramural, and rarely reveals preoperative evidence of metastatic disease. A variety of preoperative imaging modalities have been used to assess patients with this tumor. Unfortunately, even after extensive preoperative evaluation, occult unresectable disease is discovered at the time of exploratory laparotomy in more than 50% patients, respectively[9]. Tumor involvement of the portal venous system is most im-

TABLE 4
NUMBER (%) OF PATIENTS WITH DISTANT METASTASES

	Group 1 N=5 (%)	Group 2 N=14 (%)	Group 3 N=5 (%)
Total	2 (40)	7 (50)	5 (100)
N2 lymph nodes	1 (20)	4 (29)	0 (0)
Liver	1 (20)	2 (14)	1 (20)
N2+liver	0 (0)	1 (7)	3 (60)
N2+liver+peritoneum	0 (0)	0 (0)	1 (20)

portant determinant for irresectability, which can often be assessed by duplex Doppler US with accuracy of 91% compared with surgical findings. Helical CT is not so effective and it's accuracy in assessing of biliary extrahepatic and vascular involvement is about 60%[9]. Some authors have brought staging laparoscopy like preoperative procedure that correctly identifies the majority of patients with unresectable disease and prevents unnecessary laparotomy in one third of patients[10,11]. In our series, preoperative imaging studies usually consisted of a CT scan, abdominal ultrasound and ERCP were done in 22 patients (two patients were emergency operated). In all patients diagnostic evaluation revealed obstruction or stricture of extrahepatic bile duct with no evidence of locally advanced or metastatic disease. Thus, all patients in our study were candidates for curative resection.

Treatment of obstructive jaundice due to Klatskin cancer relieves pruritus, improves appetite, and reduces fat malabsorption[12]. Since Gerald Klatskin[13] in 1965 noticed increased duration of survival from 10 months to 23 months in patients who underwent successful decompression, over the years aggressive surgical therapy for this tumor has changed. The disappointing outcome in patients with Klatskin tumor arises from the difficulty in completely excising of the tumor. Because of high propensity to spread proximally and distally within the bile duct system[14,15], it is common for these tumors that surgical margins demonstrate residual microscopic tumor with perineural or perivascular invasion. In our research positive surgical margins were found in 1 (20%) of 5 patients treated by curative resection and this patient survived 18 months after curative resection.

According to Bismut et al[16] microscopic involvement of the resection margin is the most important prognostic factor, while local lymph node involvement does not influence patients' outcome and survival after curative resection for Klatskin tumor. In view of this poor prognosis and the likelihood of recurrent disease, palliative therapies have been advocated. These include surgical palliation by creation of bilioenteric anastomosis or operative stent placement and nonsurgical palliation by placing stents endoscopically or with radiologic guidance. Unfortunately, these modalities fail to improve survival despite temporary relief of the biliary tract obstruction.

Several authors have demonstrated significantly prolonged survival when resectional therapy is included in the treatment regiment[17,18]. In Childs' study, mean postoperative survival rates was 21.3 months in the group resected for cure and 12.4 months in those resected with palliative intent (resection margins were involved with tumor on pathologic examination)[18].

In our study, mean postoperative survival for patients treated by curative resection was 38 months and 10 months for patients treated by operative stent insertion. These data clearly demonstrates the impact of curative resection of all visible tumor with an en block lymphadenectomy on survival in patients suffering from Klatskin tumor. Although this procedure significantly prolonged duration of surgery (260 min. vs. 110 min.), incidence of postoperative complications (20% vs. 43%) and operative mortality (20% vs. 36%) were higher in palliative group.

Controversy exists as to whether more radical resection, including hepatic lobectomy is indicated for treatment. Hepatic resection is often performed in order to obtain microscopic tumor-free margins and curative resection. Siewert et al.[19] achieved 54.8% R0 resection in 31 patients treated by extended, local and hepatic resection. Two-and five-year survival rates in his study were 53.9% and

24.5%, respectively. Lygidakis et al.[20] in his study compared results between local and extended procedure that included hemihepatectomy. Mean survival in patients treated by local resection was 29 months and 5-years survival rate 10% compared with 39 months and 20% for those patients treated by hemihepatectomy. Therefore, combined tumor and liver resection is associated with better results when compared with those following tumor resection alone. According to Kawarada and Gadzijev[21] in some patients, hilar bile duct carcinoma can easily spread to the bile duct branches of the caudate lobe as well as to the bile duct branches of the medial segment depending on anatomical variations of these structures, and resection of the inferior portion of the medial segment together with a caudate lobectomy is then required for curative resection.

Many clinical trials showed prolonged patency in expandable biliary stent used to treat low-or distal-bile duct obstruction, but not in cases of obstruction by a tumor involving the proximal biliary system at or above the bifurcation of the right and left hepatic ducts[22]. In our study operative stent insertion had a limited effect on long-term palliation and equally had a low successful drainage rate. Namely, in 3 (21%) patients from palliative group progressive hepatic failure due to complete stent afuncion resulted in death.

It is noteworthy that patients in our study were not treated by preoperative biliary drainage, and this fact may explain low operative morbidity and mortality rate especially in resection group. This is in accordance with findings of MacPherson et al.[23] who found increased operative mortality and postoperative infections complications, in previously drained patients undergoing resection of proximal bile duct cancers. In contrast, preoperative ERCP were performed in 12 (50%) patients and following this procedure we noticed one case of cholangytes. Thus, incidence of cholangytes after the ERCP procedure was 8.3% in our study.

In conclusion, results of our study show that aggressive surgical treatment could improve survival in patients suffering from Klatskin tumor. The major weakness of this study is a small number of patients operated with curative intent. Therefore conclusions based solely on the statistical significance of the data presented in this study must be critically reviewed. Studies involving larger number of patients are required before definite judgment of the benefit of radical local resection for Klatskin tumor. Based on this study, we favor radical resection of all visible tumor with an en block lymph node dissection of the portal vein and proper and common hepatic arteries to their origin. In the cases of Bismuth III–IV tumors we support additional liver resection for the reason to achieve an RO surgery. This surgical procedure is characterized by high technical difficulties and better results can be reached by hepatobiliary surgical teams[24].

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KLATSKIN TUMOR – REZULTATI KIRURŠKOG LIJEČENJA

S A Ž E T A K

U razdoblju od 1. siječnja 1990. do 31. prosinca 1999. godine u našoj Kirurškoj Klinici operirano je ukupno 24 bolesnika s Klatskinovim tumorom. S obzirom na Bismuthovu klasifikaciju proširenosti tumora, nijedan bolesnik u našoj studiji nije imao tumor I. stupnja proširenosti, dok je u 5 (25%) bolesnika tumor bio u II. stadiju, u 6 (25%) bolesnika u III.a, u 4 (17%) bolesnika u III.b te u 9 (37%) bolesnika u IV. stadiju bolesti. 5 (21%) bolesnika bilo je podvrgnuto radikalnom operacijskom zahvatu (Grupa I) dok je kod 14 (58%) bolesnika bio učinjen samo palijacijski kirurški zahvat (Grupa II). U preostalih 5 (21%) bolesnika uznapredovalost tumora nije dozvoljava bilo koji oblik kirurškog zahvata. Radikalni kirurški zahvat sastojao se od široke resekcije tumora i žučnih vodova (uz »wedge« resekciju jetrene presadnice kod jednog bolesnika) te kreiranja bilio – digestivnih anastomoza. Palijativni kirurški zahvat sastojao se od intraoperativnog postavljanja stenta u desni ili lijevi jetreni vod. Ikterus kao vodeći simptom većine naših bolesnika, u potpunosti se povukao u svih bolesnika operiranih radikalnim kirurškim zahvatom dok kod 3 (21%) bolesnika nakon postavljanja stenta nije došlo do uspostave zadovoljavajuće bilijarne drenaže. Jedan bolesnik iz grupe 1 (20%) te 5 bolesnika (36%) iz grupe 2 umrla su u postoperativnom periodu. Ukupno srednje preživljenje naših bolesnika je 16 mjeseci. Za bolesnike operirane radikalnim kirurškim zahvatom srednje vrijeme preživljenja iznosilo je 38 mjeseci u odnosu na 10 mjeseci u bolesnika operiranih palijativnim kirurškim zahvatom. Od 5 bolesnika iz grupe III, četiri bolesnika su umrla tijekom postoperativnog perioda dok je samo jedan bolesnik preživio 7 mjeseci. Rezultati ove retrospektivne studije upućuju na zaključak da radikalni kirurški zahvat u bolesnika s Klatskinovim tumorom produžuje preživljenje i poboljšava kvalitetu života.