Liver resections for hilar cholangiocarcinoma

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Abstract. – Hilar cholangiocarcinoma (HC) is a rare tumor which has to be distinguished by intrahepatic cholangiocarcinoma invading hepatic hilum because the former has better prognosis than the latter. Patients with HC are difficult to manage because many challenging issues remain in the treatment of this tumor regarding correct diagnosis and therapeutic strategy. HC is resectable in about 30% of cases, but operative risk is highly influenced by septic complications of preoperative biliary drainage and by the need of major liver resection associated with biliary resection. We report the results of 43 resected patients (28 M/15 F; mean age 60 years, range 33-78), accounting for 29% of 149 patients with HC. Symptomless jaundice was the most common clinical presentation (87%; 130 patients). Biliary stricture was classified according to the Bismuth-Corlette classification as type 1 in 3 patients (7%); type 2 in 12 patients (28%); type 3 in 28 patients (65%). Ten patients underwent preoperative right portal vein embolization. Main biliary confluence excision associated with major hepatectomy was performed in 40 patients (93%), with R0 resection rate by 77%. Postoperative mortality rate was 6.9% (3 patients). Morbidity rate was 52.5% (21 patients), being biliary fistula (38%) and liver failure (19%) the most frequent complications. Five-year overall and disease-free survival rate were 36.1% and 28.2, respectively.

Surgical resection remains the only chance of cure for patients with HC. However, due to the complexity of surgery immediate results remain unsatisfactory with morbidity and mortality rates higher than those reported after liver resection for other malignancies. This is mainly related to septic complications, strictly linked to complications of preoperative biliary drainage. Selective biliary drainage, careful management of biliary drains, drainage of excluded ducts in case of cholangitis, bile culture guided antibiotic use and preoperative portal vein embolization are important factors to reduce the risk of cholangitis and of postoperative complications. Because of the significant perioperative risk, the demanding operative management and the rarity of this tumor, patients with HC should be referred to tertiary surgical centers.

Key Words: Hilar cholangiocarcinoma, Liver resection.

Introduction

Cholangiocarcinoma is a rare malignancy that can occur anywhere along the intrahepatic or extrahepatic biliary tree. The main biliary confluence is the most frequently involved site (around 70%)1. Cholangiocarcinoma arising here has been called hilar cholangiocarcinoma (HC) or Klatskin tumor2. However, as the boundary between the extrahepatic and intrahepatic bile ducts is unclear, cholangiocarcinoma which involves the hepatic hilum potentially includes two types of tumour: extrahepatic hilar cholangiocarcinoma, arising from the main biliary confluence, and intrahepatic hilar cholangiocarcinoma, which involves the hepatic hilum3. According to the Johns Hopkins classification these two types of tumors were defined as “perihilar tumors”, because they involve or require resection of the main biliary confluence1. However differentiating between these two categories is mandatory because it impacts the prediction of postoperative survival. Indeed the overall survival of patients with HC is significantly better than that of patients with intrahepatic cholangiocarcinoma involving the hepatic hilum3. Criteria to discriminate between these two types of neoplasm are: dominant location of the tumor which can be evaluated by histological examination of tumor location, whether inside or outside of hilar plate, and size of the tumor because Klatskin tumors never present size >5 cm.

Surgical resection is the only chance of cure for these patients with 5-year overall survival rate reported to be about 40%-1.

The primary goal of surgical treatment should be complete resection of the main biliary conflu-
ence with clear histologic margins. Addition of major hepatectomy has increased the proportion of R0 resections. Several reports have demonstrated improved survival in patients undergoing R0 resections after major hepatectomy and worse outcome in patients undergoing bile duct excision alone. Furthermore, the caudate lobe is often involved by either direct invasion or ductal extension. For this reason, several studies have shown a decrease in local recurrence and improvement in 5-year survival, when concomitant caudate lobe resection is performed.

Patients and Methods

Inclusion criteria of our study were patients with hilar cholangiocarcinoma managed at our Unit between 1992 and 2008. Patients with intrahepatic cholangiocarcinoma invading the hepatic hilum were excluded from this analysis.

The ideal strategy used in our unit is based on absolutely avoidance of biliary drainage before staging of the tumor. However 45% of patients with HC managed in our Unit underwent biliary drainage before referral and before complete imaging staging. All patients underwent staging of the tumor by abdominal computed tomography (CT) in order to evaluate portal vein involvement and liver volumetry, and by magnetic resonance cholangiopancreatography (MRCP) in order to predict the extent of bile ducts involvement.

Bile duct tumor extent was stratified according to the Bismuth-Corlette classification: Type 1, tumor below the main biliary confluence; Type 2, tumor occluding the main biliary confluence; Type 3A and 3B, tumor occluding the main biliary confluence and the second order bile duct branches of the right side or of the left side; Type 4, tumor occluding the main biliary confluence and the second order bile duct branches bilaterally.

According to Memorial Sloan-Kettering Cancer Center Classification, criteria for unresectability were: bilateral involvement up to secondary biliary radicles; encasement of the main portal vein proximal to its bifurcation; atrophy of one hepatic lobe with encasement of contralateral portal vein branch or with contralateral involvement of secondary biliary radicles; distant metastases.

All patients classified as resectable at radiologic imaging underwent staging laparoscopy before surgery. After staging laparoscopy, percutaneous unilateral biliary drainage for the future remnant liver was performed in resectable patients who did not undergo biliary drainage before referral. Resection was performed when total bilirubin levels were about 3 mg/dL.

Patients with “right sided” hilar cholangiocarcinoma with future remnant liver volume <40% underwent preoperative right portal vein embolization. The hypertrophy of the non-embolized hemiliver was assessed by CT volumetry 4 weeks after portal vein embolization.

Results

Between 1992 and 2008, 149 consecutive patients with HC were managed at our Unit. There were 87 males and 62 females (mean age 64 years, range 33-90).

Obstructive jaundice was the most common symptom (87%; 130 patients). Out of these patients, 67 (45%) underwent biliary drainage before referral (38 patients underwent endoscopic biliary drainage and 29 percutaneous). Biliary drainage in such patients was performed without preliminary radiologic staging of the tumor and rate of acute cholangitis was 61% (41 patients).

Forty-three patients were finally resected and the resectability rate was 29% (43/149). There were 28 males and 15 females (mean age 60 years, range 33-78). Ten patients underwent preoperative right portal vein embolization. Biliary stricture was classified as Type 1 according to the Bismuth-Corlette classification in 3 patients (7%); as Type 2 in 12 patients (28%) and as Type 3 in 28 patients (65%).

Main biliary confluence excision associated with major hepatectomy was performed in 40 patients (93%), extended to the caudate lobe in 27 patients.

Mortality rate was 6.9% (3 patients). Cause of death in these patients was postoperative sepsis with subsequent multiple organ failure (MOF). Mortality rate was higher in patients who presented preoperative acute cholangitis than in patients who did not (16% vs. 0, respectively).

Morbidity rate was 52.5% (21 patients): biliary fistula 38.5%; transient liver failure 19.2%; subphrenic abscess requiring percutaneous drainage 15.4%; sepsis 15.4%; pleural effusion requiring thoracentesis 11.5%.
At pathology rate of clear histologic margins (R0 resection) was 77%. The caudate lobe was invaded in 44% of cases. Lymph node involvement was present in 23% of patients.

Five-year overall and disease-free survival rate were 36.1% and 28.2, respectively.

Conclusion

Patients with HC have a chance of cure after surgical resection which remains the mainstay of treatment of this tumor. Major hepatic resection combined with bile duct resection improves the rate of negative resection margins with better long term results, and therefore has been accepted as the standard procedure for this neoplasm.

However, due to the complex biliary and hepatic resections required in this type of tumor immediate results remain unsatisfactory with high morbidity rates, ranging from 40% to 68%, and in hospital mortality rates higher than those reported after resection for all other diseases13. The main cause of such high postoperative morbidity and mortality rates is related to septic complications, which are strictly relative to complications of preoperative biliary drainage. The strategy to reduce the incidences of preoperative cholangitis and therefore postoperative complications is complex and is based on the following: selective biliary drainage, careful management of biliary drainage catheters, drainage of undrained ducts in case of cholangitis, bile culture guided antibiotics use and preoperative portal vein embolization. Because of the significant perioperative risk for complications, the demanding nature of the operative management and the rarity of this tumor, patients are best served by referral to tertiary centers.

References


