

Advances in Surgical Research of Hepatocellular Carcinoma with Bile Duct Tumor Thrombus

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Introduction

Hepatocellular carcinoma (hereinafter referred to as liver cancer) is one of the world's high incidence of malignant tumors. It ranks in the top ten in the world for the incidence of malignant tumors, while China is a large country with liver cancer. More than half of new and dead liver cancer patients occur every year in China [1]. Liver cancer is often accompanied by hepatic portal vein invasion and the formation of portal vein tumor thrombus; but liver cancer with bile duct tumor thrombus is relatively rare in clinical, and the diagnosis is easy to be confused with bile duct stones, BDT, liver failure and other diseases. The literature reports that the incidence of BDT in patients with liver cancer is only 1.2%-9% [2]. Obstructive jaundice often occurs in liver cancer with BDT. This clinical manifestation can assist diagnosis, but BDT with no obstructive jaundice has a low preoperative diagnosis rate and cannot be treated intra-operatively. Caused by intrahepatic recurrence of the tumor, the patient's tumor-free survival was significantly shortened, and the 5-year survival rate was also reduced [3]. Patients with liver cancer and BDT who have been admitted to hospital due to jaundice are still difficult to diagnose and diagnose with diseases such as BDT, bile duct stones, and hilar tumors. In recent years, magnetic resonance examinations have been used to improve the diagnosis rate. The BDT involving the hilar can simultaneously involve the caudate bile duct of the liver, which significantly reduces the surgical resection rate of the BDT [4,5]. At present, patients with liver cancer and BDT have a uniform treatment standard, but there is still no uniform operation. In this paper, we will discuss the surgical treatment of several common liver cancers complicated with BDT from the aspects of bile duct grading and pathological features of BDT.

Bile Duct Grading

The bile duct system is divided into two parts: intrahepatic and extrahepatic, including gallbladder, cystic duct, common hepatic duct, common bile duct, intrahepatic bile duct, and hepatic caudate lobe. For intrahepatic bile duct grading is mainly divided into three levels,

Grade I. Liver tube: Left and right hepatic duct.

Grade II. Hepatic duct: Left inner and outer lobe hepatic duct, right anterior and posterior hepatic duct.

Grade III. Hepatic duct: Left upper liver Tube (section II), left outer lower hepatic duct (section III), left upper hepatic duct (IVa), left inner and lower hepatic duct (IVb), right anterior superior hepatic duct (paragraph VIII), right anterior and posterior segmental hepatic duct (V segment), the right posterior segment of the liver tube (section VI), the right posterior segment of the liver tube (section VII).

It should be noted that the caudate bile duct is open to the left hepatic duct and the right posterior hepatic duct. The caudate BDT or

calculus is often accompanied by stenosis or atresia of the bile duct, so a tail may occur during routine liver or biliary surgery. Missed or residual stones in the BDT, under the general choledocholial incision, if the left hepatic duct is not cut, it is difficult to see the opening of the caudate bile duct, and the missing tumor in the caudate bile duct can cause postoperative recurrence or hemorrhage of the tumor thrombus and biliary hemorrhagic jaundice, or fibrosis and atrophy of the caudate lobe.

Bile Duct Tumor Thrombus (BDT) Classifying

According to the location of the BDT, there are two types of typing that are common in clinical practice.

One is the Japanese Satoh classification, which is divided into three types.

Type I: BDT is located in the upper and lower bile ducts, but not in the confluence.

Type II: BDT extends to the confluence of the left and right hepatic ducts.

Type III: BDT is removed from the primary tumor in the common bile duct [6].

The second is the Ueda classification, which is divided into four types [7].

Type I: BDT is located in the upper and lower bile ducts.

Type II: BDT extends to the primary bile duct.

Type III (a): BDT extends to the common hepatic duct.

Type III (b): Bile duct tumor thrombus in the manner of metastatic tumor in the common hepatic duct.

Type IV: Hepatocellular carcinoma ruptures and hemorrhages to the common bile duct tumor thrombus.

Clinico-pathological Features of BDT

At present, the research on the occurrence and development of BDT is still controversial. The main controversy focuses on the following two aspects:

I. The occurrence of BDT is the invasive growth of tumor tissue from the primary site directly or indirectly invading the bile duct tip, and then continuously grows in the biliary system until the invasion of the extra hepatic bile duct [8].

II. Most of the biliary tumor plugs have no adhesion between the embolus and the bile duct wall, or only one layer of epithelium is attached to the mucosa of the bile duct. Our research team found that

most of the visible BDT plugs were smooth, grayish-white or brown-green polypoid masses. Most of the tumor thrombi were covered with bile duct epithelium [9], therefore, we conclude that BDT may mainly grow in a Paget-like manner [10,11]. Once the BDT is formed, it will “jump” or extend to the distal side, thereby blocking the intrahepatic or extra hepatic bile ducts, and the patient's condition will be further deteriorated, and the prognosis is generally poor [12]. Common features of primary liver cancer with BDT are mainly consistent with the following five points:

- (A) The primary tumor has no more capsules. In the previous case report, the clinical data of large samples found that the liver cancer with BDT was mostly without a capsule, with unclear borders and invasive growth [13].
- (B) The primary tumor is small in size, and some even cannot find the primary tumor [14].
- (C) Liver cancer with BDT, often with vascular invasion [15].
- (D) Primary tumor histology is mostly poorly differentiated [15].
- (E) Invasive, poor prognosis [9,16].

Surgical Methods and Prognosis Analysis

Patients who cannot tolerate liver operation

Severe obstructive jaundice, cholangitis, liver dysfunction, etc. can affect the patient's ability to tolerate surgery. In view of the above situation, conventional non-surgical treatment mainly includes arterial chemoembolization (TACE), biliary stent, radiotherapy, and absolute ethanol injection. However, these treatment methods usually do not improve the condition of such patients. Oba et al., reported that among 25 patients, 1, 3, and 5 year overall survival rates were 14%, 5%, and 0%, respectively [17]; Luo et al., reported that 27 patients who underwent TACE and 40 patients who underwent biliary drainage were 5 years with a total survival rate of 0% [18].

At present, Chinese scholars have reported [19], by radiofrequency ablation, better treatment results were obtained in the case of liver cancer with BDT. Radiofrequency ablation is highly effective, minimally invasive, and safe. It is suitable for patients with cirrhosis and severe obstructive jaundice who cannot undergo surgery in a short period of time. Therefore, radiofrequency ablation is expected to be an effective minimally invasive surgical treatment for visible BDT.

Patient who can tolerate liver operation

At present, the surgical treatment of liver cancer with BDT is mainly based on individualized comprehensive treatment of liver resection. The liver function test, abdominal ultrasound examination, abdominal CT examinations are performed before operation and magnetic resonance cholangiopancreatography can be used for evaluation of the size of the BDT and the extent of the invasion. The choice of specific surgical methods depends on the general condition of the patient, tumor stage, preoperative liver function grading, preoperative diagnosis of primary tumor location, scope of invasion of biliary tract thrombus, and estimation of residual liver parenchyma size and function.

The surgical methods of liver cancer mainly include radical resection, palliative resection, recurrence and resection, and unresectable liver cancer before and after chemotherapy and reduction of tumor resection. The surgical treatment of liver cancer with BDT is

based on the above surgical treatment of liver cancer. However, there is still no specific surgical method for standardization of liver cancer with BDT. Currently, different research centers focus on their centers. Retrospective analysis by patients summed up different treatment experiences. Combined with our research, the current choice of surgical treatment options for liver cancer patients with BDT is mainly concentrated in three aspects: Is there a regular resection of the affected side? Do you need extra hepatic bile duct resection? Is the liver transplant considered if the patient meets the Milan criteria? Therefore, the surgical methods are mainly divided into relatively aggressive surgical methods and relatively conservative surgical methods. The main difference between the two is whether to expand the scope of hepatectomy and whether to combine extra hepatic bile duct resection and whether to remove the caudate lobe of the liver. The study center found that the total recurrence rate of liver cancer patients with BDT with bile duct preservation was as high as 67%. At the same time, we also found that patients in the conservative treatment group had a postoperative tumor recurrence rate of 77.8%, which was significantly higher than the 36.8% recurrence rate in the relative radical treatment group; the follow-up period of 1-90 months showed that the conservative treatment group 1, 2 The 3 year overall survival rate was 54.5%, 15.2%, and 0%, respectively, which was significantly lower than the overall survival rate of the radical treatment group (73.3%, 61.5%, 35.2%) [10,20].

Hee et al., reported [21], for patients in their medical center, the overall median survival time, overall survival, and tumor-free survival of patients undergoing hepatectomy and extra hepatic bile duct resection were significantly higher than those with bile duct incision. The median time to recurrence was significantly lower in the conservative surgery group. Hee et al., pointed out that the most important cause of recurrence is that the tiny bile duct cancer plug jumps into the bile duct wall. Patients with long-term survival after surgery, have four main characteristics; first is that these patients are young patients, the primary liver cancer is in the early stage and the patient's liver function is good; Secondly, the preoperative AFP and other indicators are not high; In addition, these patients performed a relatively radical approach, namely, hemi-hepatic resection+extrahepatic bile duct resection+caudate lobe resection; finally, postoperative pathology suggests that the tumor invasion mode of these patients is extended rather than jumping infringement. Based on the theory of mitral metastasis of BDT, Hee et al., summarized the “jaundice-type liver cancer” for the treatment of liver cancer with BDT. The most effective method is hemihepatectomy+caudate lobe resection+extrahepatic hepatectomy [21].

It is still controversial whether liver transplantation can be performed in patients with liver cancer with BDT. So far, only a few medical centers around the world have reported on liver cancer cases treated with liver transplantation for BDT [22-24], in one of the reports, four patients who underwent liver transplantation died of liver cancer recurrence within three years; other reports have similar conclusions. In 2012, our research team reported a 42 year old male patient with previous history of hepatitis B virus cirrhosis, liver cancer, left hepatectomy, tumor recurrence in five years after surgery, and radiofrequency ablation of two right recurrences in the right liver. Surgery, magnetic resonance examination found that the patient has lesions in the common bile duct, intrahepatic bile duct dilatation is obvious, the patient's liver function is poor, and it is considered to be treated by liver transplantation. By preoperative hemodialysis and other methods, the patient's bilirubin was reduced to the safe range of surgery. During the liver transplantation operation, we found that the

patient's common bile duct was full of tumor thrombus and was not directly related to the right hepatic lobe recurrence. At 21 days after liver transplantation, serum alpha-fetoprotein levels returned to normal levels. After the patient was discharged from the hospital, he or she was regularly returned to the hospital for review. After the follow-up, the patient survived for five years without tumor [25]. Therefore, liver transplantation for patients with BDT is an effective treatment, but there is still a high risk of liver cancer recurrence.

Summary

Since the first report of "jaundice type liver cancer" in 1949, it has been a controversial type of liver cancer. Their diagnosis, patient treatment, and prognosis after hepatectomy have been the subject of speculation and discussion. Patients who received only symptomatic treatment and palliative surgery such as "reducing yellow" had a poor prognosis, with a median survival time of less than 5 months [16]. Therefore, surgical resection is the only option to increase the survival time of such patients.

The incidence of liver cancer with BDT is not high, but its prognosis is poor. Although surgery is the only option for radical treatment, there is still much debate about the specific surgical approach and techniques. In most patients with liver cancer with BDT, hepatectomy is performed only in selected patient populations due to differences in liver function and cirrhosis. However, hepatic resection still has intrahepatic bile duct recurrence, which makes the surgeon need to consider the choice of the initial surgical approach, whether to expand the resection range, such as the removal of extra hepatic bile ducts.

In the past, most of the research focused on tumor invasion in the bile duct, such as the invasion of grade I and II bile ducts. On the contrary, there are few studies on tumor invasion of grade III bile ducts. Some scholars have concluded through retrospective analysis that whether the removal of extra hepatic bile ducts has no significant effect on the survival rate of patients. This view is biased. Is the inclusion criteria uniform in the process of retrospective analysis? Are multiple types of BDTs included in the analysis? If the BDT only affects grade I and grade II bile ducts, although the extra hepatic bile duct is not removed, the regular bile duct resection has been extended when regular hepatectomy; if the BDT involves the grade III bile duct, the patient is often accompanied by the hilar invasion of arteries and veins, obstructive jaundice, etc., the overall prognosis of this type of patients is poor, the effect of resection of extra hepatic bile duct on the prognosis of patients should be analyzed separately. Retrospective analysis of bulk data, comparing all types of BDT, we believe that if the patient's liver function is good, should be actively undergoing hemi-hepatic resection, extra hepatic bile duct resection and caudate lobe resection; liver cancer with BDT often accompanied Obstructive jaundice, it is difficult to assess the patient's liver function reserve before deciding the treatment plan. Conversely, if the patient's liver function cannot tolerate surgery, bile duct drainage and bile duct stent placement should be performed in time for hepatic artery embolization.

According to our previous study, the growth process of BDT may be skip growth and may extend to the contralateral and or distal extension. Despite the continuous improvement in imaging methods, it is still difficult to find out whether liver cancer patients have a small BDT. Combined with the results of multicenter studies, the tiny tumor thrombus of the distal bile duct is a detrimental factor affecting the prognosis of patients with liver cancer [12].

Regardless of domestic or foreign research, all of them are small-scale single-center retrospective studies. The total number of cases is still small. In the research process, the inclusion criteria of the analysis indicators are different. The analysis process often has bias and bulk data analysis. The comparison of all types of BDT and different surgical procedures is an important means of reducing bias.

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