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SURGICAL METHODS AND PROGNOSTIC ANALYSIS OF ACCIDENTAL DISCOVERYOF BILE DUCT STONES AND CHOLANGIOCARCINOMA

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ABSTRACT

Obejective: To investigate the surgical plan and curative effect analysis of cholangiocarcinoma accidentally discovered during the diagnosis and treatment of bile duct stones. **Methods:** Through retrospective analysis of 25 cases of bile duct stones admitted to our hospital, patients with cholangiocarcinoma found before or during the operation, the clinical data and relevant laboratory examination and imaging data of the patients were collected, and the surgical patients were classified according to whether the operation was performed or not. For the simple extrahepatic bile duct resection group and the combined liver resection group, the postoperative complications and prognosis of patients with extrahepatic bile duct resection and combined liver resection were compared. **Results:** All 25 patients underwent surgical resection. The surgical resection rate was 100%, of which R0 resection was 88.00% (22/25) and R1R2 resection was 12.00% (3/25). The total postoperative complication rate in the extrahepatic bile duct resection group was 13.63% (3/22), and the total complication rate in the combined hemihepatectomy group was 100% (3/3). Postoperative complications in the extrahepatic bile duct resection group were significantly lower than those in the combined hemihepatectomy group. The R0 resection rate of TNM stage I-II patients was significantly higher than that of stage III-IV (95.6% vs 50%). The RO resection rate of hilar cholangiocarcinoma in Bismuth type I patients was 100% (15/15), the resection rate of type II RO was 75% (3/4), and the resection rate of type IIIa RO was 50% (1/2). In the combined hemihepatectomy group, the type I RO resection rate was 100% (1/1), the type II RO resection rate was 66.66% (2/3), and the type IIIa RO resection rate was 0% (0/0). In the simple extrahepatic bile duct resection group, the R0 resection rate was 90.47% (19/21), and in combined hemihepatectomy or combined hemihepatectomy, the R0 resection rate was 75.00% (3/4). The 3-year and 5-year survival rates of the R0 resection group were significantly higher than those of the R1R2 resection group (P <0.05). **Conclusion:** For patients with bile duct tumors accidentally found due to bile duct stones, full evaluation shouldbe done before surgery. Increasing the R0 resection rate can significantly improve the prognosis of patients.

KEYWORDS: Cholelithiasis, laparoscopic choledocholithotomy, bile duct tumor, cholangiocarcinoma, survival rate.

I. INTRODUCTION

Choledocholithiasis is a common benign biliary disease in hepatobiliary surgery, which is currently treated with endoscopic and interventional techniques.[1] Laparoscopic common bile duct exploration (LCBDE) has become theideal method for the treatment of common bile duct stones.[2,3] In recent years, the number of patients with stone bile duct tumors has increased significantly. When they have obvious symptoms, most of them have advanced to thelate stage of the disease and cannot undergo radical surgery. Therefore, early detection and diagnosis of bile duct tumors should be emphasized.[4,5]

Painless jaundice and abdominal pain are the most common complaints of patients with cholangiocarcinoma. Most patients with cholangiocarcinoma are usually difficult to diagnose and treat at an early stage. The best preoperative evaluation requires multidisciplinary discussion. Surgical resection is currently the main treatment method.Cholangiography has been used for the treatment of bile duct stones and the diagnosis of various bile duct tumors. However, the choledochoscopy characteristics of various types of bile duct tumors are still unclear. At present, surgical resection is the main method for the treatment of cholangiocarcinoma, and the preoperative diagnosis cannot be clear. For cholangiocarcinoma that is suspected before surgery and accidentally discovered during surgery, intraoperative choledochoscopy and biopsy have obvious advantages. We reviewed the diagnosis and treatment of patients with

cholangiocarcinoma after admission or during surgery with bile duct stones, and analyzed postoperative complications and surgical methods to explore the diagnosis and treatment of bile duct tumors accidentally discovered by bile duct stones.

II. MATERIALS AND METHODS

1. General information

The clinical data of 25 patients diagnosed with cholangiocarcinoma and undergoing surgical treatment in the east hospital of Yangzhou affiliated hospital from January 2010 to 2020 were respectively analyzed the diagnosis methods, complication and surgical methods of the patients. We selected patients based on AJCC (American Joint Committee on Cancer, 7th edition) criteria who successfully underwent curative resections. There were 25 patients in the study. Among the 25 patients, 22 patient had local resection of hilar cholangiocarcinoma and 3 patient had a hilar cholangiocarcinoma combined with hemihepatectomy.

Table 1: Basic information of 25 patient.

Personal characteristic	cases	percentages
Age		
≤65	19	76.00%
>65	6	24.00%
Gender		
Male	10	40.00%
Female	15	60.00%
Abdominal pain	19	76.00%
Choledocholithiasis	17	68.00%
Jaundice	12	48.00%
TNM staging	cases	percentages
Stage I	16	64.00%
Stage II	6	24.00%
Stage IIIa-c	3	12.00%
Bismuth Colette typing		
Type I	18	72.00%
Type II	4	16.00%
Type IIIa	3	12.00%

2. Inclusion and exclusion criteria

Inclusion criteria: ①Admission with gallbladder stones or bile duct stones, complete alkaline phosphatase (AF), γ- glutamyltransferase (GGT), total bilirubin (TBI), amylase (AMIL), aspartic acid Laboratory tests such as aminotransferase (AST) or alanine aminotransferase (ALT), as well as abdominal ultrasound suggest bile duct dilation and/or bile duct occupying. ② CT scan of the whole abdomen and MR scan of the upper abdomen + MRCP showed: (i) multiple stones in the bile duct, dilatation of the bile ducts inside and outside the liver, and biliary space occupation; (ii) multiple stones in the gallbladder, chronic cholecystitis.

Exclusion criteria: ①peritoneal metastasis, ②extensive hilar lymph node metastasis, ③bilateral intrahepatic metastasis, ④bilateral bile duct infiltration reaching or exceeding grade 2, ⑤simultaneous infiltration of the left and right liver or right hepatic artery, ⑥direct infiltration and enveloping the main The portal vein or the trunks of the bilateral portal veins are affected by tumors, ⑦ severe heart, liver and kidney insufficiency, ascites and cachexia.

3. Preoperative examination

After admission, all patients underwent laboratory tests and imaging examinations. After eliminating surgical contraindications, no serious heart, liver or kidney dysfunction was found, and surgical treatment was arranged as soon as possible. For patients with high preoperative serum bilirubin levels (TBIL> 170umol) or long duration of obstruction (> 2 weeks), percutaneous transhepatic biliary drainage can be used to relieve the symptoms of obstruction and reduce total bilirubin (TBIL < 100umol). Among them, 18 patients (72.00%) had elevated CA19-9 (>31u/ml), and 11 patients (44.00%) had elevated CEA (>3.06ng/L). Among the 25 patients, 14 had CT positive or suspected positive tumors (56.00%), and 13 had MRI positive tumors (52.00%). The results of abdominal CT and upper abdominal MR scan + MRCP are roughly as follows: (1) Multiple bile duct stones, intrahepatic and extrahepatic bile duct dilation; (2) Multiple gallstones, chronic cholecystitis; (3) Hilar bile duct Occupation is possible, see Table 2. Finally, 22 cases underwent extrahepatic bile duct resection, and 3 cases in the combined hemihepatectomy group.

Table 2: Pre-operative investigation of 25 patient.

Personal characteristic	cases	percentages
CT Positive or suspected (+)	14	56.00%
MRI Positive or suspected (+)	13	52.90%
USG	15	60.00%
MRCP	16	64.00%
CEA Increased	11	44.00%
CA19-9 Increased	18	72.00%

4. Surgical contraindications

Contraindications: ① peritoneal implantation metastasis, ② extensive hilar lymph node metastasis, ③ bilateral intrahepatic metastasis, ④ bilateral bile duct invasion of grade 2 or above, ⑤ simultaneous invasion of left and right hepatic artery or proper hepatic artery, ⑥ direct invasion and wrapping of main portal vein or bilateral portal vein trunk by tumor, and ⑦ severe cardio hepatic renal insufficiency, ascites and cachexia. It is suggested that surgical treatment should be arranged as soon as possible if no severe cardiac, hepatic or renal insufficiency is found in the preoperative examination after excluding surgical contraindications. For patients with high preoperative serum bilirubin level (TBIL > 170 umol) or long duration of obstruction (> 2 weeks), percutaneous trans hepatic biliary drainage can be used to relieve the symptoms of obstruction, and the operation can be performed after the decrease of total bilirubin (TBIL < 100 umol).

5. Surgical approach

Take a reverse "L" incision in the right upper abdomen and enter the abdomen layer by layer to explore the tumor size, scope, vascular invasion, intrahepatic metastasis and invasion of the second hepatic portal. Excluding distant metastases outside the lymph nodes, radical resection was confirmed during the operation, followed by Bismuth Colette classification. According to the extent of tumor invasion of bile ducts and blood vessels and the preoperative liver reserve function, hemihepatectomy should be selected if necessary under the premise of ensuring R0 resection. Type Ⅰ and type Ⅱ tumors did not invade the caudate lobe bile duct orifice and underwent perihilar bile duct resection. Type Ⅱ patients located at the bifurcation of the hepatic duct underwent perihilar cholangiotomy or combined left and right hepatectomy. All patients underwent regional lymph node dissection. The scope of lymph node dissection includes: hepatoduodenal ligament lymph nodes (12 groups), posterior pancreatic lymph nodes (13 groups) and common hepatic artery lymph nodes (8 groups). A quick-freezing pathological examination was performed during the operation, and it was confirmed that the bile duct had a negative margin. If the bile duct has a positive margin, hemihepatectomy should be performed on the premise of ensuring the safety of the operation. When R0 or R1 cannot remove tumor metastasis, the specimen is taken for biopsy, and then external T tube drainage is performed. After the operation, the bleeding was completely stopped, the abdominal cavity was flushed with double cannula, and the jejunal nutrition tube was placed.

6. Evaluation index

The operation methods were summarized, the complications were analyzed, and the 3 and 5-year survival rates wereobserved.

7. Follow up results

The patients were reviewed regularly, including CT, Serum CA19-9 and CEA. The follow-up period was until September 25, 2020.

8. Statistical analysis

SPSS21.0 software was used for data analysis, count data was analyzed by t-test and or variance analysis, measurement data was analyzed by chi-square test, survival data was analyzed by COX regression model, and $p<0.05$ was considered statistically significant.

III. RESULT

Among the 25 patients, 15 were women and 10 were men. The ratio of men to women was 3:2, the minimum age was 27 years old, and the maximum age was 74 years old and the average age was 58 years old. The operations are performed by the same surgeon, which reduces the influence of human factors on preoperative evaluation and surgical skills. All 25 cases underwent surgical resection, and the surgical resection rate was 100%. Among them, 22 cases of hilar cholangiocarcinoma, the surgical resection rate was 100% (22/22). Postoperative pathological results showed 3 cases of adenoma and 22 cases of adenocarcinoma. Among the 25 patients, R0 resection accounted for 88.00% (22/25), and R1R2 resection accounted for 12.00% (3/25).

Table 3: Surgical resection of 25 patients.

Surgical resection	cases	Percentages
Ro Resection	22	88.00%
R1 R2 Resection	3	12.00%

Analysis of postoperative complication rate and mortality of patients with different surgical methods

In this study, in the two groups of patients with cholangiocarcinoma, the total postoperative complication rate was 13.63% (3/22) in the local resection group, and the mortality within 1 month was 0%. In the combined hemihepatectomy or hemihepatectomy group, the total complication rate was 100% (3/3), and the mortality within one month was 0%.In the local resection group, there were 2 cases (9.09%) with bile leakage after operation, which were cured after giving drainage, bacterial culture, changing antibiotics according to the results of drug sensitivity test and nutritional support. There was 1 case (4.54%) with upper gastrointestinal bleeding, which stopped bleeding after hemostasis and acid suppression. In hemihepatectomy 2 cases (66.66%) had bile leakage, 1 case (33.33%)) had abdominal infection and had no incision infection.

Table 4: Postoperative complication of the patients.

Postoperative complication	local excision group Incidence(%,N)	The incidence rate of hemihepatectomy (%,N)
Bile leakage	9.09%(2)	66.66(2)
Upper gastrointestinal	4.54% (1)	0.0%(0)Bleeding
Abdominal infection	0.0%(0)	33.33(1)
Incision infection	0.0%(0)	0.0%(0)

Surgical resection of patients with different stages and types

Among the 25 cases of surgical resection, 15 cases were TNM stage I, including 15 cases of RO resection, accounting for 100.0% (15/15), 8 cases of stage II, including 8 cases of RO resection, accounting for 87.5% (7/8), 2 cases of stage a ~ C, including 2 cases of RO resection, accounting for 50% (1/2) (table 5).

In the bismuth corlette classification, 100% (15/ 15) of

the 25 patients underwent Type I local resection of hilar cholangiocarcinoma, 75% (3/ 4) of type II RO, 50% (1/ 2) of type IIIa, while in the hemihepatitis group Type I local resection rate was 100% (1/1), 66.66% (2/ 3) of type II RO resection(table 6).

Table 5: Surgical Ro Resection in patients with different stages.

TNM staging	Total N	local resection group	combined with hemihepatis	Ro Resection rate
Phase	15	15	0	100%(15/15)
Phase II	8	7	1	87.5%(7/8)
Phase III a-c	2	1	1	50%(1/2)

Table 6: Surgical Ro Resection in patients with different stages.

Bismuth Colette typing	Total N	local resection group		combined with hemihepatis	
		Ro resection	R1R2 resection	Ro resection	R1R2 resection
Type I	16	15	0	1	0
Type II	7	3	1	2	1
Type IIIa	2	1	1	0	0

As shown in Table 7 the R0 resection rate was 90.47% (19/21) in the local resection group of hilar cholangiocarcinoma, and 75.00% (3/4) in the combined hemihepatectomy or combined hemihepatectomy of hilar cholangiocarcinoma. The R0 local resection rate of hilar cholangiocarcinoma was significantly higher than R0 local resection combined with combined hemihepatectomy especially for patients with bismuth type I Type IIhilar cholangiocarcinoma.

Table 7: Ro resection with different surgical methods.

Operation method	Ro resection	R1R2 resection
Local diagnosis of cholangiocarcinoma Resection group	90.47%(19/21)	9.52%(2/21)
Combined with hemi hepatitis Or hemihepatectomy	75.00%(3/4)	25.00%(1/4)

Survival analysis of 25 patients after operation

The results of the study showed that the 3-year survival rate and 5-year survival rate of the R0 resection group were 88.0% and 48.3%, respectively, and the 3-year survival rate and 5-year survival rate of the R1R2 resection group were 56.0% and 12.1%, respectively. The 3-year and 5-year survival rates of the R0 resection group were significantly higher than those of the R1R2 resection group (P<0.05), as shown in Figure 1.

Survival analysis of 21 patients.

Therapeutic method	number of cases	Survival rate	
		3 year	5 year
Ro Resection	22	88.0%	48.3%
R1 R2 Resection	3	56.0%	12.1%

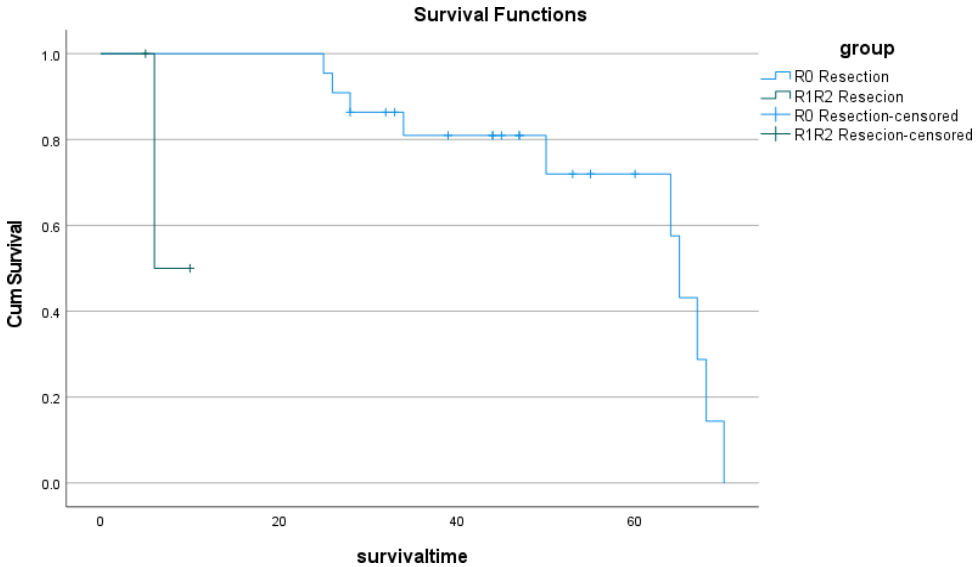

Figure 1: Comparison of survival analysis between R0 resection and R1R2 resection.

IV. DISCUSSION

Cholangiocarcinoma is the cancer caused by malignant transformation of bile duct epithelial cells. It can be divided into intrahepatic and extrahepatic cholangiocarcinoma in primary cholangiocarcinoma, which is next to that of hepatocyte cancer. Because of its complicated etiology, no special typical clinical manifestations in the early stage, lack of specific tumor markers, and atypical imaging manifestations, the diagnosis of cholangiocarcinoma is complex and high in concealment[6], while the clinical manifestations of cholangiocarcinoma and cholelithiasis are not easy to distinguish, the specificity is not strong, and the preoperative early diagnosis rate of cholangiocarcinoma with stones is low,[4,7,8] The incidence rate of bile duct stones and bile duct tumors is increasing in recent years. According to a large number of clinical observation data at china and abroad, bile duct stones are one of the inducing factors of bile duct tumors. The incidence of bile duct tumor in foreign countries reported by choledocholithiasis is 2%-10%[9,10], the incidence rate of 0.36%-10%[11] is reported in China, while the incidence rate of bile duct tumor with bile duct stones is 26%-48%,[10,12] A large number of studies show that there is a close relationship between them. Therefore, we should correctly understand the relationship between them, which can often guide clinical reduction of missed diagnosis and improve the detection of stones accompanying bile duct tumor.

Therefore, we believe that patients with cholelithiasis, recurrent cholangitis or bleeding during surgery should pay attention to the possibility of common bile duct tumors. For the preoperative diagnosis of cholangiocarcinoma, we can combine tumor marker detection with imaging examination. Among them, CA19-9 is the most commonly used with a cutoff value of 129u/ml. The sensitivity of CA 19-9 greater than 129u/ml is 78.6% and the specificity is 98.5%.[12] Obstructive jaundice caused by other causes can also lead to an increase in CA 19-9. If CA19-9 still increases after bile duct decompression, it should be highly suspected of cholangiocarcinoma.[13] The diagnostic sensitivity of CA19-9 and CEA is higher than that of a single test.[7] MRCP can show the condition of the bile duct very well and determine whether it is dilated and narrowed. In addition, histological examination can also be performed.

If the patient can undergo a radical resection, a needle biopsy is usually not recommended to prevent implant transfer during the puncture process. Even if the preoperative diagnosis is cholelithiasis, intraoperative choledochoscopy, intraoperative B-ultrasound and intraoperative cholangiography should also be combined toidentify bile duct lesions, so as to find bile duct tumors and infiltrative lesions. In the process of exploring unexpected tumors, the pathological tissue of the bile duct wall should be taken for rapid histopathological examination, and three or more tissues should be taken for examination.[14] After confirming the diagnosis, surgery should be performed as soon as the patient's physical condition permits. The radical resection of cholangiocarcinomastones is not exactly the same as that of cholangiocarcinoma, but it should focus on the treatment of tumors, remove the lesion tissue and consider the treatment of stones. We believe that the specific scope of surgical resection should be based on the location and size of the tumor, the degree and degree of infiltration of the surrounding bile ducts and blood vessels, whether it involves other adjacent organs, the actual situation of lymph node metastasis and other factors. Consider choosing an appropriate surgical plan.[15] to make the patient's treatment more targeted. For patients who cannot be resected or who cannot tolerate surgery, the overall condition of the patient can be improved first to obtain opportunities for surgical treatment or palliative treatment, such as placement of T-tube drainage, placement of biliary stents, etc. Patients who survive more than six months are recommended to use metal stent.

Sometimes, extrahepatic cholangiocarcinoma is at an advanced stage when it is discovered. Surgical removal of extrahepatic cholangiocarcinoma can ensure the highest survival rate, so surgery should be considered whenever possible. There are many complications after hilar cholangiocarcinoma, such as bile leakage, gastrointestinal hemorrhage, and abdominal infection, obstruction caused by anastomotic stenosis, biliary tract infection, abdominal hemorrhage, liver failure, hepatic encephalopathy and hepatorenal syndrome. In this study, there were 2 cases (9.09%) with postoperative bile leakage. According to the results of the drug susceptibility test, they are cured after drainage, bacterial culture, antibiotic replacement and nutritional support. One case (4.54%) had upper gastrointestinal bleeding after surgery. After hemostasis and acid suppression, the bleeding stopped. Other complications: 1 case of abdominal infection. The perioperative mortality rate of local resection of hilar cholangiocarcinoma was 0%, while the perioperative mortality rate of hemihepatectomy or extended hepatectomy and caudate lobectomy was 1.8%. We are deeply aware that the wound needs strict hemostasis during the operation, especially for combined hemihepatectomy. For the resection and reconstruction of arteries and veins, the anastomosis should be accurate and should not form an angle.

At the same time, some patients are prone to gastrointestinal bleeding after surgery, which is caused by a large amount of blood coagulation material consumed during the operation. Therefore, hemostatic drugs or hemostatic factors should be used in time after the operation, and the drainage of each drainage tube should be always paid attention to. First of all, it is necessary to ensure the normal operation of the drainage tube to prevent the drainage tube from falling out, deforming and blocking, and pay close attention to the

amount and color of the drainage fluid in the drainage tube. In case of leakage, the patient should actively receive treatment and make an open hemostasis. Patients with postoperative biliary leakage should observe whether the patient has exhaust, whether there is abdominal distension, whether there is bile outflow from the drainage tube, whether there is peritoneal irritation, and check the body carefully to find positive signs of peritoneal irritation. Strengthen abdominal washing to prevent infection, regularly review the patient's liver function, and emergency ultrasound-guided puncture and drainage when necessary. In view of the occurrence of postoperative complications, we should calmly face, analyze the cause, and take timely treatment measures to create more favorable conditions for the patient's recovery.

V. CONCLUSION

In summary, for patients with bile duct stones, we must consider the possibility of bile duct tumors, achieve early detection of bile duct tumors, and strive for early radical resection. For patients who accidentally find bile duct tumors due to bile duct stones, surgery it should be fully evaluated beforehand. Increasing the R0 resection rate can significantly promote the prognosis of the patient and prolong the survival time and quality of the patient.

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