

# Diagnostic and surgical therapeutic features of extrahepatic bile duct carcinoma without jaundice

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## Abstract

**AIM:** To analyze the diagnostic and therapeutic features of extrahepatic bile duct carcinoma (EBDC) without jaundice.

**METHODS:** Between 1985 and 1999, 101 patients underwent surgery for EBDC in Xiangya Hospital. These patients were divided into two groups: 84 jaundiced patients and 17 non-jaundiced patients according to preoperative serum total bilirubin levels. The clinical manifestations, laboratory findings, location, pathology and surgical resectability of the tumors were compared between the two groups.

**RESULTS:** The laboratory parameters such as hemoglobin, serum albumin ALB, AKP,  $\gamma$ -GT, and sonography appearance were similar between the two groups, and there was no significant difference in tumor location, pathological type and resectability. However, the number of non-jaundiced patients associated with cholelithiasis was significantly greater than that of jaundiced patients ( $P = 0.008$ ).

**CONCLUSION:** The presence of jaundice is not a reliable criterion for the prediction of the resectability and the extent of tumor progression in extrahepatic bile duct carcinoma. Decreased levels of blood hemoglobin and serum albumin, elevated levels of AKP and  $\gamma$ -GT, and /or abnormal sonography may be suggestive. Biopsy of a stenotic or thickened bile duct is strongly recommended for a correct diagnosis before the appearance of jaundice.

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## INTRODUCTION

Primary carcinoma of the extrahepatic bile duct is an uncommon malignant tumor, with reported incidence rate of about 0.01-0.46%. About 2% of patients who died of cancer were autopsied to have this disease<sup>[1-4]</sup>. Jaundice is generally thought to be the most important factor in the diagnosis of this disease, but there are still few cases seeking doctors' consultation before jaundice appears<sup>[5-9]</sup>. Those patients could be underdiagnosed or misdiagnosed because of atypical clinical symptoms. In this study, the diagnostic and therapeutic features of bile duct carcinoma without jaundice were compared with those with jaundice.

## MATERIALS AND METHODS

From January 1984 to December 1999, two hundred and thirty-nine patients who were diagnosed as extrahepatic bile duct carcinoma were admitted to Xiangya Hospital. One hundred and one were operated and the diagnosis was confirmed by pathology. Patients with carcinomas of gallbladder, intrahepatic bile duct and ampulla of Vater were excluded from the study. The patients under studies consisted of 58 males and 43 females, aged 27 to 76 years (an average age of 61.7 years).

According to the level of serum total bilirubin (STB), the patients were divided into non-jaundiced group (17 patients,  $STB \leq 2.0$  mg/dL at the time of diagnosis) and jaundiced group (84 patients,  $STB > 2.0$  mg/dL). Clinical data included symptoms, laboratory results, imaging findings, pathological results, treatments and resectabilities.

## Statistical analysis

The difference between the two groups was compared using chi-square analysis and Student's *t* test.  $P < 0.05$  was considered statistically significant.

## RESULTS

### Symptoms and signs

Fifteen (88.2%) patients in the non-jaundiced group had anorexia or/and vomiting, abdominal pain compared with 63 (75.0%) in the jaundiced group. Eight (47.1%) patients in the non-jaundiced group and fifty-seven (67.9%) patients in the jaundiced group were found to show positive signs in liver, spleen or gallbladder enlargement. (Table 1).

### Laboratory examination

The patients showed no difference in the levels of abnormal serum albumin, alkaline phosphates (AKP),  $\gamma$ -glutamyltranspeptidase ( $\gamma$ -GT), except STB level (Table 2).

### Image examination

All patients in the non-jaundiced group underwent sonography. The results showed segmental stenosis of extrahepatic bile duct, thickening of the bile duct wall, and dilatation of intra- or extra-hepatic bile duct proximal to the stenosis. Sixty-seven out of 78 patients showed stenosis or neoplastic space-occupying lesions within the extrahepatic bile duct.

### Operation findings

During the operation, 59 patients had neoplasms located in the upper extrahepatic bile duct while 8 in the middle and 34 in the lower. There was no difference with regard to localization of the tumor between the two groups.

### Pathological features

All patients were proved to have adenocarcinoma. The patients were categorized into three different grades by the degree of differentiation. The results showed that there was no difference between the patients with or without jaundice.

### Treatment

Radical resection, biliary bypass, external drainage or biopsy

were performed according to the surgical findings. There was no difference in tumor resectability between the two groups ( $P>0.05$ , Table 3).

**Table 1** Symptoms and signs

Symptom	Non-jaundiced		Jaundiced		P value
	No.	%	No.	%	
Abdominal discomfort	15	88.2	63	75.0	>0.05
Liver or gallbladder palpable	8	47.1	57	67.9	>0.05
Cholelithiasis	11	64.7	26	31.0	<0.05 <sup>a</sup>

No significant difference was found between the two groups in the clinical symptoms and signs. In the non-jaundice group, the rate of combined cholelithiasis was obviously higher than in the jaundice group.

**Table 2** Laboratory data

	Non-jaundiced		Jaundiced		P value
	No.	%	No.	%	
Descending of HB	8	47.1	45	53.6	>0.05
Ascending of AKP	8	72.7	56	86.2	>0.05
Ascending of $\gamma$ -GT	4	66.7	28	93.3	>0.05
Descending of ALB	4	23.5	39	47.0	>0.05

No significant difference was found between the two groups in laboratory data.

**Table 3** Tumor location, pathological type, treatment

	Non-jaundiced		Jaundiced		P value
	No.	%	No.	%	
Location					
Upper	11	64.7	48	57.1	
middle	0	0.0	8	9.6	>0.05
Lower	6	35.3	28	33.3	
Differential					
Good	6	35.3	48	57.1	
mild	8	47.1	27	32.1	>0.05
Poor	3	17.7	9	10.8	
Biopsy	3	17.7	8	9.5	
Treatment					
drainage	9	52.9	43	51.2	>0.05
By pass	0	0.0	1	1.2	
Radical	5	29.4	32	38.1	

No significant difference was found between the two groups in tumor locations, pathological types and treatment methods.

## DISCUSSION

Jaundice is the early and main manifestation of extrahepatic bile duct carcinoma. It has been reported to be the initial sign in 83-97% of patients<sup>[5-9]</sup>. However, there are few patients coming to hospital before the appearance of jaundice. In the present study 16.8% of the patients with EBDC were diagnosed before the presence of jaundice. These patients were likely to be neglected during busy outpatient service. We found that, there were still some clues to the diagnosis of bile duct carcinoma for these patients without jaundice. Some laboratory parameters, such as hemoglobin, serum albumin, AKP and  $\gamma$ -GT may be suggestive.

Sonography is almost the first tool for the diagnosis of extrahepatic bile duct carcinoma because it is non-invasive and less expensive. Ninety-five of the patients underwent sonography in our study, of whom 84 (88.4%) had positive findings, such as duct stenosis, thickness of the bile duct wall or space-occupying lesions within the duct. The results were in accordance with those documented in the literature<sup>[10-12]</sup>.

The relationship between choledocholithiasis and bile duct carcinoma is still unclear. As reported, 6-37% of extrahepatic bile duct carcinomas were associated with bile duct stones<sup>[13]</sup>. In the present study the number of patients who suffered from choledocholithiasis in the non-jaundiced group was significantly higher than that in the jaundiced group ( $P<0.05$ ). Two factors may contribute to this finding. First, for patients with bile duct stones, the clinical manifestations were so typical that the doctor would pay more attention to the biliary system. Second, during the operation for choledocholithiasis, we usually took the whole layer of bile duct wall for biopsy whenever there was stenosis, sclerosis or nodular change in the bile duct. Eight patients were diagnosed by this means and radical resection was performed.

It was reported that extrahepatic bile duct carcinoma without jaundice occurred in the early stage of the disease. The tumor was well differentiated and the resection rate was usually high<sup>[8]</sup>. However, there was no difference between the two groups in our study. The radical resection rate was 29.4% in the non-jaundiced group and 38.1% in the jaundiced group ( $P>0.05$ ). Liver and/or intrabdominal lymph node metastases were found in 12 patients without jaundice. We suggest that the presence of jaundice cannot be taken as the major criterion to predict the tumor resectability or the extent of tumor progression.

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