

Retrospective Study

Prognosis after resection for hepatitis B virus-associated intrahepatic cholangiocarcinoma

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Supported by National Natural Science Foundation of China, No. 81402523.

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Received: May 14, 2014

Peer-review started: May 14, 2014

First decision: June 18, 2014

Revised: July 12, 2014

Accepted: September 18, 2014

Article in press: September 19, 2014

Published online: January 21, 2015

Abstract

AIM: To investigate the prognostic factors after resection for hepatitis B virus (HBV)-associated intrahepatic cholangiocarcinoma (ICC) and to assess the impact of different extents of lymphadenectomy on patient survival.

METHODS: A total of 85 patients with HBV-associated ICC who underwent curative resection from January 2005 to December 2006 were analyzed. The patients were classified into groups according to the extent of lymphadenectomy (no lymph node dissection, sampling lymph node dissection and regional lymph node dissection). Clinicopathological characteristics and survival were reviewed retrospectively.

RESULTS: The cumulative 1-, 3-, and 5-year survival rates were found to be 60%, 18%, and 13%, respectively. Multivariate analysis revealed that liver cirrhosis (HR = 1.875, 95%CI: 1.197-3.278, $P = 0.008$) and multiple tumors (HR = 2.653, 95%CI: 1.562-4.508, $P < 0.001$) were independent prognostic factors for survival. Recurrence occurred in 70 patients. The 1-, 3-, and 5-year disease-free survival rates were 36%, 3% and 0%, respectively. Liver cirrhosis (HR = 1.919, $P = 0.012$), advanced TNM stage (stage III/IV) (HR = 2.027, $P < 0.001$), and vascular invasion (HR = 3.779, $P = 0.02$) were independent prognostic factors for disease-free survival. Patients with regional lymph node dissection demonstrated a similar survival rate to patients with sampling lymph node dissection. Lymphadenectomy did not significantly improve the survival rate of patients with negative lymph node status.

CONCLUSION: The extent of lymphadenectomy does not seem to have influence on the survival of patients with HBV-associated ICC, and routine lymph node

dissection is not recommended, particularly for those without lymph node metastasis.

Key words: Intrahepatic cholangiocarcinoma; Hepatitis B virus; Lymph node metastases; Postoperative survival; Lymph node dissection

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Core tip: Some recently published studies show a relation between chronic hepatitis B infection and the development of intrahepatic cholangiocarcinoma. Hepatitis B-associated patients with cholangiocarcinoma appear to have different clinicopathological characteristics compared with seronegative patients. In this context, the authors analyzed the data of patients with hepatitis B virus-associated intrahepatic cholangiocarcinoma who underwent curative resection retrospectively. They found in multivariate analysis that liver cirrhosis and multiple tumors were independent prognostic factors for overall survival. Independent prognostic factors for disease-free survival were liver cirrhosis, vascular invasion and advanced TNM stage. The patients were divided into three groups depending on the extent of lymph node dissection (no lymph node dissection, sampling lymph node dissection and regional lymph node dissection). The outcomes were not statistically different between the three groups.

Wu ZF, Wu XY, Zhu N, Xu Z, Li WS, Zhang HB, Yang N, Yao XQ, Liu FK, Yang GS. Prognosis after resection for hepatitis B virus-associated intrahepatic cholangiocarcinoma. *World J Gastroenterol* 2015; 21(3): 935-943 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v21/i3/935.htm> DOI: <http://dx.doi.org/10.3748/wjg.v21.i3.935>

INTRODUCTION

Intrahepatic cholangiocarcinoma (ICC), which arises from the more peripheral branches of the intrahepatic bile duct, is the second most common primary liver cancer after hepatocellular carcinoma (HCC), accounting for 5%-10% of primary liver malignancies^[1,2]. It demonstrates a relatively high prevalence in parts of East Asia^[3].

Recently, an increasing number of studies have shown that viral hepatitis B and C are statistically related to ICC^[4-8]. The mechanism for the development of ICC in patients with HBV infection is still uncertain. Hepatitis B and C virus infections are the most common risk factors for HCC. Hepatitis-associated HCC contains elements of cholangiocarcinoma^[9,10], suggesting that the two malignancies share a common origin from bipotential stem cells and pathogenic mechanisms^[9,11]. Clinically, some studies have also found that both viral hepatitis-associated ICC and HCC have similar age profiles and different age distributions between patients with chronic

hepatitis B and those with chronic hepatitis C^[7,8,12]. In addition, in our previous study, we have found that HBV-associated ICC have specific clinicopathological characteristics^[13]. Compared with seronegative ICC patients, HBV-associated ICC patients tend to be male and younger, with higher α -fetoprotein levels and a lower frequency of lymphatic metastasis, which has been proved by other studies^[7,12]. It is suggested that HBV-associated ICC and HCC share common disease processes for carcinogenesis, and should be distinguished from those without HBV infection, because they have different clinicopathological characteristics and surgical outcomes^[14].

The prognosis of ICC is generally poor as compared with that of HCC^[15,16], because it is frequently associated with lymph node involvement, intrahepatic metastasis, and peritoneal dissemination^[17,18]. In consideration of similar pathogenesis and clinicopathological characteristics, studies should be conducted to ascertain whether HBV-associated ICC can be successfully treated by the methods used to treat HCC. Curative resection is still known to be the only effective therapeutic measure. However, there is no established consensus on the prognostic significance of lymph node dissection (LND), or even the extent of LND^[19]. Prognostic factors after resection for HBV-associated ICC have not been confirmed due to its rarity and low resectability. Therefore, this study was conducted to investigate the outcomes of HBV-associated ICC patients after hepatic resection, and to analyze the prognostic factors affecting the survival and recurrence of the patients. The study also investigated the impact of the extent of LND on survival.

MATERIALS AND METHODS

Patients

Primary curative resection was performed in 127 out of 146 patients diagnosed with ICC at Eastern Hepatobiliary Surgery Hospital, Second Military Medical University (Shanghai, China) from January 2005 to December 2006. Only 114 patients were available for data analysis, and the rest of the patients could not be followed after operation.

With respect to a case of hepatitis B surface antigen being positive [HBsAg (+)], it is impossible to determine whether it is a chronic infection, acute infection, or false positive result. Generally speaking, the case of anti-hepatitis B core (HBc) being positive [anti-HBc (+)] only indicates that there may be past infection or that it may be present after the disappearance of HBsAg and the appearance of anti-HBs antibody, thus indicating recent infection. It can also be considered a sentinel marker for detection of occult HBV infection (HBsAg carrier)^[20]. Therefore, the present study defined chronic HBV infection as either HBsAg (+) or anti-HBc (+)^[21].

Data analysis was conducted on 85 patients (74.6%) with chronic HBV infection. The diagnosis of ICC was confirmed by pathological examination. Patients with hilar cholangiocarcinoma, gallbladder cancer, or

combined type carcinoma consisting of HCC and ICC were excluded from this study. Curative resection was defined as negative surgical margins on microscopic examination, absence of macroscopic intrahepatic metastasis in the residual liver at the time of surgery, and absence of abdominal dissemination. The study protocol was approved by the clinical research ethics committee of the hospital. Written consent was obtained from all patients according to the policies of the committee.

Preoperative investigations

Preoperative evaluation was conducted before the decision for surgery was made. We evaluated resectability of ICC by ultrasonography, computed tomography (CT), and magnetic resonance image (MRI) examinations. Liver function was evaluated *via* Child-Pugh classification. Before the operation, patients at or over the age of 60 were routinely evaluated for formal cardiopulmonary and general conditions. Resection criteria were constant during the study period, including the number of resectable tumors, presence or absence of tumor thrombus and gross metastatic focus, and adequate liver function reserve, as reported in our previous study^[22,23].

Surgical procedures and parameter definitions

Liver resection was carried out using finger fracture and clamp crushing with intermittent Pringle's maneuver under room temperature. Lymphadenectomy was not conducted uniformly for every patient. 35 out of 85 patients did not undergo lymphadenectomy, neither did they present lymph node metastasis in the preoperative evaluation and intraoperative assessment. We classified the extent of lymphadenectomy into lymph node sampling and regional LND. Lymph node sampling was performed in 22 patients, and the lymph nodes along the hepatoduodenal ligament were removed. Regional LND was performed in 28 patients who underwent complete excision of soft tissue and lymph nodes at the hepatic hilum, common hepatic artery stations, hepatoduodenal ligament, and posterior to the upper portion of the pancreatic head. The extent of LND was similar for right- and left-sided tumors, with the exception of dissection of lymph nodes along the lesser curvature of the stomach for tumors located in the left lobe of the liver. The patients were divided into three groups according to the extent of LND: (1) LND (-) group: with no lymphadenectomy; (2) lymph node sampling group: with lymph node sampling; and (3) regional LND group: with regional lymphadenectomy.

ICC was classified on the basis of gross appearance, as raised by the Liver Cancer Study Group of Japan (LCSGJ), including types of mass-forming (MF), periductal infiltrating (PI), and intraductal growth (IG). Tumor-node-metastasis (TNM) staging of tumors complied with the guidelines of the 7th edition of the American Joint Committee on Cancer/International Union against Cancer (AJCC/UICC). In this study, multiple tumors referred to more than one tumorous node (including micrometastases

that could be discovered only on pathological examination); tumor size referred to the maximum tumor diameter; major liver resection was defined as resection of three or more hepatic segments; minor liver resection was defined as resection of one or two hepatic segments.

Follow-up

The clinical data from all patients were recorded prospectively. Follow-up after resection consisted of routine blood tests, physical examination, and abdominal ultrasonography every 3 mo postoperatively for the first 2 years and twice a year thereafter at our hospital. Suspected recurrences were confirmed by CT or MRI. If unavailable to undergo this procedure, the patient was followed by telephone or letter every year, as reported in our previous study^[22,23].

Statistical analysis

Overall survival (OS) and disease-free survival (DFS) rates and curves were analyzed by the Kaplan-Meier method, and differences were compared by the log-rank test. Comparisons between groups were made using the Chi-square test or Fisher's exact test. After univariate analysis, only significant variables with $P < 0.05$ were adopted in the multivariate analysis. Multivariate analysis was conducted by means of the Cox proportional hazards model to identify prognostic factors. All statistical analyses were carried out with software package SPSS 18.0 (SPSS Inc., Chicago, IL). A P value < 0.05 was considered statistically significant.

RESULTS

Clinicopathological characteristics of the patients

The follow-up duration was calculated from the day of operation to either the day of death or the date of December 31, 2012. There were a total of 66 males and 19 females with a median age of 54 years (range: 28-79 years). Out of the 85 patients, 40 underwent major liver resection while 45 underwent minor resection. Additional procedures were carried out in 10 patients (Table 1). Eight patients had surgical complications, including biliary leakage in 3 cases, subphrenic infection in 2 cases, liver abscess in 1 case, bowel obstruction in 1 case, and bleeding in 1 case.

Survival and recurrence

The cumulative 1-, 3-, and 5-year survival rates were 60%, 18%, and 13%, respectively (Figure 1). The median survival time was 25 mo. Univariate analysis revealed that the following prognostic factors were predictive of worse survival: liver cirrhosis ($P = 0.002$), tumor number ($P < 0.001$), tumor size ($P = 0.006$), lymph node metastasis ($P = 0.005$), vascular invasion ($P = 0.013$), and TNM classification ($P < 0.001$; Table 2). Age, gender, and other tumor-related factors were not significantly related with survival. Through multivariate analysis by means of Cox's proportional hazards model, liver cirrhosis (HR = 1.875, 95%CI: 1.197-3.278, $P = 0.008$) and multiple tumors (HR

Table 1 Operative procedures for intrahepatic cholangiocarcinoma

Operative modality	Number
Hepatic resection (<i>n</i> = 85)	
Major resection (<i>n</i> = 40)	
Partial hepatectomy	24
Right trisectionectomy	1
Left trisectionectomy	4
Right hemihepatectomy	1
Left hemihepatectomy	8
Central bisectionectomy	2
Minor resection (<i>n</i> = 45)	
Partial hepatectomy	33
Right anterior sectionectomy	2
Right posterior sectionectomy	3
Left lateral sectionectomy	4
Bisegmentectomy	3
Combined resection (<i>n</i> = 10)	
Spleen	2
Gallbladder	8

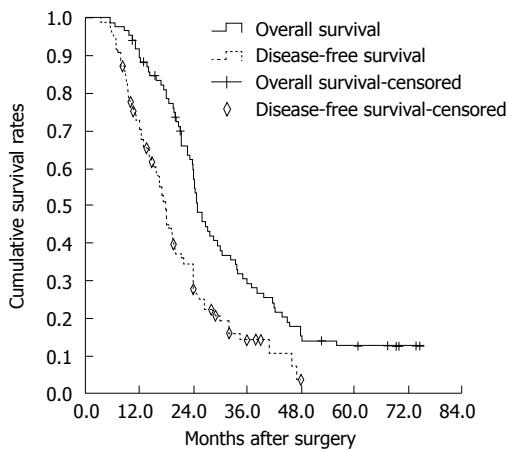


Figure 1 Overall survival and disease-free survival curves of the 85 hepatitis B virus-associated intrahepatic cholangiocarcinoma patients after curative resection. The median overall survival was 25 mo. The median disease-free survival was 17.9 mo.

= 2.653, 95%CI: 1.562-4.508, *P* < 0.001) were identified as independent prognostic factors (Table 2).

Seventy patients had recurrence (82.4%). The 1-, 3-, and 5-year DFS rates were 36%, 3% and 0%, respectively (Figure 1). The sites of recurrence are shown in Table 3. The most common recurrence pattern was intrahepatic. Two patients (2.9%) with recurrence underwent further liver resection, while 48 patients (68.6%) underwent post-recurrence TACE. Other measures taken against recurrence included radiotherapy (*n* = 11), systemic chemotherapy (*n* = 2), and supportive therapy or Chinese herbal therapy (*n* = 7) in patients with liver dysfunction. Univariate analysis revealed that liver cirrhosis (*P* = 0.003), tumor number (*P* < 0.001), lymph node metastasis (*P* < 0.001), vascular invasion (*P* < 0.001), and TNM classification (*P* < 0.001) were significant risk factors for recurrence (Table 4). Multivariate analysis revealed that liver cirrhosis (HR = 1.919, *P* = 0.012), advanced TNM stage (stage III or IV) (HR = 2.027, *P* < 0.001), and vascular invasion (HR = 3.779, *P* = 0.02) were

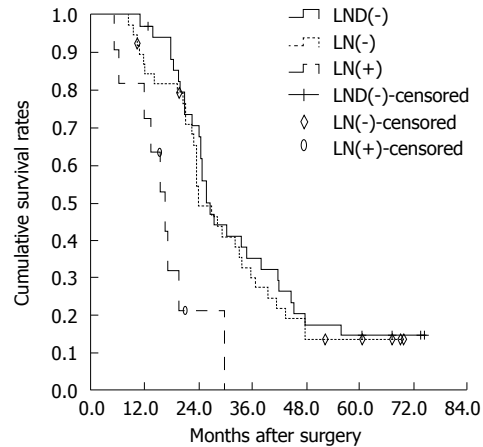


Figure 2 Overall survival curves of patients in lymph node dissection (-), lymph node (-) and lymph node (+) groups. There was no statistically significant difference in OS between the lymph node dissection (LND) (-) and LN (-) groups (*P* = 0.729). There were significant differences between LN (-) and LN (+) groups (*P* = 0.033). A statistically significant difference between LND (-) and LN (+) groups was observed (*P* = 0.004). LND: Lymph node dissection; LN: Lymph node.

independent prognostic factors affecting DFS (Table 4).

Influence of LND on survival

The pathological characteristics associated with the extent of lymphadenectomy are as shown in Table 5. The LND (-) group did not demonstrate lymph node metastases as revealed by preoperative imaging (CT and MRI) and intraoperative assessment. No survival difference was recorded between the LND (-) group and the group of patients without lymph node metastasis [LN (-) group] (*P* = 0.729). Among patients who underwent lymph node sampling or dissection, the LN (-) group showed better survival than the group of patients with lymph node metastasis [LN (+) group] (*P* = 0.033) (Figure 2). No survival difference was recorded between the lymph node sampling and regional LND groups (*P* = 0.089) (Figure 3). Among the patients with negative lymph node status, a survival difference was not present between the lymph node sampling group and regional LND group (*P* = 0.182). Therefore, lymphadenectomy did not significantly improve the survival rate in node negative patients (Figure 4).

DISCUSSION

We analyzed a group of 85 patients who underwent potentially curative surgery for HBV-associated ICC. The cumulative 1-, 3-, and 5-year survival rates were 60%, 18%, and 13%, respectively. Several clinicopathological factors that were suspected to significantly influence survival and recurrence were examined. In some studies, vascular invasion, lymph node metastasis, microscopic presence of tumor cells on the resection margin, multiple tumors, and tumor size were found to be significant prognostic factors for survival^[24-30]. In this study, univariate analysis showed that liver cirrhosis, tumor number, tumor size, lymph node metastasis, vascular invasion, and TNM classification were

Table 2 Univariate and multivariate analyses of prognostic factors for overall survival of hepatitis B virus-associated intrahepatic cholangiocarcinoma patients included in this study

Variable	n	Univariate analysis			Multivariate analyses		
		1-yr	5-yr	P value	HR	95%CI	P value
Gender				0.205	NA	NA	NA
Female	19	66%	23%				
Male	66	58%	10%				
Age				0.769	NA	NA	NA
≤ 60	59	64%	13%				
> 60	26	50%	12%				
Capsule formation				0.522	NA	NA	NA
Yes	32	55%	10%				
No	53	63%	14%				
Cirrhosis				0.002	1.981	1.197-3.278	0.008
Yes	48	56%	0%				
No	37	65%	27%				
Child-Pugh class				0.257	NA	NA	NA
A	76	61%	14%				
B	9	18%	0%				
AFP (ng/mL)				0.342	NA	NA	NA
≤ 20	48	51%	11%				
> 20	37	72%	15%				
CA19-9 (U/mL)				0.342	NA	NA	NA
≤ 37	55	66%	14%				
> 37	30	50%	10%				
Gross type				0.402	NA	NA	NA
MF	63	61%	13%				
PI + IG	22	56%	11%				
Differentiation				0.119	NA	NA	NA
Well or Moderate	63	64%	16%				
Poor	22	50%	0%				
Tumor number				< 0.001	2.653	1.562-4.508	< 0.001
Single	60	69%	17%				
Multiple	25	38%	0%				
Tumor size				0.006	NA	NA	NA
< 5 cm	43	70%	21%				
≥ 5 cm	42	49%	5%				
LN metastasis				0.005	NA	NA	NA
Yes	11	31%	0%				
No	74	64%	14%				
Vascular invasion				0.013	NA	NA	NA
Yes	11	24%	0%				
No	74	64%	14%				
TNM classification				< 0.001	NA	NA	NA
Stage I or II	61	66%	17%				
Stage III or IV	24	43%	0%				
Width of resection margin				0.274	NA	NA	NA
< 1 cm	37	69%	17%				
≥ 1 cm	48	53%	9%				
Surgical procedure				0.962	NA	NA	NA
Major hepatectomy	40	61%	13%				
Minor hepatectomy	45	59%	12%				

AFP: Alpha-fetoprotein; CA19-9: Carbohydrate antigen 19-9; MF: Mass-forming; PI: Periductal infiltrating; IG: Intraductal growth; TNM: Tumor-node-metastasis; NA: Not available; HR: Hazard ratio; LN: Lymph node.

Table 3 Sites of initial recurrences in hepatitis B virus-associated intrahepatic cholangiocarcinoma patients after curative resection

Site of initial recurrence	No. of patients
Liver, lymph nodes	6
Liver, lung	1
Liver	46
Lymph nodes	8
Peritoneum	5
Wound site	1
Bone	1
Lung	2

significant prognostic factors for survival. Multivariate analysis showed that liver cirrhosis and multiple tumors were independent prognostic factors for survival.

The recurrence rate was reported to be 61%-65%^[24,25,28,29]. The most common recurrence site was the remnant liver, as reported in other studies^[24,25,28]. In this study, liver cirrhosis, vascular invasion, and advanced TNM stage (stage III or IV) were independent prognostic factors for DFS.

The presence of liver cirrhosis was obviously more common in HBV-associated ICC. In this study, there were

Table 4 Univariate and multivariate analyses of prognostic factors for disease-free survival in hepatitis B virus-associated intrahepatic cholangiocarcinoma patients included in this study

Variable	n	Univariate analysis			Multivariate analyses		
		1-yr	5-yr	P value	HR	95%CI	P value
Gender				0.312	NA	NA	NA
Female	19	50%	0%				
Male	66	32%	4%				
Age				0.853	NA	NA	NA
≤ 60	59	33%	1%				
> 60	26	42%	5%				
Capsule formation				0.970	NA	NA	NA
Yes	32	40%	7%				
No	53	33%	0%				
Cirrhosis				0.003	1.919	1.153-3.192	0.012
Yes	48	22%	0%				
No	37	52%	5%				
Child-Pugh class				0.237	NA	NA	NA
A	76	50%	20%				
B	9	27%	0%				
AFP (ng/mL)				0.648	NA	NA	NA
≤ 20	48	32%	3%				
> 20	37	40%	2%				
CA19-9 (U/mL)				0.189	NA	NA	NA
≤ 37	55	39%	3%				
> 37	30	29%	2%				
Gross type				0.917	NA	NA	NA
MF	63	37%	3%				
PI + IG	22	30%	0%				
Differentiation				0.076	NA	NA	NA
Well or Moderate	63	42%	3%				
Poor	22	18%	0%				
Tumor number				< 0.001	NA	NA	NA
Single	60	48%	3%				
Multiple	25	5%	0%				
Tumor size				0.091	NA	NA	NA
< 5 cm	43	44%	1%				
≥ 5 cm	42	27%	5%				
LN metastasis				< 0.001	NA	NA	NA
Yes	11	0%	0%				
No	74	40%	3%				
Vascular invasion					3.779	1.601-8.923	0.020
Yes	11						
No	74						
TNM classification				< 0.001	NA	NA	NA
Stage I or II	61	0%	0%				
Stage III or IV	24	51%	20%				
Width of resection margin				< 0.001	NA	NA	NA
< 1 cm	37	49%	4%				
≥ 1 cm	48	0%	0%				
Surgical procedure				0.391	NA	NA	NA
Major hepatectomy	40	41%	2%				
Minor hepatectomy	45	31%	3%				

AFP: Alpha-fetoprotein; CA19-9: Carbohydrate antigen 19-9; MF: Mass-forming; PI: Periductal infiltrating; IG: Intraductal growth; TNM: Tumor-node-metastasis; NA: Not available; HR: Hazard ratio; LN: Lymph node.

48 patients (56.5%) with liver cirrhosis. Cirrhosis was an independent prognostic factor for HCC. However, there is little documentation showing that this is associated with ICC. We have demonstrated that cirrhosis not only is an independent prognostic factor for DFS, but also is significantly related to poor survival of the patients with HBV-associated ICC after surgery. It may be due to the fact that HBV-associated ICC shares common disease processes for carcinogenesis with HCC.

Lymph node metastasis was found to be an important

prognostic factor in previous studies^[27,30]. It was associated with OS and DFS on univariate analysis, but not on multivariate analysis in this study, probably because the sample size was relatively small.

It remains unclear whether the clearance of the route of lymph node metastasis is beneficial to survival^[24]. There are no clear guidelines on LND. It is reported that extended lymphadenectomy in ICC patients did not seem to show any advantage without control of liver metastases, because most recurrences occurred

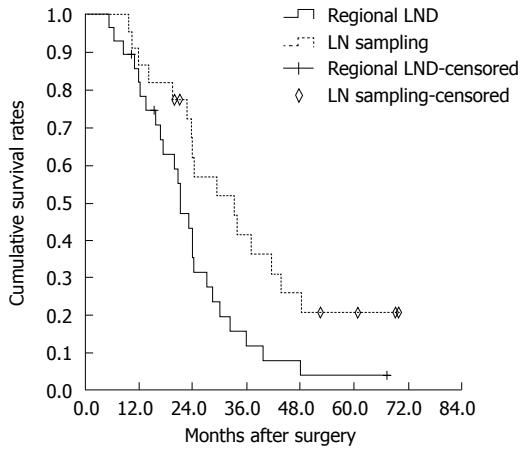


Figure 3 Overall survival curves of hepatitis B virus-associated intrahepatic cholangiocarcinoma patients undergoing sampling lymph node sampling and regional lymph node dissection. There were no significant differences between the two groups ($P = 0.089$). LND: Lymph node dissection; LN: Lymph node.

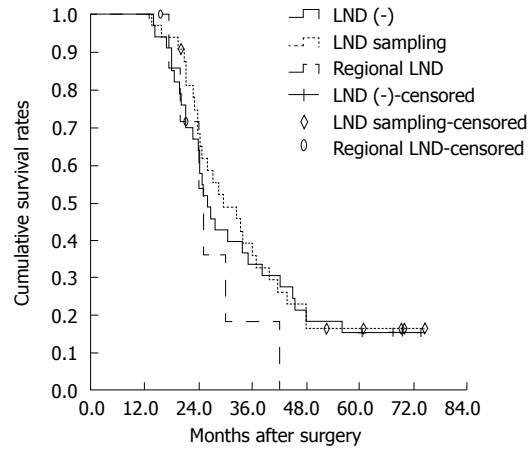


Figure 4 Overall survival curves of hepatitis B virus-associated intrahepatic cholangiocarcinoma patients without lymph node involvement. There was no survival difference between lymph node sampling and regional LND groups ($P = 0.182$). There was no statistically significant difference in overall survival between LND (-) and lymph node sampling groups ($P = 0.709$). There were also no significant differences between LND (-) and regional LND groups ($P = 0.309$). LND: Lymph node dissection.

Table 5 Comparison of the pathological factors according to the extent of lymph node dissection

Variable	LND (-)	LN sampling	Regional LND	P value
Cirrhosis				0.439
Yes	17	13	18	
No	18	9	10	
Gross type				0.617
MF	24	17	22	
PI + IG	11	5	6	
Differentiation				0.478
Well or Moderate	25	15	23	
Poor	10	7	5	
Capsule formation				0.931
Yes	14	8	10	
No	21	14	18	
Tumor number				0.512
Single	27	14	18	
Multiple	8	8	10	
Tumor size				0.145
< 5 cm	21	12	10	
≥ 5 cm	14	10	18	
Pathologica LN metastasis				0.085
Yes	NA	2	9	
No	NA	20	19	
Vascular invasion				0.181
Yes	2	3	6	
No	33	19	22	

MF: Mass-forming; PI: Periductal infiltrating; IG: Intraductal growth; LN: Lymph node; LND: Lymph node dissection; NA: Not available.

in patients with known liver metastases^[17,24]. However, other reports indicated that extensive hepatectomy with extended LND produced a better outcome^[31,32]. Defining the role of lymphadenectomy is important, because lymphadenectomy is a factor controllable by a surgeon out of numerous prognostic factors. The present study has demonstrated that regional LND group has a survival rate similar to that of the lymph node sampling group. The extent of lymphadenectomy (lymph node sampling *vs* regional LND) does not affect the survival. The

patients without LND have similar survival to patients with LND or negative lymph node status. It is revealed that lymphadenectomy does not significantly improve the survival of patients with negative lymph node status.

Nevertheless, this study was limited by its retrospective design. More than five surgeons were involved in treating ICC in this study. It was difficult to determine the exact reasons and extent of LND performed for each patient.

In conclusion, liver cirrhosis and multiple tumors are independent prognostic factors for survival in patients with HBV-associated ICC. The extent of LND does not seem to have influence on the survival of patients with HBV-associated ICC. LND cannot significantly improve the survival of patients with negative lymph node status. We recommend intraoperative lymph node exploration, as opposed to routine regional LND. Regional LND should be performed when lymph node involvement is clinically recognized or it is positive as demonstrated by a frozen section examination.

COMMENTS

Background

Some recently published studies show a relation between chronic hepatitis B infection and the development of intrahepatic cholangiocarcinoma. Patients with hepatitis B-associated cholangiocarcinoma appear to have different clinicopathological characteristics compared with seronegative patients.

Research frontiers

Hepatitis B virus (HBV)-associated intrahepatic cholangiocarcinoma (ICC) have different clinicopathological characteristics and surgical outcomes, and should be distinguished from those without HBV infection. Because of the rarity and low resectability of HBV-associated ICC, prognostic factors after resection for HBV-associated ICC have not been clearly established. The influences of the extent of lymph node dissection (LND) on survival were also not been clearly established.

Innovations and breakthroughs

This study was conducted to investigate the outcomes of HBV-associated ICC patients after hepatic resection, and analyzed the prognostic factors affecting the survival and recurrence. The impact of the extent of LND on survival was

also investigated.

Applications

Liver cirrhosis and multiple tumors are independent prognostic factors for survival in patients with HBV-associated ICC. The extent of lymph node dissection does not seem to have influence on the survival of patients with HBV-associated ICC. Lymphadenectomy cannot significantly improve the survival of lymph node negative patients.

Peer review

The reported data are interesting. Some recently published studies show a relation between chronic hepatitis B infection and the development of intrahepatic cholangiocarcinoma. Patients with hepatitis B-associated cholangiocarcinoma appear to have different clinicopathological characteristics compared with seronegative patients.

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P- Reviewer: Bo J, Chiang TA, Shaikh S **S- Editor:** Qi Y
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ISSN 1007-9327

