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Original Research

Prognostic factors in patients with recurrent intrahepatic cholangiocarcinoma after curative resection: A retrospective cohort study

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ABSTRACT

Background: The aim of this study is to determine the outcomes and prognostic factors in patients with recurrent intrahepatic cholangiocarcinoma after curative hepatectomy.

Methods: Clinical, histopathological, and treatment data of 53 patients with recurrent cholangiocarcinoma after curative resection from 2005 to 2015 at our institutes were investigated and analyzed by univariate and multivariate analyses (E-788).

Results: Recurrent cholangiocarcinoma occurred in 53 of 97 patients who underwent curative resection for intrahepatic cholangiocarcinoma. The median overall survival after recurrence was 13.6 months (range, 1–55 months). Multivariate analysis revealed that recurrent treatment without surgery ($p = 0.0007$), gross appearance except for mass-forming type ($p = 0.0183$) and bile duct invasion at the initial surgery ($p = 0.0093$) were significant poor prognostic factors in recurrent cholangiocarcinoma. Median survival of patients after surgical treatment for recurrent cholangiocarcinoma was 36.7 months versus 13.1 months in patients who did not undergo surgery ($p = 0.029$).

Conclusions: Surgical treatment, gross appearance in mass-forming type and the absence of bile duct invasion were independent favorable factors for survival among patients with recurrent cholangiocarcinoma. We recommend surgical treatment for localized recurrence, even if it occurs early after the initial hepatectomy.

1. Introduction

Intrahepatic cholangiocarcinoma (ICC) carries poor prognosis [1]. The possible causative risk factors of ICC are similar to those of hepatocellular carcinoma (HCC), such as cirrhosis, chronic hepatitis B and C, obesity, diabetes, and alcohol consumption [2]. Partial liver resection is the only established therapy to achieve a possible cure in patients with ICC [1]. However, the incidence of recurrence is very high and the 5-year survival rate after partial hepatectomy is only 20–40% [3–6]. The risk factors for ICC recurrence after surgery included multiple tumors, vascular invasion, and lymph node metastasis [1]. Regarding the overall survival of patients with ICC, lymph node metastasis, vascular invasion, multifocal lesions, tumor diameter, old age, and cirrhosis were associated with poor prognosis [3,7,8]. However, limited data are available in patients with recurrent ICC after curative resection.

The aim of this multi-center study was to identify the predictive factors of survival in patients who had recurrent ICC after curative resection.

2. Methods

From January 2005 to December 2015, 97 patients underwent the initial operation for ICC at the following 7 institutions of our study group. The institutional Review Board of each institution approved this

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Table 1
Univariate and multivariate analysis for prognostic factors after recurrent ICC following curative hepatectomy.

Factors	n	Univariate		Multivariate		
		Median survival months after recurrence (95% CI)	p value	HR	95% CI	p value
Age (years)			0.860			
< 70	28	13.3 (8.4–23.0)				
> 70	25	13.7 (7.8–22.7)				
Sex			0.8362			
M	26	13.7 (8.4–23.0)				
F	27	13.3 (7.8–24.1)				
BMI (kg/m2)			0.2514			
< 23	28	14.6 (8.4–22.7)				
> 23	19	13.0 (5.3–17.3)				
HBV			0.5685			
Yes	7	17.3				
no	46	13.7 (10.4–17.0)				
HCV			0.4969			
Yes	8	15.0				
no	45	13.3 (10.4–19.8)				
Recurrence-free survival (years)			0.4645			
< 1	33	13.3 (7.8–19.8)				
> 1	20	13.8 (10.4–36.8)				
Post-operative complications			0.5612			
Yes	11	12.8 (5.3–44.6)				
No	42	13.8 (8.4–22.7)				
Macroscopical findings			0.0211			0.0183
MF	37	16.3 (11.3–24.0)		1		
Others (PI, IG, MF + PI)	16	10.2 (4.0–13.8)		4.01	1.27–13.42	
im			0.3512			
Yes	14	13.3 (4.1–36.8)				
No	35	13.7 (8.4–19.8)				
vp			0.3475			
Yes	27	13.8 (5.3–17.3)				
No	23	13.7 (11.3–36.6)				
vv			0.1129			
Yes	15	8.4 (4.4–13.8)				
No	35	17.0 (11.3–24.1)				
b			0.0221			0.0094
Yes	29	10.6 (5.9–14.8)		4.88	1.45–20.46	
No	18	22.7 (12.8–25.6)		1		
Tumor differentiation			0.3060			
wel, mod	36	13.1 (8.4–16.8)				
por	12	17.3 (4.4–44.6)				
Lymph node metastasis			0.1435			
Yes	11	10.6 (5.9–19.8)				
No	42	14.6 (11.3–23.0)				
CEA (initial)			0.0025			0.4761
< 5 ng/ml	35	17.3 (13.1–24.2)		1		
> 5 ng/ml	16	7.8 (4.4–14.8)		1.74	0.37–8.41	
CEA (at recurrence)			0.0024			0.9507
< 5 ng/ml	34	22.7 (13.0–36.6)		1		
> 5 ng/ml	14	8.4 (4.4–14.8)		1.05	0.23–4.24	
CA19-9 (initial)			< 0.0001			0.3939
< 40 U/ml	27	24.2 (16.4–36.8)		1		
> 40 U/ml	23	10.6 (7.2–13.0)		2.46	0.30–20.18	
CA19-9 (at recurrence)			< 0.0001			0.2097
< 40 U/ml	30	23.0 (16.4–36.6)		1		
> 40 U/ml	18	8.4 (5.3–11.3)		3.52	0.50–32.09	
GPS (initial)			0.2541			
0	39	14.6 (12.8–23.0)				
1	13	8.4 (4.4–22.7)				
GPS (at recurrence)			0.0023			0.8886
0	33	17.3 (13.0–25.6)		1		
1,2	11	7.8 (1.0–14.6)		1.16	0.14–9.48	
NLR (initial)			0.0040			0.6640
< 1.6	15	7.8 (3.4–13.7)		1.34	0.33–4.93	
> 1.6	36	17.0 (12.8–24.2)		1		
NLR (at recurrence)			0.5579			
< 2.1	24	13.8 (11.3–36.6)				
> 2.1	23	13.3 (8.4–22.7)				
PNI (initial)			0.0599			
< 45	10	8.2 (0.7–13.7)				
> 45	41	14.8 (12.8–24.1)				
PNI (at recurrence)			0.0043			0.5952
< 45	15	10.4 (3.8–13.3)		1.56	0.27–7.50	
> 45	30	17.3 (13.0–25.6)		1		

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