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Clinicopathological Prognostic Factors and Impact of Surgical Treatment of Mass-forming Intrahepatic Cholangiocarcinoma

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Abstract. The clinicopathological characteristics relevant to prognosis after surgical treatment of intrahepatic cholangiocarcinoma (ICC) remain unclear. In this study, the clinicopathological features of 19 patients with mass-forming ICC, the most common form of the disease, were reviewed to analyze prognostic determinants. Two or more segmentectomies of the liver with systematic lymphadenectomy were performed in 18 patients. Resection of the extrahepatic bile duct was performed in 14 patients, and reconstruction of the portal vein was accomplished in 5 patients. Stage IVA or IVB tumors were seen in 13 patients, and lymph node (LN) metastasis was present in 14 patients. The estimated 5-year survival rate after surgery for mass-forming ICC was 28%, with median survival time of 18 months. In univariate analysis, five variables were determined to be significantly correlated with poor survival of patients with mass-forming ICC after surgery. These variables include mass-forming ICC with periductal infiltration, perineural invasion, portal vein invasion, presence of intrahepatic metastasis, and two or more LN metastases. Survival rates of 5 patients without LN metastasis and 6 patients with a single LN metastasis were 80% and 33% at 5 years, respectively, while 8 patients with two or more LN metastasis failed to survive beyond 2 years. Multivariate analysis revealed the presence of intrahepatic metastasis to be an independent prognostic factor of poor survival. Hepatectomy with resection of the extrahepatic bile duct and systematic lymphadenectomy yields a good chance for prolonged survival for patients with mass-forming ICC when the lesion is singular and LN metastasis is limited to a regional LN. Because the presence of intrahepatic metastasis was closely related to a poor prognosis in patients with mass-forming ICC, efficacious chemotherapy would be needed to control development of the lesion.

Intrahepatic cholangiocarcinoma (ICC) is the second most common primary liver cancer originating from the intrahepatic bile ducts, although it accounts for only about 6% of primary liver cancers as determined by the Liver Cancer Study Group of Japan [1]. Most cases of ICC are not diagnosed until the disease has reached an advanced stage, as it has proven difficult to identify high-risk patients with ICC [1, 3–5]. In addition to direct invasion to the portal region, ICC tends to spread by perineural invasion, lymphatic involvement, and metastasis to local or distant lymph node (LN) [2, 6–8]. Thus, the poor prognosis after surgical treatment of ICC may be associated with its various patterns of tumor extension as well as delayed diagnosis. Several studies on ICC have reviewed its clinical, radiological, and pathological aspects [2, 6, 9–21]. This neoplasm may show differences in biological behavior depending on tumor location and morphology [5, 7, 9, 11, 17, 18]. Intrahepatic cholangiocarcinoma is macroscopically classified into the following three types; mass-forming, periductal infiltrating, and intraductal growth type [22]. Among these classifications, mass-forming tumors are the most common [23]. It remains unclear which factors affect prognosis after surgical treatment for ICC. Therefore, analysis of prognostic determinants after surgical treatment of mass-forming ICC may be useful not only in clarifying the clinicopathological characteristics of this tumor, but also in determining the appropriate treatment for resectable disease.

We have adopted an aggressive surgical policy in the treatment of ICC. Based on a retrospective analysis of patients with mass-forming ICC who underwent hepatectomy, we determined the prognostic factors and evaluated the efficacy of surgical treatment for this tumor.

Patients and Methods

Patients

Between April 1, 1978, and November 30, 1998, 42 patients with ICC were admitted to our hospital. Surgical resection was indicated when (1) patients were in good health and (2) ICC did not show the findings of extensive tumor involvement of the portal hepatis, paraaortic LN metastases, peritoneal tumor dissemination, or distant organ metastases. Twenty-seven patients with ICC underwent hepatectomy for ICC. Another 15 patients were excluded from resection because of extensive tumor involvement of

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the portal hepatis in 7 patients, the presence of intrahepatic metastases in 3, and distant organ metastases in 5. According to the guidelines for the classification of primary liver cancer published by The Liver Cancer Study Group of Japan [22], ICC was defined as cholangiocarcinoma arising from a segmental duct (the first major branch of each hepatic duct) or from a more peripheral duct. The resected tumors were also divided into the categories of intraductal growth (1 patient), periductal infiltrating lesions (5 patients), and mass-forming lesions (21 patients). Because there were two operative deaths within 30 days of surgery, the clinical features and tumor histology of the remaining 19 patients with mass-forming ICC were retrospectively reviewed to analyze the prognostic determinants of this disease. Of these patients, 12 were men and 7 were women, with a mean age of 63 years (range: 48 to 75 years). Their tumors were staged according to the pTNM classification based on the criteria of the Union International Contre la Cancer (UICC) [24]. Patients with mixed or combined hepatocellular and cholangiocellular carcinoma as well as hepatic cystadenocarcinoma and cholangiocarcinoma arising from the bile duct confluence were not included in this study.

Symptoms

The most common symptom was obstructive jaundice in 7 patients, followed by upper abdominal pain or discomfort in 6 patients, and fatigue in 3 patients. Preoperative percutaneous transhepatic biliary drainage was performed in the patients with jaundice.

Surgical Procedures

The type of surgical procedure performed was dependent on both the tumor location and the mode of extension. Eleven tumors were located in right hepatic lobe and eight in left hepatic lobe. Eighteen patients with mass-forming ICC underwent major liver resection. The type of liver resection was right trisegmentectomy or extended right lobectomy in 9 patients, right lobectomy in 1, left trisegmentectomy or extended left lobectomy in 5, left lobectomy in 2, central bisegmentectomy in 1, and posterior segmentectomy in 1. All but one patient underwent systematic lymphadenectomy (clearance of the hepatoduodenal ligament, retropancreatic, and paraaortic LN as well as LN located along the common hepatic and celiac arteries). In addition, dissection of LN along the left gastric artery and of perigastric LN along the lesser curvature was performed for ICC located in the left hepatic lobe. One patient with a 19-cm hypervascular tumor was preoperatively diagnosed as having hepatocellular carcinoma, and no enlargement of the regional LN was seen at laparotomy, so right hepatic trisegmentectomy alone was performed. Biliary reconstruction by Roux-en-Y hepaticojejunostomy combined with resection of the biliary confluence and extrahepatic bile duct was performed in 14 patients (74%), including 4 with peripheral tumors and 10 with central tumors. Vascular reconstruction was performed in 5 patients (26%), including portal vein reconstruction in all 5 and right hepatic artery reconstruction in 2 (Table 1). No patient received postoperative radiation therapy or adjuvant chemotherapy.

Table 1. Surgical treatment in 19 patients with mass-forming ICC.

Treatment	Number of patients
Type of hepatectomy	
Right trisegmentectomy	4
Extended right lobectomy	5
Right lobectomy	1
Left trisegmentectomy	1
Extended left lobectomy	4
Left lobectomy	2
Central bisegmentectomy	1
Posterior segmentectomy	1
Systematic lymphadenectomy	18
Biliary reconstruction	14
Vascular reconstruction	
Portal vein	5
Right hepatic artery	2

ICC: intrahepatic cholangiocarcinoma.

Prognostic Determinants

The influence of gender, age, tumor location, gross appearance, tumor size, tumor differentiation, portal vein invasion, extrahepatic bile duct involvement, intrahepatic metastasis, LN involvement, perineural invasion, clearance margins of resected surface, and tumor stage were analyzed to determine prognostic factors associated with survival after surgery for mass-forming ICC.

Statistical Analysis

For each variable, survival was estimated by the Kaplan-Meier method and was checked for statistical significance by the log-rank test. Cox's proportional hazard model was used in stepwise multivariate analysis to identify factors independently associated with prognosis after surgery. The relationship between the macroscopic appearance of the mass and the pathological findings was assessed using the chi-square test with Fisher's exact method. Probability values < 0.05 were considered significant.

Results

Tumor Extension and Pathological Features

Liver cirrhosis was present in 1 patient, but no patient had hepatolithiasis. The mean tumor size was 6.3 cm (range: 1.5 to 19 cm). Seven tumors of mass-forming ICC had periductal infiltration. Tumor invasion of a major branch of the portal vein was observed in 7 patients, and invasion of the extrahepatic bile duct was observed in 5 patients. Examination of the resected specimens showed that 13 patients had solitary lesions and 6 (32%) had intrahepatic metastasis. Lymph node metastasis was found in 14 (78%) of the 18 patients undergoing lymphadenectomy. A single LN metastasis was observed in 5 patients, affecting the hepatoduodenal ligament in 2 and being located along the common hepatic artery in 3. Perineural invasion was observed in 13 patients (68%). Clearance margins of the resected surface were more than 5 mm in 15 patients. Three patients had stage II disease, 3 were in stage III, 5 were in stage IVA, and 8 were in stage IVB (Table 2).

Table 2. Univariate analysis of prognostic factors for mass-forming ICC.

Variable	No. of patients	Survival (%) 3-Year	5-Year	*p* Value
Gender				
Male	12	22	11	0.2648
Female	7	57	57	
Age (years)				
< 65	7	29	29	0.6678
≥ 65	12	33	25	
Tumor factors				
Location				
Right lobe	11	55	41	0.2032
Left lobe	8	13	13	
Tumor size (cm)				
< 5	7	38	19	0.8697
≥ 5	12	33	33	
Gross appearance				
Mass-forming type				
Without periductal infiltration	12	58	47	0.0028
With periductal infiltration	7	0	0	
Differentiation				
Well differentiated	11	18	18	0.5967
Not well differentiated	8	50	38	
Portal vein invasion				
Yes	7	0	0	0.0081
No	12	56	44	
Extrahepatic bile duct invasion				
Yes	5	0	0	0.0918
No	14	48	38	
Intrahepatic metastasis				
Yes	6	0	0	0.0005
No	13	51	41	
Lymph node metastasis				
No	5	80	80	0.0193
Single lymph node	6	50	33	
Multiple lymph nodes	8	0	0	
Perineural invasion				
Yes	13	15	8	0.0059
No	6	83	83	
Resection margin (mm)				
≤ 5	4	0	0	0.1832
> 5	15	44	36	
Tumor stage				
II and III	6	67	67	0.0882
IV	13	23	15	

Morbidity and Mortality

Postoperative complications occurred in 7 (33%) of the 21 patients with mass-forming ICC. The complications included development of subphrenic abscess in 2 patients, leakage of hepaticojejunostomy in 1 patient, and biliary fistula in 2, all of which resolved with conservative management. There were 2 operative deaths (mortality rate, 9.5%) after hepatopancreatoduodenectomy and right hepatic trisegmentectomy in patients with advanced disease. There were no complications associated with vascular reconstruction.

Recurrent Sites and Survival Rates

Recurrence was observed in 15 patients, with the main sites being the remnant liver in 8, systemic LN metastasis in 4, and the anastomosis for biliary reconstruction in 2. For 3 patients with recurrent disease, total gastrectomy with resection of the pancreatic tail, splenectomy, and partial resection of the diaphragm was performed in 1 patient, and repeat hepatectomy was accomplished in 2 without morbidity or mortality. Whereas the median survival time from the diagnosis based on medical imaging in the 15 patients with unresectable ICC was 6 months (range, 2 to 20 months), the median survival among the 19 patients with resectable mass-forming ICC was 18 months. The 1-, 3- and 5-year survival rates after surgery for mass-forming ICC were 63%, 35%, and 28%, respectively, showing a significant difference from the unresectable cases ($p < 0.01$) (Fig. 1). In our series, 4 patients have survived beyond 5 years after surgical resection of mass-forming ICC. Of these, 2 patients with limited metastasis to a LN along the common hepatic artery have survived without recurrence for 75 and 82 months after extended right hepatic lobectomy with resection of the extrahepatic bile duct and systematic lymphadenectomy. The other 2 patients treated with repeat resection have survived for 121 and 131 months after the initial resection for mass-forming ICC (Table 3).

Prognostic Determinants

In univariate analysis, five variables were significantly associated with poor survival after surgical treatment. These include mass-forming ICC with periductal infiltration, portal vein invasion, perineural invasion, presence of intrahepatic metastasis, and two or more LN metastases ($p < 0.05$) (Table 2). Periductal infiltration in mass-forming ICC was significantly associated with perineural invasion along Glisson's sheath ($p = 0.046$). Six patients with intrahepatic metastasis did not survive beyond 14 months after surgery, while 13 patients without intrahepatic metastasis had a 5-year survival rate of 41% (Fig. 2). Six patients with a single LN metastasis had a 5-year survival rate of 33%, and 8 patients with two or more LN metastases failed to survive beyond 2 years (Fig. 3). Multivariate analysis revealed that intrahepatic metastasis ($p = 0.0166$) was an independent and a significantly poor prognostic factor (Table 4).

Discussion

Intrahepatic cholangiocarcinoma can extend in a different manner from hepatocellular carcinoma [4, 7, 14, 17, 18]. Multimodal and locoregional extension such as infiltration of the parenchyma, the presence of intrahepatic satellite nodules, vascular invasion, and the high incidence of regional LN metastasis is frequently observed at the time of diagnosis of ICC. According to previous reports, the incidence of LN metastasis was 14% to 58%, and intrahepatic metastasis or satellite lesions were present in 26% to 58% of patients treated surgically [2–7, 13, 14, 17–21] (Table 5). The resectability of ICC varies from 19% to 70% in reports from different institutions [2–7, 12, 16], and such differences in resectability may be associated with variations in the extent of the disease. In our series, 13 stage IVA or IVB tumors were resected with five vascular reconstructions based on our aggressive surgical policy, which resulted in a 63% resectability rate for ICC. Although the improved resectability rate did not yield an increased survival benefit for ICC as shown in Table 5, long-term survival may be possible even after resection of the tumors of advanced stage [16]. It is therefore important to determine which tumor characteristics meet the expectation of prolonging survival after surgical treatment. This retrospective study was designed to clarify

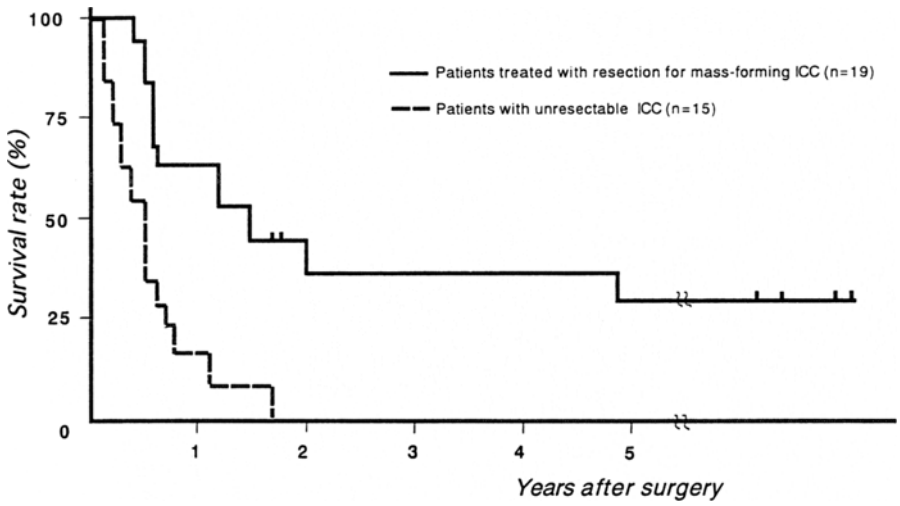

Fig. 1. Overall survival of mass-forming intrahepatic cholangiocarcinoma (ICC) patients after surgery stratified by resectability. Survival time in 15 patients with unresectable ICC represented the period from the diagnosis of ICC based on medical imagings.

Table 3. Long-term survivors beyond 5 years after surgery for mass-forming ICC.

No. of patient	pTNM staging	Gross appearance	Tumor involvement		Intrahepatic metastasis	Lymph node metastasis	Perineural invasion	Treatment	Outcome
			PV	BD					
1	III	Mass-forming ICC without PI	Absent	Absent	Absent	Absent	Absent	Left lobectomy Partial gastrectomy ↓ Total gastrectomy Splenectomy Resection of pancreatic tail	Recurrence at 28 months ↓ Alive for 131 months after the initial resection
2	II	Mass-forming ICC without PI	Absent	Absent	Absent	Absent	Absent	Right trisegmentectomy ↓ Partial hepatectomies	Recurrence at 96 months ↓ Alive for 121 months after the initial resection
3	IVB	Mass-forming ICC without PI	Absent	Absent	Absent	Present	Present	Extended right lobectomy	Alive for 82 months
4	IVB	Mass-forming ICC without PI	Absent	Absent	Absent	Present	Absent	Right trisegmenectomy	Alive for 75 months

PV: portal vein, BD: extrahepatic bile duct, PI: periductal infiltration.

the prognostic determinants through the analysis of outcome after surgery for patients with mass-forming ICC in our own series.

Cherqui and associates [13] indicated three criteria (no LN metastasis, a clearance margin ≧ 1 cm, and a solitary tumor) as important for determining whether surgery for ICC was curative. It was reported that the 2-year actuarial survival was 100% after surgery when the three criteria were met in patients who underwent liver resections for ICC [13]. According to their criteria, most of our patients had non-curative resections, but a good prognosis was obtained in 2 patients with a single metastasis to LN along the common hepatic artery. In our study on the prognostic determinants after surgery for mass-forming ICC, a decline in survival was implicated in mass-forming ICC with periductal infiltration, portal vein invasion, the presence of intrahepatic satellite lesions, LN metastases, and perineural invasion in univariate analysis. Among those factors, the presence of intrahepatic satellite lesions was independently associated with a poor prognosis after surgery, corresponding to the results of Madariaga and associates [5], although the power of multivariate analysis in the present study is low because of a limited sample size of mass-forming ICC. Yamamoto and colleagues also [6] indicated that a salient feature in recurrence pattern of mass-forming ICC was intrahepatic metastasis, corresponding to our findings that the main sites were the remnant liver in 8 of 15 patients with recurrent disease after surgery for mass-forming ICC. Regional LN metastases were reported to be a significant prognostic factor in several studies of ICC [5, 14, 19, 20]. In our series, the reason that LN metastasis was not independently associated with a significantly poor prognosis in multivariate analysis may be explained by the existence of 2 disease-free survivors who are alive more than 5 years after hepatectomy. Although systematic lymphadenectomy combined with hepatectomy is an efficacious strategy for patients with a limited metastasis in regional LN from mass-forming ICC, adjuvant therapy for potential intrahepatic satellite lesions would

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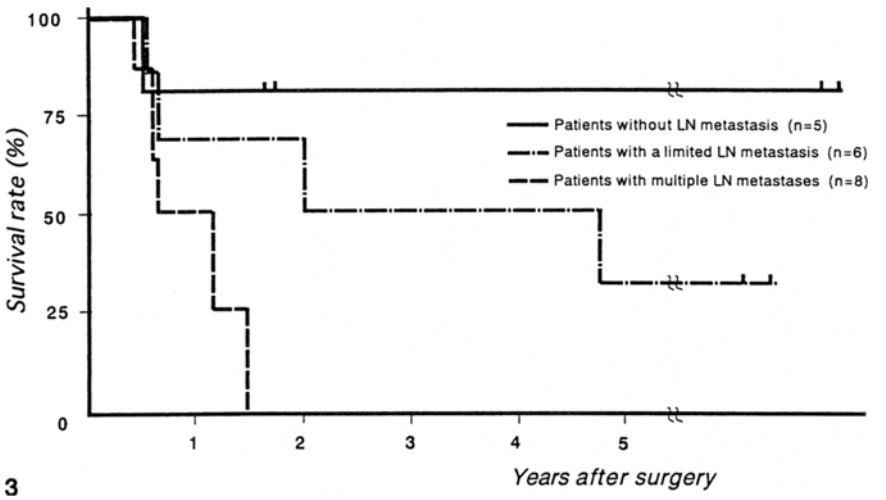

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Fig. 2. Actuarial survival of mass-forming ICC patients after surgery according to the presence of intrahepatic metastasis. $p < 0.01$ by the log rank test.

Fig. 3. Actuarial survival of mass-forming ICC patients after surgery, stratified by the extent of lymph node (LN) metastasis. $p < 0.05$ by the log rank test. One patient who had no macroscopic LN metastasis at laparotomy and no LN recurrence beyond 5 years after hepatectomy is included in the patients without LN metastasis.

Table 4. The results of a multivariate analysis using Cox's proportional hazard model.

Variable	Category	Hazard ratio (95% CI)	*p* Value
Gross appearance In mass-forming ICC	1: without periductal infiltration 2: with periductal infiltration	0.361 (0.095–1.367)	0.1335
Portal vein invasion	1: absent 2: present	0.755 (0.136–4.181)	0.7475
Intrahepatic metastasis	1: absent 2: present	11.348 (1.554–82.881)	0.0166
Lymph node metastasis	1: none or single lymph node 2: multiple lymph nodes	0.768 (0.127–4.637)	0.7733
Perineural invasion	1: absent 2: present	0.150 (0.015–1.466)	0.1028

be needed to improve the prognosis after surgical treatment [5]. Research into chemotherapy regimens may open up a new vista in the treatment of mass-forming ICC.

The perineural space is a lymphatic channel and a major pathway for LN metastasis. Bhuiya and colleagues [25] demonstrated that perineural invasion has a profound impact on survival in analysis of hilar cholangiocarcinoma. Mass-forming ICC with periductal infiltration also showed a poor prognosis after surgical resection, which was significantly associated with perineural invasion. Chijiiwa et al. [26] indicated that perineural invasion might be a reason for poor prognosis of ICC after surgery even in a symptom-free stage without extrahepatic bile duct involvement and LN metastases. Perineural invasion as well as a high incidence of LN metastases in mass-forming ICC may explain the aggressive invasive behavior of this type of tumor. Considering that cancer readily spreads through the perineural space, dissection of nerve fibers and plexus around the hepatic and celiac arteries and portal vein should be performed in systematic lymphadenectomy for patients with mass-forming ICC.

The recurrence rate after surgery for mass-forming ICC is high,

Table 5. Outcome after surgery for primary intrahepatic cholangiocarcinoma.

Authors	No. of patients	Incidence (%)		Median survival (months)	Survival rate (%)		
		LN metastasis	Intrahepatic metastasis		1-Year	3-Year	5-Year
Chen et al. [12]	20	NR	NR	21	70	56	—
Yamamoto et al. [6]	20	25	35	—	66	36	36
Schlinkert et al. [2]	6	17	40	34	83	30	—
Cherqui et al. [13]	14	14	29	14	58	—	—
Chou et al. [14]	19	58	NR	9	49	37	—
Yamanaka et al. [7]	26	58	46	—	41	14	14
Pichlmayr et al. [3]	32	22	41	13	—	25	21
Nakeeb et al. [15]	9	NR	NR	26	—	—	44
Berdah et al. [4]	19	37	26	15	67	—	32
Madariaga et al. [5]	34	18	47	19	67	40	35
Lieser et al. [16]	28	NR	NR	—	85	60	—
Nozaki et al. [17]	47	32	36	—	59	30	27
Sasaki et al. [18]	12	NR	58	16	—	—	—
Isaji et al. [19]	36	46	54	—	44	24	24
Valverde et al. [20]	30	37	26	15	67	—	32
Kim et al. [21]	28	39	NR	17	51	22	—
Present series	19	74	32	18	63	35	28

LN: lymph node, NR: not reported.

with 79% recurrence in our series. Treatment for recurrent disease varies in the site and pattern of recurrence. In 2 patients treated with repeat hepatectomy, 1 patient died of recurrent disease at 40 months and another is alive for 16 months with recurrence after reresection. Another patient with resection of locoregional recurrence between the diaphragm and the stomach has survived disease-free for 103 months after repeat resection. Cherqui et al. performed three repeat resections including one liver transplantation for ICC patients and they were reported to be alive with recurrence for 34 months and without disease for 24 and 32 months, respectively [13]. Thus, aggressive surgical treatment is recommended for recurrent disease in patients with mass-forming ICC under careful patient selection criteria.

In conclusion, systematic lymphadenectomy combined with hepatectomy is a reasonable surgical treatment for mass-forming ICC. However, considering the presence of intrahepatic satellite lesions as a prognostic determinant, adjuvant chemotherapy would be needed to improve survival after surgical resection of mass-forming ICC.

Résumé. Les caractéristiques clinicopathologiques influençant le pronostic après traitement des cholangiocarcinomes intra-hépatiques (CIH) ne sont pas claires. Dans cette étude, les caractéristiques clinicopathologiques chez 19 patients porteurs de CIH à forme tumorale, la forme la plus fréquente, ont été analysés à des fins pronostiques. On a réalisé une segmentectomie de deux segments ou plus avec lymphadénectomie systématique chez 18 patients, une résection des voies biliaires extra-hépatiques chez 14 et une reconstruction de la veine porte chez 5 patients. Treize patients avaient une tumeur stade IVA ou IVB; 14 avaient des métastases ganglionnaires. La survie à 5 ans après chirurgie pour CIH à forme tumorale a été de 28%; la médiane de survie a été de 18 mois. En analyse univariée, on a trouvé cinq variables significativement associées à une survie médiocre chez les patients opérés de CIH à forme tumorale. Ces variables sont un CIH avec infiltration péricanulaire, un envahissement périneural, un envahissement portal, la présence de métastases hépatiques, et des métastases de deux ganglions ou plus. La survie de cinq patients sans métastase ganglionnaire et de six patients avec une seule métastase ganglionnaire ont été, respectivement, de 80% et de 33% à 5 ans, alors qu'aucun des huit patients avec deux métastases ganglionnaires ou plus n'a survécu au-delà de deux ans. En analyse multivariée, la présence de métastases intrahépatiques était un facteur indépendant de mauvais pronostic. Une hépatectomie avec résection des voies biliaires extra-hépatiques associée à un curage lymphatique systématique améliore les chances de survie prolongée en cas de CIH à forme tumorale lorsque la lésion est unique et les métastases ganglionnaires sont limitées à un seul ganglion lymphatique régional. Puisque la présence de métastases intrahépatiques est étroitement en rapport avec un mauvais pronostic chez les patients porteurs de CIH à forme tumorale, une chimiothérapie efficace est nécessaire pour contrôler l'évolution.

Resumen. Tras el tratamiento quirúrgico, las características clínicopatológicas pronósticas más importantes para los pacientes con colangiocarcinomas intrahepáticos (ICC) son poco conocidas. En este estudio se revisan las características clínicopatológicas más frecuentes en 19 pacientes con grandes tumores ICC, con objeto de determinar los factores pronósticos más importantes. 18 casos fueron tratados mediante dos o más segmentectomías hepáticas y linfadenectomía sistemática. En 14 pacientes se procedió a la resección y subsiguiente reconstrucción de la vía biliar extrahepática y en 5 de la vena porta. 13 pacientes pertenecían al estadio IV A o IV B y adenopatias metastásicas (LN) se registraron en 14 enfermos. Tras el acto quirúrgico el porcentaje medio estimado de supervivencia a los 5 años fue del 28%, con un tiempo de supervivencia de 18 meses. En pacientes con ICC que cursan con una tumoración macroscópicamente visible y palpable, el análisis univariante detectó 5 variables significativas por lo que a la escasa supervivencia se refiere: tumoración ICC con infiltración periductal, invasión perineural o de la vena porta, existencia de metástasis intrahepáticas y 2 o más adenopatías (LN) metastásicas. La supervivencia a los 5 años de 5 pacientes sin metástasis ganglionares (LN) y con una sola adenopatía metastásica fue del 80% y 33%, mientras que 8 pacientes con dos o más adenopatias metastásicas (LN) no sobrevivieron más de 2 años. El análisis multivariante demostró que las metástasis intrahepáticas constituyen un factor pronóstico independiente, de escasa supervivencia. La hepatectomía con resección de la vía biliar extrahepática asociada a una sistemática linfadenectomia puede, con suerte, prolongar la supervivencia de pacientes con tumores ICC palpables, cuando la tumoración es única y las adenopatias metastásicas son exclusivamente regionales. Dado que la presencia de metástasis intrahepáticas es signo de mal pronóstico, se precisa una eficaz quimioterapia para controlar el desarrollo de este tumor.

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