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Anatomic resection reduces the recurrence of solitary hepatocellular carcinoma ≤5 cm without macrovascular invasion

Atsushi Kudo, M.D., Ph.D.*, Shinji Tanaka, M.D., Ph.D., Daisuke Ban, M.D., Ph.D., Satoshi Matsumura, M.D., Ph.D., Takumi Irie, M.D., Ph.D., Noriaki Nakamura, M.D., Ph.D., Shigeki Arii, M.D., Ph.D.

Department of Hepato-Biliary-Pancreatic Surgery, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo 113-8519, Japan

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Milan criteria

Abstract

BACKGROUND: In patients with solitary hepatocellular carcinoma ≤5 cm without macrovascular invasion, it is unknown whether the initial anatomic resection improves the long-term survival.

METHODS: Among 545 initial hepatectomies for hepatocellular carcinoma between 2000 and 2012, the 233 patients with the aforementioned criteria of hepatocellular carcinoma were enrolled.

RESULTS: The mean observation time was 1,125 days. Disease-free 5-year survival rates with and without anatomic resection were 46% and 23%, respectively ($P = .009$). Multivariate analyses for disease-free survival rates revealed the risk factors to be α-fetoprotein (odds ratio, 1.6; $P = .028$) and anatomic resection (odds ratio, .7; $P = .048$), while increased Child-Pugh score (>5) was the only independent risk factor for overall survival (odds ratio, 1.8; $P = .043$). The 5-year overall survival rates with and without Child-Pugh score 5 were 74% and 40%, respectively ($P < .0001$, log-rank test).

CONCLUSIONS: Initial anatomic resection for small solitary hepatocellular carcinoma without macrovascular invasion improved disease-free survival rates remarkably.

The most important aim when performing hepatectomy is to accurately estimate the functional liver volume to avoid liver failure and completely remove hepatocellular carcinoma. Some authors have reported that anatomic resection is superior to nonanatomic resection and reduces intrahepatic metastases of hepatocellular carcinoma through the portal vein.[1,2] Moreover, anatomic resection exposing the length of the hepatic veins reduces the incidence of accidental bleeding and the unexpected impairment of the Glisson that results in the development of ischemic areas.[3] Anatomic resection requires precise information about individual anatomic variations and markedly reduces postoperative morbidity and improves long-term mortality in patients with hepatocellular carcinoma.[4] The unexpected development of the ischemic area and the stasis of the hepatic vein may result in liver dysfunction as well as postoperative morbidity and mortality.[5]

However, discussion of the benefits of anatomic resection is controversial. Some reports state that the indications

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* Corresponding author. Tel.: +81-3-5803-5928; fax: +81-3-5803-0263.

E-mail address: kudomsrg@tmd.ac.jp

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for anatomic resection should be limited. Excessive resection often leads to serious postoperative liver failure and operative mortality.[6] In chronic hepatitis and liver cirrhosis, it increases severe bleeding from hepatic veins and liver parenchyma, leading to postoperative liver dysfunction. Anatomic resection is beneficial for the treatment of solitary small hepatocellular carcinoma in patients with α-fetoprotein levels >100 μg/L.[7] Liver functional reserve dictates the indication for anatomic resection and resectable liver volume.[8] The severity of cirrhosis and tumor characteristics rather than the type of resection determine long-term survival in patients with hepatocellular carcinoma.[9] An adequate resection margin is required in nonanatomic resection. Anatomic resection is preferred to avoid micrometastases,[10] though it has been shown to decrease disease-free survival and overall survival rates in patients with liver dysfunction.[11] For patients with small liver cancer and poor liver function, the limited procedure leads to a comparatively longer survival.[12]

In the present study, we aimed to elucidate whether anatomic resection improves long-term survival and to identify the preoperative determinants influencing the survival of the patients. To exclude the malignancy factor of the tumor, single small hepatocellular carcinoma without macroscopic vascular invasion (within the Milan criteria) were included in this study. Through our findings, we noted that initial anatomic resection reduces disease-free survival rate, and liver dysfunction was the best predictor of overall survival, irrespective of whether the patient had undergone initial anatomic resection.

Methods

Between April 2000 and March 2012, 545 patients received initial curative hepatic resection for hepatocellular carcinoma in the Department of Hepato-Biliary-Pancreatic Surgery at Tokyo Medical and Dental University. Among these patients, 233 with single, small, noninvasive hepatocellular carcinomas were selected for this study. The operative procedures are shown in Table 1. The indication for hepatic resection with anatomic resection were determined by the indocyanine green retention rate at 15 minutes according to Makuuchi's criteria and the Child-Pugh score. In anatomic resection, the liver was divided according to the demarcation line, after occlusion of the portal vein and hepatic artery. When necessary, an intravenous injection of Sonazoid was used to detect the main feeding artery.[13] As shown in Fig. 1, the liver is resected along the demarcation line after Glisson clamping. The anatomic resection procedure included segmentectomy, sectoriectomy, and hemilobectomy. For nonanatomic resection, the liver was resected to maintain a surgical margin of 5 mm, if possible, without referring to the demarcation line. The nonanatomic resection procedure did not include segmentectomy, sectoriectomy, and hemilobectomy, as shown in Table 1.

Table 1 Baseline characteristics

Variable	Nonanatomic (n = 112)	Anatomic (n = 121)	P
Background			
Age (y)	66.9 ± 10.6	67.3 ± 9.5	.789
Men	73 (65%)	95 (79%)	.028*
Hepatitis B virus	21 (19%)	20 (17%)	.732
Hepatitis C virus	65 (58%)	64 (53%)	.507
Liver function			
AST (IU/L)	50.9 ± 43.8	47.0 ± 33.7	.445
Platelet count ($\times 10^4/\mu L$)	13.1 ± 6.6	16.1 ± 6.8	.001*
Child-Pugh score	5.0 ± 1.6	4.9 ± 1.3	.533
Prothrombin time (%)	84.3 ± 15.2	88.8 ± 15.3	.028*
Albumin (g/dL)	3.9 ± .6	4.0 ± .5	.028*
Total bilirubin (mg/dL)	1.0 ± .7	.8 ± .5	.062
ICG R15 (%)	21.1 ± 13.9	15.7 ± 10.1	.001
Tumor Factors			
Size (cm)	2.6 ± 1.1	3.3 ± 1.1	<.0001*
α-fetoprotein (ng/mL)	125 ± 377	583 ± 4118	.245
DCP (mAU/mL)	219 ± 641	973 ± 3576	.029*
Operative procedures			
Segmentectomy	0	59	<.0001*
Sectoriectomy	0	45	
Hemihepatectomy	0	17	
Histology			
Surgical margin	11 (10%)	6 (5%)	.208
Liver cirrhosis	68 (61%)	53 (44%)	.012

AST = aspartate aminotransferase; DCP = des-gamma-carboxy prothrombin; ICG = indocyanine green.
*Statistically significant ($P < .05$).