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World J Gastroenterol 2004;10(14):2134-2135
World Journal of Gastroenterology
 ISSN 1007-9327

• BRIEF REPORTS •

A report of 28 cases of 3-year follow-up after liver transplantation for advanced hepatocellular carcinoma

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Received: 2003-12-28 **Accepted:** 2004-01-08

Abstract

AIM: To investigate the therapeutic value of liver transplantation for advanced hepatocellular carcinoma (HCC).

METHODS: Twenty-eight patients with advanced HCC were treated by liver transplantation from August 2000 to October 2003 at Peking University Third hospital. All the patients were followed up to evaluate the result.

RESULTS: The longest follow-up duration was 3 years and 3 mo. Till the end of the follow-up period, 17 patients had already died and 11 were alive. Of those who died, 10 patients died of tumor recurrence, 4 died during the perioperative period, 2 died of variceal bleeding, and 1 died of biliary complication. According to life table method, the 1-, 2-, and 3-year survival rates were 87.5%, 52.5%,and 42.9%, respectively.

CONCLUSION: Liver transplantation provides a new treatment under the circumstance of lacking of an effective treatment for advanced HCC at present. Some patients can survive for a relatively long time free of tumor. In our country, if the patients can afford liver transplantation, advanced HCC without extrahepatic metastasis is an indication for liver transplantation at present.

Wang DC, Zhang TL, Song SB, Yuan J, Xiu DR, Yang XX. A report of 28 cases of 3-year follow-up after liver transplantation for advanced hepatocellular carcinoma. *World J Gastroenterol* 2004; 10(14): 2134-2135
http://www.wjgnet.com/1007-9327/10/2134.asp

INTRODUCTION

Hepatocellular carcinoma (HCC) is a common malignant tumor in China. The methods of treatment for advanced HCC are limited, and the prognosis is so poor. Peking University Third Hospital began to carry out liver transplantation since August 2000. Some of the patients suffered from advanced HCC. In our study, the result of treatment has been found to be somewhat accepted at present.

MATERIALS AND METHODS

Materials

Twenty-eight patients with advanced HCC were treated by liver transplantation from August 2000 to October 2003 at our hospital. Of them, twenty-six patients were male. The average age was 46.3 years, ranging from 20 to 63 years. All the patients suffered from cirrhosis caused by hepatitis B. Child-Pugh classes A, B, and C patients were 13, 8, and 7, respectively. The diagnosis was made by ultrasound, computed tomography, magnetic resonance imaging, arteriography and serum alpha-fetoprotein levels. Postoperative pathologic examination confirmed that all the patients had HCC. The patients with extrahepatic spread were excluded by ultrasound, chest film and bone scan. All the patients met the following criteria: solitary tumor $\geqslant$5 cm or with multiple nodules and total diameter >8 cm; and the mean diameter of single nodule was 10.3 cm, ranging from 3 cm to 20 cm. There were 12 patients with tumor involving bilateral hepatic lobes, 5 with positive porta hepatis nodes, and 18 with portal invasion.

Methods

All the patients underwent orthotopic liver transplantation (OLT) and were taken care of by the same medical team perioperatively. The donors were healthy male who had brain death with the age of 20-40 years. The initial 11 patients did not undergo formal chemotherapy postoperatively, and only the eighth patient underwent transarterial chemoembolization preoperatively (hot lipiodol 10 mL and cisplatin 100 mg). Seventeen patients underwent the formal intravenous chemotherapy postoperatively when the hepatic function was normal. The chemotherapy regime was: administration of adriamycin 40 mg, cisplatin 60 mg, calcium folinate-SF 200 mg and 5- Fluorouracil 1 000 mg on the first day, the same doses of calcium folinate-SF and 5- Fluorouracil from the second day to the fifth day. The course of chemotherapy was 5 d once a month, and there were 6 courses altogether. All the patients were followed up and the longest duration was 3 years and 3 mo.

Statistics

The survival rate was calculated according to the life table method. Patients who died of non-tumor and who stopped the follow-up in the intervals were listed into the lost.

RESULTS

Till the end of the follow-up period, 17 patients had already died, and 11 were alive. Of those dead patients (Table 1), 10 patients died of tumor recurrence, 4 died within perioperative period, 2 died of variceal bleeding, and 1 died of biliary complication. Among the patients who survived (Table 2), there were 1, 2, 2, and 3 patients survived for 8 mo, 1, 2, and 3 years free of tumor, respectively; and there were 1 and 2 patients survived for 8 mo and 1 year with tumor-recurrence, respectively. In the first year, 8 patients were lost, 3 were dead, and the 1-year survival rate was 87.5%. In the second year, 4 patients were lost, 6 were dead, and the 2-year survival rate was 52.5%. In the third year, 3 patients were lost, 1 was dead, and the 3-year survival rate was 42.9%.

Of the patients with single tumor of more than 10 cm, there was 1 patient who survived for more than 3 years. No patients with tumors involving many hepatic lobes could survive for more than 3 years, but there were 2 patients survived for more

than 2 years. There was 1 patient with positive portal lymph node survived for more than 3 years. Of the patients with portal invasion, 2 survived for more than 3 years, and 3 survived for more than 2 years. The cases were divided according to the different standards, and their survival time can be seen in Table 3.

Table 1 Causes and time of the death of patients

Cause	Peri-operatively	Variceal bleeding	Biliary complication	Tumor-recurrence		
				<1 yr	1-2 yr	>2 yr
Number	4	2[1]	1[2]	3	6	1

[1]2 years and 2 mo, and 6 mo after OLT, respectively, [2]6 mo after OLT.

Table 2 Survival time of the patients

Time	<1 yr	1-2 yr	2-3 yr	>3 yr
Number	1+1[1]	2+2[1]	2	3

[1]Survive with recurrence.

Table 3 Survival time of the different groups

Groups	<1 yr	12 yr	2-3 yr	>3 yr
Tumor diameter				
>10 cm	5	4	0	1
<10 cm	6	6	4	2
Portal invasion				
Yes	7	6	3	2
No	4	4	1	1

DISCUSSION

Among the surgical therapies of HCC, the dominant treatment is hepatic resection. A study showed that the 5-year survival rate is up to 50% after hepatic resection[1]. But HCC always occurs in the presence of liver cirrhosis, hepatic resection is limited by the poor hepatic function and the presence of portal hypertension. In general, Child' s C` stage is considered an absolute contraindication for any type of resection[1].

According to the principle of tumor surgery, replacing an allograft after total hepatectomy is an ideal curative resection of HCC[2]. Herrero *et al*. reported that in the patients with solitary HCC nodule less than 6 cm and those with 2-3 HCC nodules less than 5 cm in diameter,1- and 3-year recurrence free suvival rates were 87% and 79%, respectively[3]. In the study by Yao *et al*.[2], patients with HCC meeting the following criteria: solitary tumor $\leqslant$6.5 cm, or $\leqslant$3 nodules with the largest lesion $\leqslant$4.5 cm and total tumor diameter $\leqslant$8 cm, had survival rates of 90% and 75.2%, at 1 and 5 years after OLT, respectively. So they concluded that the current criteria for OLT based on tumor size might be modestly expanded while preserving excellent survival. Since OLT for early HCC is not fit for the situation of our country as well as the economic status, and the result of hepatic resection is good in our country, OLT is not accepted by the patients except that the patients having early HCC with serious cirrhosis can not tolerate hepatic resection.

The diagnosis of early HCC is achieved in around 30% of the cases[4]. As to the unresectable HCC, the chief therapy is a non-surgical treatment. But it always leads to poor prognosis for it is not a curative treatment. Now the generally accepted non-surgical treatment is transarterial chemoembolization. Lo *et al.* undertook a randomized controlled trial of transarterial chemoembolization for unresectable HCC[5]. The patients were excluded if they had 1 or more of the following criteria: poor hepatic function (presence of hepatic encephalopathy, ascites not controlled by diuretics, history of variceal bleeding within last three months, a serum total bilirubin level over 50 μmol/L, a serum total albumin level below 28 g/L, or a prothrombin time of more than 4 s over the control); extrahepatic metastasis; main portal vein thrombosis *etc*[5]. The chemoembolization group underwent transarterial chemoembolization, and the control group received only treatment for symptoms and complications. The estimated 1-, 2- and 3-year survival rates were 57%, 31% and 26% for the chemoembolization group, and 32%, 11%, and 3% for the control group, respectively.

There is no effective therapy for the patients with advanced HCC who do not meet the chemoembolization criteria, such as poor hepatic function and/or portal thrombosis, and they have poor prognosis even if there is no extrahepatic spread when the diagnosis of HCC is made. In the initial stage of OLT, the patients with advanced HCC were also treated by OLT in abroad, and the 3-year survival rate was 20-30%[1]. Due to the poor prognosis and the shortage of donor, OLT for advanced HCC was abandoned in foreign countries. From the year of 2000, our hospital began to perform OLT and chose advanced HCC for the initial trial just as peers at home and abroad. Till now, 28 patients with advanced HCC underwent OLT at our hospital. We can not conclude that the result is excellent through the 3-year follow-up. Many patients who underwent OLT did not meet the chemoembolization criteria, but the total survival rate was higher than that of the chemoembolization group reported by Lo *et al*. Some patients survived for a relatively long time free of tumor after OLT. Thus, liver transplantation provides a new treatment under the circumstance of lacking of an effective treatment for HCC at present, and some patients have a chance to lengthen their lives. But the expense of liver transplantation is very high. In our country, if the patients can afford liver transplantation, advanced HCC without extrahepatic metastasis is an indication for liver transplantation at present.

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Edited by Kumar M and Xu FM