

## INFLUENCE FACTORS TO RECURRENCE OF HEPATOCELLULAR CARCINOMA AFTER SURGICAL RESECTION

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### ABSTRACT

**Objective:** To analyze the influence factors to recurrence of hepatocellular carcinoma (HCC) after its resection according to pathologic findings of the resected primary tumor and angiographic features of the recurrence tumor. **Methods:** In this series, 142 cases with recurrence HCC were analyzed with respect to (1) size, number, gross and histologic findings of the primary tumor; (2) time when recurrence occurred; (3) size, number, blood supply, staining property, and accumulation of lipiodol oil in the recurrence tumor. **Following angiography, arterial chemoembolization was performed. Results:** In 101 of the 142 (71.1%) cases, the primary tumor was >5 cm in diameter, and in 41 cases (28.9%) it was <5 cm. In 67.7% of the cases, the capsule of the primary tumor was incomplete or absent. In 67.7% of the cases, the capsule of the primary tumor was incomplete or absent. In 47 cases (33.1%), satellite tumor nodules were seen during operation but they were seen on pathologic sections in 94 cases (66.2%). Tumor thrombus was present in the portal vein in 26 cases (18.3%) during operation and 121 cases (85.2%) on pathologic examination, respectively. In the majority of the cases (99/142), recurrence had occurred within 6 months after operation. The recurrence foci consisted of multiple tumor nodules of <5 cm in 68.3% of the cases. **On angiography, the recurrence tumors were rich in blood supply and with good accumulation of lipiodol after embolization. Conclusion:** Recurrence is apt to occur in HCC patients with large (>5 cm) primary tumor which has incomplete or no capsule, with satellite tumor nodules and portal vein tumor thrombus. It is suggested to perform angiography 1-2 months after surgery to detect early recurrence and, if confirmed,

the patients may be treated by trans-catheter arterial chemoembolization.

**Key words:** Hepatocellular carcinoma, Embolization, Surgery, Recurrence

Due to many reasons, the recurrence of hepatocellular carcinoma (HCC) after surgical resection is easily taken place. The focus of recurrence can not be re-resected for the great part of the patients. The treatment of transcatheter arterial chemoembolization (TAE) was performed for these patients. How to decrease the recurrence rate and increase survival rate of these patients is one of important problems. The current study was established to find the relationship with primary hepatocellular carcinoma and recurrence tumors, by surgical resection findings, pathological examinations, angiography and TAE experience.

### MATERIALS AND METHODS

Subjects were recurrence 142 patients who received hepatic angiography and chemoembolization after surgical resection with HCC. There were 91 males and 44 females in the study group. Their ages ranged from 21 to 77 years with a mean of 45.6 years. The diagnostic standard of recurrence was that patients had a medical history of resection HCC and histological diagnosis and then new tumor focus of the liver in the patients were discovered by later imaging examination. A catheter was inserted into the femoral artery by the Seldinger technique. Celiac artery angiography and the common hepatic artery angiography were performed in order to show the blood supply, then the tip of the catheter was placed to the right or left hepatic artery. The embolization was produced using Ultra-Fluid lipiodol (laboratoire guerbet, Aulnay-Sous-Bois, France). The anticancer

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drug were Doxorubicin Hydrochloride, Pharmorubicin, Pirarubicin hydrochloride, Fluorouracil, Carboplatin or Paraplatin. Three kinds of these drugs were selected and injected. The dose of drug and Lipiodol was made up by size and number of tumor, hepatic function of patient and intratumor lipiodol full up. If no tumor embolus in the main trunk of the portal vein, the tumor artery was embolized with gelatin sponge. We had reviewed the size, number, gross pathological features and histological types of the primary tumor; analyzed the size, number, recurrence time, blood supply, staining property and Lipiodol accumulation of the recurrence

tumors, so as for finding the relationship of them.

**RESULTS**

During the primary tumor, there were 114 cases (80.3%) with single nodules, 24 cases (16.9%) with multiple nodules and 4 cases (2.8%) with multiple nodule fusion. In the single nodule, the size of tumor of 32 cases (28.1%) was less than 5 cm, 36 cases (31.6%) was 5-10 cm and 46 cases (40.4%) was larger than 10 cm in diameter, respectively.

The histological classification of the primary HCC was divided into 11 types (Table 1).

Table 1. The 11 types of histological classification of the primary HCC

Type	1	2	3	4	5	6	7	8	9	10	11
Case	72	18	16	12	8	6	4	2	2	2	2
Percentage(%)	50.7	12.7	11.3	8.5	5.6	4.2	2.8	1.4	1.4	1.4	1.4

Type: 1. Thick trabecular type; 2. Compact type; 3. Compact-clear-cell type; 4. Compact-thin trabecular type; 5. Cholangiocarcinoma type; 6. Compact-pseudoglandular type; 7. Thin trabecular-pseudoglandular type; 8. Scirrhous type; 9. Thin trabecular type; 10. Clear-cell type; 11. Compact scirrhous type.

In surgical and gross pathological examination, we found that a complete fibrous capsule was seen in 46 cases (32.4%), an incompleated capsule and infiltrative type tumor grow was seen in 42 cases (29.6%) and absence of encapsulation was seen in 54

cases (38%). Daughter nodules and tumor thrombus were seen in operation with 47 (33.1%); and 26 (18.3%) cases, 94 (66.2%) and 121 (85.2%) in pathological examination.

Table 2. Recurrence time

Time	1m	2m	3m	4m	6m	7~12m	1~2y	2~3y	3~4y	4~5y	5y
Case	24	38	15	17	5	20	12	5	2	3	1
Percentage(%)	16.9	26.8	10.6	12.0	3.5	14.1	8.5	3.5	1.4	2.1	0.7

M: month, Y: year

About the recurrence time, new mass was discovered in 1 month in 24 cases (16.9%), 2 month in 38 cases (26.8%), 3 month in 15 cases (10.6%), 4 month in 17 cases (12.0%), 6 month in 5 cases (3.5%), 7-12 month in 12 cases (14.1%), 1-2 year in 12 cases (8.5%), 2-3 year in 5 cases (3.5%), 3-4 year in 2 cases (1.4%), 4-5 year in 3 cases (2.1%) and 5 year in 1 case (0.7%). The location of recurrence tumor was in right hepatic lobe with 74 cases (35.1%), in left lobe with 17 cases (12%) and in both lobes with 51 cases (35.9%). The metastases tumor of lung and abdominal cavity were seen in 18 and 3 cases, respectively. The bile duct tumor thrombus of the HCC was found in 5 patients. The single recurrence tumor was seen in 45 cases (31.7%), in which had a diameter less than 3 cm in 18 cases (40.0%), 23 cases (51.1%) had 3 to 5 cm, and 4 cases (8.9%) had greater than 5 cm. The multiple nodules was 97 cases

(68.3%), the size was less and equate 2 cm in diameter with 21 cases (21.7%) and 0.5 cm in diameter with 41 cases (42.3%). The multiple nodule fusion type was found in 35 cases (36.1%). In recurrence tumor, the tumor blood supply was hypervascularized in 48 cases (33.8%), and hypovascularized in 42 cases (29.6%). The accumulation of lipiodol was satisfaction in 74 cases (51.1%) and relatively poor in 33 cases (23.2%).

**DISCUSSION**

Even though the HCC had a radical operation resection, the recurrence rate still was higher (45.2%-60.0%).<sup>[1-3]</sup> In imaging examination, the discovery rate of angiography was 93.4% and at same time the patient could be treated with

chemoembolization.<sup>[4]</sup> The cause of recurrence was quite complicated. Present series of cases showed that the most cases were with occurrence, no matter what the classification of gross and histological, the capsule was completed or absent, the primary tumor was large or small, single or multipel nodule. In the primary tumor, when the size was large than 5 cm, the recurrence rate was higher (71.9%, n=84/114), when the size less than 5 cm, the recurrence rate was lower (28.1%). When the primary cancer was multinodular or diffuse type, most of them should be recurrence after surgical resection. The case with incomplete and absent capsule of primary tumor had a higher recurrence rate (67.6%, n=96), and lower recurrence rate with the complete capsule (32.4%, n=46). This is because that degree of differentiation was lower in the tumor of incomplete and absent of capsule. It easy brought the blood vessel tumor thrombus and cancer cells spread and infiltrated into liver tissue. The residual of satellite nodules and cancer cell in resection boundary after surgical operation was also one of reason of recurrence. This study suggested that the pathological classification of tumor cells had no significant relationship with the occurrence and prognosis. Pre-operation imaging examination has benefit to discover metastasis nodules in liver and tumor thrombus of port vein, but the detectable rate was relative lower when the tumor was smaller than 1 cm and thrombus were extremely minor in the portal vein, but all of these were closely related with the recurrence. The recurrence nodules of pro-resection in a month were mostly less than 1 cm. This discovers suggested that the tumor had been metastasis or multi-center existence of the tumor cells before the surgical resection, but it was too small to be discovered. Suenaga et al.<sup>[5]</sup> observed 118 patients of surgical resection and found that the tumor easy recurrence and worse prognosis was closely related with the tumor was multinodules, larger than 5 cm and the blood vein had been invaded. Ikeda et al<sup>[6]</sup> reported also that the early recurrence was closed related to a higher AFP lever, metastasis of cancer cells in the liver and infiltration of the portal vein before the surgery. Because the number and position of the tumor before surgery was not easy make clear, and the tiny thrombus of the portal vein can not identified and dealt with, the satellite tumor and the tiny thrombus of the portal vein be left over in the operation.

In general consideration, the recurrence rate was

higher in the 1~2 years after operation. In this study series, the higher recurrence rate was in the 6 month (n=99, 69.7%). This was related to perform the hepatic angiography after 1~2 month of operation, because there were satellite tumor, thrombus of the portal vein, incomplete and absent capsule of tumor in the operation or pathological examination. After hepatic angiography, the lipiodol oil and anticancer drug were be injected, and CT scan of liver was performed after 3 week of TAE.

Recurrence is apt to occur in HCC patients with large (>5 cm) primary tumor which has incomplete or no capsule, satellite tumor nodules and portal vein tumor thrombus. It is necessarily to perform angiography 1~2 months after surgery to detect early recurrence and, if confirmed, the patients can be treated by chemoembolization. Before the operation, we must carefully examine the shape, size, number and capsule of the mainly tumor, satellite nodule and portal vein tumor thrombus. The boundary of resection of hepatic cancer must be 2 cm around the tumor.

## REFERENCE

- [1] Adachi EA dachi E, Maeda T, Matsumata t, et al. Risk factors for intrahepatic recurrence in human hepatocellular carcinoma. *Gastronterology* 1995; 108: 768.
- [2] Nagasue N, Uchida M, Makino Y, et al. Incidence and factors associated with intrahepatic recurrence following resecting of hepatocellular carcinoma. *Gastronterology* 1993; 105: 488.
- [3] Ezaki T, Koyanagi N, Yanmagata M, et al. Postoperative recurrence of solitary small hepatocellular carcinoma. *J Surg Oncol* 1996; 62: 115.
- [4] Cheng Jimin, Wang jianhu, Yan Zhiping, et al. The diagnostic value of hepatic arterial angiography in the intrahepatic node and subclinical cases of postoperative hepatocellular carcinoma (HCC) recurrence (A report of 61 cases). *Acta Academia Medicina Shanghai* 1997; 24: 259.
- [5] Suenaga M, Nakao A, Harada A, et al. Hepatic resection for hepatocellular carcinoma. *World J Surg* 1992; 16: 97.
- [6] Ikeda Y, Kajiyama K, Adachi E, et al. Early recurrence after surgery of hepatocellular carcinoma. *Hepatogastroenterology* 1995; 42: 469.