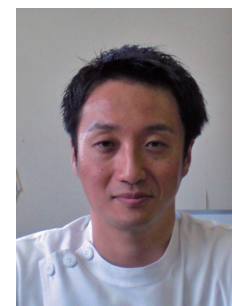


Serum alpha-fetoprotein monitoring after curative resection of hepatocellular carcinoma: clinical significance of postoperative level

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Background: The high incidence of recurrence after curative resection is a major challenge in hepatocellular carcinoma (HCC) treatment. Although serum alpha-fetoprotein (AFP) and des-gamma-carboxy prothrombin (DCP) were well known as tumor markers of HCC, the clinical usefulness for early detection of HCC recurrence remains controversial. The aim of this study was to evaluate the clinical value of perioperative serum AFP and DCP levels in predicting HCC recurrence after curative resection, with a focus on the kinetics as surveillance tools.

Methods: From January 2005 to December 2007, 165 patients with HCC underwent hepatectomy with curative intent at National Cancer Center Hospital East, Japan. Among them, 108 were initial treatment cases and 57 were recurrence cases. The serum AFP and DCP concentrations were determined within 1 month before operation and at least once within 4 months after operation. The minimum values of postoperative tumor markers examined several different times within 4 months after operation were used for analyses. Then the levels of the tumor markers before and after operation were compared. In this study, the cut-off levels for AFP and DCP were set to 10 ng/ml and 40 mAU/ml, respectively. Tumor recurrence was defined as newly developed lesion on computed tomography (CT).

Results: The sensitivity rates of preoperative AFP and DCP were 50.3% (83/165) and 61.2% (101/165), respectively. The combination of both tumor markers increased the sensitivity to 78.8% (130/165). Until the end of follow-up, tumor recurrence was identified in 114 patients (69.1%). Of these, 106 had intrahepatic recurrence distant from the primary site, 3 had local tumor recurrence, and 13 had extrahepatic recurrence (some patients had a first relapse at more than one site). The cumulative probability of overall recurrence was 46.2%, 64.5%, and 74.5% at 1, 2, and 3 years, respectively. The sensitivity of AFP, DCP, and the combination at the time of detecting recurrence were 55.3% (63/114), 40.4% (46/114), and 71.9% (82/114), respectively. In the patients with positive levels of AFP at preoperation, the number of patients whose AFP levels changed to negative after operation in the group without recurrence was more than that in the group with recurrence. And the difference was significant ($P < 0.001$). In contrast, there was no significant difference between two groups in DCP ($P = 0.118$). The differences in cumulative recurrence rate of patients among the various risk factors stratified were evaluated by log-rank tests. Age ($P = 0.031$), tumor occurring ($P < 0.001$), postoperative minimum AFP level ($P < 0.001$), postoperative minimum DCP level ($P = 0.002$), tumor size ($P = 0.026$), number of nodules ($P = 0.007$), microscopic vascular invasion ($P < 0.001$), intrahepatic metastasis ($P < 0.001$), and pathological stage ($P < 0.001$) were found to be significantly related to recurrence. Thereafter, multivariate analysis using Cox's proportional hazard model was performed to assess the independent importance of each variable studied. Tumor occurring ($P < 0.001$), postoperative minimum AFP level ($P < 0.001$), and intrahepatic metastasis ($P = 0.004$) were found to be independent and significant risk factors for recurrence after hepatectomy. To evaluate the correlation between AFP levels and hepatitis activity, univariate regression analysis was used. Statistically, there was no significant correlation between postoperative minimum AFP and ALT levels ($P = 0.297$).

Conclusions: Postoperative serum AFP level is a useful tool for predicting recurrence after curative hepatectomy.

However, the sensitivity is as yet unsatisfactory. We are trying to find novel useful serum markers that have better sensitivity for early detection of recurrence.