

E24

**Multiple primary Malignancies in patients with HCC
Is it a poor prognosis factor for overall survival?**

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Background/Aim: Multiple primary malignancies are defined as two or more different malignancies detected synchronously or metachronously in different organs in a single patient. However, studies for the clinicopathologic features regarding multiple primary malignancies in patients with hepatocellular carcinoma (HCC) are insufficient. In this study, we performed a retrospective study to investigate the clinicopathologic features for the HCC patients with multiple primary malignancies.

Methods: Between May 1997 and July 2016, 1043 HCC patients received radical surgical treatment including hepatectomy and liver transplantation in our institute. Among them, 58 (5.6%) cases were diagnosed with extrahepatic primary malignancies. The comparison between single primary HCC and multiple primary malignancies was performed. The demographics and clinicopathologic features including HBs Ag (positive), HCV Antibody (positive) status, serum AFP (more than 400ng/ml), tumor size (more than 5cm), number of multiple tumors, presence of microvascular invasion, Edmondson grade (grade 3 and 4), presence of liver cirrhosis (fibrosis stage 4), AJCC staging for HCC (stage 1) were reviewed.

Results: The median follow up time is 53 months in the present study. Among the 58 (5.6%) patients with multiple malignancies, 8 were diagnosed synchronously and 50 ; metachronously: 14 patients' extrahepatic primary malignancies were found in prior to the diagnosis of HCC, and 36; after their HCC diagnoses. The five most common extrahepatic primary malignancies are stomach (15 cases, 25.9%), lung (10 cases, 17.2%), colorectal (9 cases, 15.5%), renal (6 cases, 10.3%) and bladder (4 cases, 6.9%) cancers. The patients with multiple primary tumors had a significantly longer overall survival (OS), compared to those with single primary HCCs. The 5-year OS rates for multiple and single primary tumor were 77.8% and 66.9%, respectively (P=0.036). The multiple primary tumor patients had the following clinicopathologic features: older mean age, more patients with non-viral background liver, fewer patients with liver cirrhosis and more patients with AJCC stage I for HCC.

Conclusion: The patients with multiple primary tumors have a relatively good prognosis compared to those with no extrahepatic malignancy. This is thought to be mostly due to non-viral background liver and less invasive tumor characteristics.