

中文題目:肝癌合併肝外原發性惡性腫瘤:其年代變遷, 臨床表徵和存活

英文題目: Hepatocellular Carcinoma associated with Extra-hepatic Primary Malignancy: its Secular change, Clinical Manifestations and Survival

作者: 紀廣明<sup>1</sup> 盧勝男<sup>1</sup> 王景弘<sup>1</sup> 王植熙<sup>2</sup> 鄭汝汾<sup>3</sup>

服務單位: 高雄長庚醫院 內科部 胃腸肝膽科系<sup>1</sup> 外科部 一般外科<sup>2</sup> 放射診斷科<sup>3</sup>

**Background and aims:** We aimed to investigate the secular change, clinical manifestations, and survival in patients with hepatocellular carcinoma (HCC) associated with extra-hepatic primary malignancy (EHPM).

**Patients and Methods:** Between 1986 and Dec 2013, all consecutive HCC patients were enrolled. The EHPM was classified as prior, synchronous and metachronous group based on before, within and after 6 months of HCC diagnosis, respectively.

**Results:** Overall incidence rate is 3.91% (570/14555) and increasing over time with significant linear trend ( $r^2=0.768$ ,  $p<0.001$ ). Incidence rates of bladder and kidney cancers were higher than general populations. Multivariate analysis shows age $>60$  (odds ratio [OR], 1.74; 95% confidence interval [CI], 1.43~2.10), normal AST levels (1.32; 1.08~1.61), Child-Pugh A (1.43; 1.14~1.80), AFP  $<400$  ng/ml (1.38; 1.11-1.72), negativity of anti-HCV (1.49; 1.20-1.87) and HBsAg (1.70; 1.36-2.11), and earlier BCLC staging (stage 0, A, B and C vs. stage D was (2.56; 1.32-4.99), (3.42; 1.87-6.24), (2.27; 1.24-4.15) and (1.73; 0.94-3.16), respectively), are associated factors to EHPM. The survival rates of EHPM is better than HCC-alone group ( $P<0.001$ ), metachronous group was better than prior, synchronous and HCC-alone groups (all  $p<0.001$ ). Survival of EHPM also improve over time (period 2003-2013,  $n=337$  vs. 1986- 2003,  $n=233$ ,  $p<0.001$ ). Cox proportional hazards regression shows independent factors associated with better poorer HCC survival are age  $>60$  (hazard ratio [HR] = 1.19, 95% CI = 1.11-1.27), male (1.18, 1.10-1.27), AFP levels  $\geq 400$  (1.47, 1.37-1.58), negativity positivity of HBsAg (1.10, 1.03-1.17), Child-Pugh B vs. A (1.32, 1.21-1.43), HCC-alone, prior and synchronous vs. metachronous group was (1.32, 1.09-1.59), (1.59, 1.23-2.05) and (1.52, 1.09-2.12), respectively, treated with local ablation, transcatheter arterial embolization, radiotherapy and supportive vs. surgery was (2.08, 1.83-2.37), (2.65, 2.39-2.93), (4.88, 4.09-5.81) and 3.70 (3.27-4.18), respectively, and earlier TNM stage IIIA vs. I (1.20, 1.07-1.35) and BCLC stages A, B, C and D vs. 0 was (1.41, 1.23-1.63), (1.98, 1.71-2.31), (3.50, 2.80-4.39) and (3.25, 2.61-4.04), respectively.

**Conclusions:** Older in age, Child-Pugh A cirrhosis, negativity of HBsAg and anti-HCV, and earlier BCLC staging are factors associated with EHPM. EHPM incidence is increasing over time and survival rate is better than HCC, these might be mostly related to early diagnosis and improve treatment of HCC.