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Epidemiological and Clinical Characteristics of Five Rare Pathological Subtypes of Hepatocellular Carcinoma

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Abstract : Background: This study aimed to characterize the epidemiological and clinical features of five rare subtypes of hepatocellular carcinoma (HCC) and to create a competing risk nomogram for predicting cancer-specific survival. Methods: This study used the Surveillance, Epidemiology, and End Results database to analyze the clinicopathological data of 50,218 patients with classic HCC and five rare subtypes (ICD-O-3 Histology Code=8170/3-8175/3) between 2004 and 2018. The annual percent change (APC) was calculated using Joinpoint regression, and a nomogram was developed based on multivariable competing risk survival analyses. The prognostic performance of the nomogram was evaluated using the Akaike information criterion, Bayesian information criterion, C-index, calibration curve, and area under the receiver operating characteristic curve. Decision curve analysis was used to assess the clinical value of the models. Results: The incidence of scirrhous carcinoma showed a decreasing trend (APC=-6.8%, P=0.025), while the morbidity of other rare subtypes remained stable from 2004 to 2018. The incidence-based mortality plateau in all subtypes during the period. Clear cell carcinoma was the most common subtype (n=551, 1.1%), followed by fibrolamellar (n=241, 0.5%), scirrhous (n=82, 0.2%), spindle cell (n=61, 0.1%), and pleomorphic (n=17, ~0%) carcinomas. Patients with fibrolamellar carcinoma were younger and more likely to have non-cirrhotic liver and better prognoses. Scirrhous carcinoma shared almost the same macro clinical characteristics and outcomes as classic HCC. Clear cell carcinoma tended to occur in the Asia-Pacific elderly male population, and more than half of them were large HCC (Size>5cm). Sarcomatoid (including spindle cell and pleomorphic) carcinoma was associated with larger tumor size, poorer differentiation, and more dismal prognoses. The pathological subtype, T stage, M stage, surgery, alpha-fetoprotein, and cancer history were identified as independent predictors in patients with rare subtypes. The nomogram showed good calibration, discrimination, and net benefits in clinical practice. Conclusion: The rare subtypes of HCC had distinct clinicopathological features and biological behaviors compared with classic HCC. Our findings could provide a valuable reference for clinicians. The constructed nomogram could accurately predict prognoses, which is beneficial for individualized management.

Keywords : hepatocellular carcinoma, pathological subtype, fibrolamellar carcinoma, scirrhous carcinoma, clear cell carcinoma, spindle cell carcinoma, pleomorphic carcinoma
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