Limited epidemiological evidence suggests a protective role for plant foods rich in flavonoids and antioxidants in hepatocellular cancer (HCC) etiology. Our aim was to prospectively investigate the association between dietary intake of flavonoids, lignans and nonenzymatic antioxidant capacity (NEAC) and HCC risk. Data from the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort including 477,206 subjects (29.8% male) recruited from ten Western European countries, was analyzed. Flavonoid, lignan and NEAC intakes were calculated using a compilation of existing food composition databases linked to dietary information from validated dietary questionnaires. Dietary NEAC was based on ferric reducing antioxidant capacity (FRAP) and total radical-trapping antioxidant parameter (TRAP). Hepatitis B/C status was measured in a nested case-control subset. During a mean follow-up of 11-years, 191 incident HCC cases (66.5% men) were identified. Using Cox regression, multivariable adjusted models showed a borderline nonsignificant association of HCC with total flavonoid intake (highest versus lowest tertile, HR=0.65, 95% CI: 0.40-1.04; \( p_{\text{trend}} = 0.065 \)), but not with lignans. Among flavonoid subclasses, flavanols were inversely associated with HCC risk (HR=0.62, 95% CI: 0.39-0.99; \( p_{\text{trend}} = 0.06 \)). Dietary NEAC was inversely associated with HCC (FRAP: HR 0.50, 95% CI: 0.31-0.81; \( p_{\text{trend}} = 0.001 \); TRAP: HR 0.49, 95% CI: 0.31-0.79; \( p_{\text{trend}} = 0.002 \)), but statistical significance was lost after exclusion of the first 2 years of follow-up. This study suggests that higher intake of dietary flavanols and antioxidants may be associated with a reduced HCC risk.

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