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Secondary Primary Cancers and Survival among Neuroendocrine Tumor Patients

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BACKGROUND: Higher rates of second cancer (SC) are suggested for patients with neuroendocrine tumors (NET), but data on SC are scare and their impact on outcomes is unknown. We evaluates the association between SC after NET diagnosis and survival.

METHODS: We identified gastrointestinal (GI), pancreatic, and lung NET from the SEER registry (2000-2016). Standardized incidence ratios (SIR) established the SC incidence for NET compared to the US population. Multivariable Cox models examined the effect of SC on overall survival (OS) and Fine-Gray accounting for the competing risk of death from other causes assessed the effect on disease-specific survival (DSS), with SC as a time-varying covariate.

RESULTS: Of 58,596 patients, NET had higher than expected incidence of SC for all cancers (SIR 1.35, 95%CI 1.31-1.39), and common cancers, such as GI (SIR 1.90, 95%CI 1.79-2.00), lung (SIR 1.36, 95%CI 1.26-1.47), and prostate cancer (SIR 1.28, 95%CI 1.18-1.38). Median time to SC was 40 months (IQR 17-77). SC was independently associated with worse OS (HR 2.02, 95%CI 1.88-2.17), but better DSS (sub-hazard ratio [SHR] 0.75, 95%CI 0.67-0.83). Stratifying by NET type, SC was independently associated with worse OS (HR 2.92, 95%CI 2.68-3.19) and comparable DSS (SHR 1.01, 95%CI 0.87-1.17) for GI NET, worse OS (HR 1.33, 95%CI 1.17-1.51) and better DSS (SHR 0.66, 95%CI 0.55-0.78) for lung NET, and comparable OS (HR 1.15, 95%CI 0.90-1.48) and better DSS (HR 0.51, 95%CI 0.37-0.69) for pancreatic NET.

CONCLUSION: Observed increased incidence of SC after NET diagnosis negatively impacts OS separately from NET-related survival, as outlined by lower OS but higher DSS with SC. Long-term follow-up strategies for NET should include detection of SC for timely management.

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