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Overall Survival and Prognostic Factors in Patients with Gastroenteropancreatic Neuroendocrine Carcinoma: A Large Population-Based Analysis

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BACKGROUND

Gastroenteropancreatic neuroendocrine carcinomas (GEP-NECs) are rare, poorly differentiated, high-grade neuroendocrine malignancies characterized by aggressive clinical behavior, for which systemic chemotherapy has long remained the standard of care. Contemporary population-level outcomes data with systemic chemotherapy for patients with GEP-NECs remain sparse.

METHODS

We queried the Surveillance, Epidemiology, and End Results (SEER) database to identify patients with GEP-NECs. Key inclusion criteria included gastroenteropancreatic site of origin, histology consistent with neuroendocrine carcinoma, poorly differentiated morphology, receipt of systemic chemotherapy, and diagnosis after 2015. Demographic, clinicopathologic, and treatment variables were extracted. OS was estimated using the Kaplan-Meier method. Univariate analysis was performed using the log-rank test to identify covariates for consideration in the multivariable model based on a threshold for statistical significance of $p<0.05$. Multivariable Cox proportional hazards regression was performed using forward stepwise selection based on the Akaike Information Criterion (AIC) to identify covariates independently associated with OS.

RESULTS

A total of 862 patients were included. Median age at diagnosis was 63 years (IQR 53–70), 59% were male, and 66% were non-Hispanic White. Median OS for the entire cohort was 12 months (95% CI 10–13). Younger age was not associated with improved survival (HR 1.00, p=0.979); age >75 years was associated with inferior OS (HR 1.37, p=0.010). On univariable

analysis, esophageal primary (HR 1.29, p=0.029), liver metastases (HR 2.29, p<0.001), and lung metastases (HR 1.70, p<0.001) were associated with worse OS. In contrast, anal primary (HR 0.45, p=0.003), gastric primary (HR 0.71, p=0.020), and isolated lung metastases without liver involvement (HR 0.62, p=0.041) were associated with improved OS. No significant differences in survival were observed by sex, race, income status, marital status, or rurality. On multivariable analysis, liver metastases (HR 2.06, p=0.006), lung metastases (HR 1.44, p=0.008), age >75 years (HR 1.51, p=0.009), and gastric primary site (HR 0.67, p=0.033) remained independently associated with OS.

CONCLUSIONS

In this contemporary population-based analysis of chemotherapy-treated GEP-NECs, metastatic burden and advanced age emerged as key prognostic factors, with liver metastases conferring a twofold higher risk of death. Unlike well-differentiated neuroendocrine tumors, younger age at diagnosis did not confer a survival advantage, suggesting uniformly aggressive disease biology of GEP-NECs across age sub-groups. Notably, sociodemographic factors were not independently associated with survival, suggesting tumor biology may outweigh traditional disparities-related determinants in this aggressive disease. The persistently short survival observed despite treatment with systemic chemotherapy highlights an urgent need for more effective novel therapeutic strategies.

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