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Two decades of advances in neuroendocrine neoplasms care: has survival changed over time?

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BACKGROUND

The incidence of gastro-entero-pancreatic neuroendocrine neoplasms (GEP-NENs) has risen worldwide over the past two decades, paralleling significant evolution in care through new systemic therapies, consensus guidelines, and the emergence of specialized multidisciplinary centres. Whether these advances have translated into improved overall survival (OS) for patients with GEP-NENs remains unknown. We examined temporal trends in OS after GEP-NEN diagnosis.

METHODS

We conducted a population-based retrospective cohort study using linked administrative datasets. Adults diagnosed with GEP-NENs between 2000 and 2019 were identified and followed until death, last contact, or five years after diagnosis. All had an opportunity for 5 years of follow-up. The primary outcome was death from any cause. OS was computed from date of diagnosis under a time-to-event framework. Restricted cubic spline (RCS) models assessed non-linear associations between year of diagnosis and the log-transformed hazards of death. Multivariable Cox regression examined the association of time period of diagnosis with OS, adjusting for age, sex, primary site, and metastatic status. Analyses were stratified by primary site and metastatic status at diagnosis.

RESULTS

Of 9,420 patients included, median age was 60 years and 51.4% were male. Metastases at diagnosis were present in 40.6%. The actual 5-year OS was 75.8% (95%CI 74.9-76.7%) overall, 88.8% (95%CI 87.9-89.6%) for non-metastatic disease, and 57.0% (95%CI 55.4-58.6%) for metastatic disease. A non-linear relationship was identified between year of diagnosis and hazards of death, with hazards dropping below 1 after 2013, consistent with improving OS in more recent years. Diagnosis between 2013-2019 was independently associated with lower hazards of death (adjusted HR 0.91, 95%CI 0.83-0.99). On stratified analysis, the reduction in hazards of death was confined to non-metastatic disease, with

no improvement observed for metastatic disease. By primary site, OS improved for pancreas, stomach, and rectum NENs, but not for small bowel and appendix NENs. When pancreas and small bowel NENs were further stratified by metastatic status, improvement was observed only for non-metastatic diagnoses.

CONCLUSIONS

Over two decades, OS for GEP-NENs has modestly improved. Gains were driven by non-metastatic diagnoses, particularly for primary NEN sites where incidental and early-stage detection has risen most sharply. This suggests that observed improvements reflect stage migration.

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