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Increased Incidence, Prevalence, and Surgical Management of Enteropancreatic Neuroendocrine Tumors Is Associated with Improvements in Survival - A Contemporary Analysis

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BACKGROUND

Neuroendocrine tumors (NETs) are increasing in incidence and prevalence. Small intestine, rectum, pancreas and appendix are the most common enteric sites of NETs, and when identified early, surgical resection can be curative. We hypothesized that observed increases in incidence and prevalence of NETs are primarily driven by earlier detection of loco-regional tumors. In turn, increases in incidence of early-stage tumors is associated with increases in resection and overall improved survival duration.

METHODS

Patients with NETs were identified in the Surveillance, Epidemiology and End Results (SEER) Program data, spanning 2000-2019. Age-adjusted incidence, 20-year limited duration prevalence, surgical resection and 5-year survival rates were calculated. Annual percent changes (APC) were calculated for each.

RESULTS

Overall incidence of NETs continued to increase from 4.83/100,000 in 2000 to 8.24/100,000 in 2019 (APC 3.30, $p<0.001$), whereas incidence of all malignancies remained stable 436.14/100,000 in 2019 (APC $p>0.05$). Incidence of small intestine (APC 2.82, $p<0.001$), rectum (APC 2.41, $p<0.001$), pancreas (APC 8.32, $p<0.001$), and appendix (APC 15.7, $p<0.001$) NETs increased from 2000 to 2019.

Overall increased incidence was primarily driven by localized and regional NET for small intestine (localized APC 2.75, regional APC 3.01 $p<0.001$), pancreas (localized APC 15.66, regional 7.13, $p<0.001$), and appendix (APC 18.28, regional 13.68 $p<0.001$) NET. Rectal NET showed increased incidence of local, but not regional disease (APC 1.97, $p<0.001$). The prevalence of localized (0.004% to 0.04%), regional (0.001% to 0.01%) and metastatic (0.001% to 0.006%) NET increased significantly, likely due to the indolent nature of NET.

Overall rate of patients undergoing resection increased significantly from 2000 to 2019, 4.06/100,000 to 7.38/100,000. Rates also increased for each disease site; small intestine (APC 2.19, $p<0.001$), rectum (APC 2.25, $p<0.001$), pancreas (APC 10.21, $p<0.001$), and appendix (APC 16.05, $p<0.001$).

Overall improvement in survival was associated with more recent diagnosis from 2000 to 2019 (HR 0.95, $p<0.001$). When controlling for sex and tumor grade, more recent diagnosis was associated with improvements in survival; small intestine (HR 0.96, $p<0.001$), rectum (HR 0.92, $p<0.001$), pancreas (HR 0.97, $p<0.001$), appendix (HR 0.94, $p<0.001$), though this may represent significant lead time bias in a relatively indolent tumor.

CONCLUSIONS

Continued increases in incidence and prevalence of locoregional NETs has been accompanied by a rise in surgical resection rates and is associated with improvements in survival. These trends may be due in part to greater detection of early-stage tumors, and in turn an earlier window for curative surgical intervention.

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