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WHO Mitotic/Ki-67 Grading Completeness and Distribution in Neuroendocrine Neoplasms (NENs), in the Surveillance, Epidemiology, and End Results (SEER) Program

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BACKGROUND

NENs are a heterogeneous group of malignancies whose classification has evolved over time. The implementation of the WHO mitotic count/Ki-67 grading and histological classification developed for gastroenteropancreatic (GEP) NENs in the Surveillance, Epidemiology, and End Results (SEER) program in 2018 provided the first opportunity to characterize population-level grade & histological distributions.

METHODS

We analyzed SEER data from 2018–2022 for NENs (WHO mitotic/Ki-67 grading was not captured in SEER prior to 2018) arising at GEP, lung and other primary sites. Grading was assessed using the WHO mitotic count/Ki-67 classification (G1–G3), with cases also characterized by histological differentiation coding (well-, moderately-, poorly- and un-differentiated) where available. Demographic characteristics were evaluated by sex, race/ethnicity, and age group.

RESULTS

Among 40,849 NEN cases diagnosed from 2018–2022, grade, G remained unassigned in 23,970 (58.7%). Of the 13,446 (32.9%) cases with a definitive WHO grade, 10,280 (76.5%) were G1, 1,755 (13.1%) were G2, and 1,411 (10.5%) were G3. Within the GEP NEN sites, appendiceal (94%) and colorectal (87%) NENs were overwhelmingly G1 while esophageal (90%) and anal (78.3%) were predominantly G3. Other sites with high G3 NENs included cervix and uterus (89-91%). Females comprised 54.7% of G1 and 53.7% of G2 cases, while G3 tumors were more common among males (57.3%). Higher-grade tumors occurred more frequently in older adults, with 59.1% of G3 cases diagnosed among individuals aged 65 years or older compared with 40.7% of G1 cases. Of note, lung NENs were also classified according to the 2018 WHO GEP NEN criteria in the SEER program and exhibited a relatively greater proportion of G3 tumors (19.7%). Of the 3,433 patients across all sites (8.4%) with histological differentiation, 89% were well-, 4% were moderately- and 7% were

poorly differentiated. However, these patients were coded only with histological differentiation and excluded from grade coding.

CONCLUSIONS

The incorporation of WHO classification into the SEER program provides the first opportunity for a population-based analysis of grade distribution for NENS. However, several opportunities for improvement still exist: a) grade was unrecorded in nearly 60% of cases that underscores a fundamental limitation of current cancer registry infrastructure b) grade & histological classifications were mutually exclusive limiting ability to classify G3 NENs and c) GEP NEN classification was used for lung NENs as well in contrast to current guidelines. Additional details regarding grade and histological distribution across sites and demographic information will be presented at the conference.

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