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Analysis of patient selection for germline testing in early-onset gastroenteropancreatic neuroendocrine neoplasms (GEPNENs) at a single institution

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BACKGROUND

In our previous work, we found a high rate of pathogenic/likely pathogenic germline mutations (PGM) in patients with early-onset GEPNENs (EO-GEPNENs) at UCSF, particularly in pancreatic primaries. However, germline testing practices in EO-GEPNENs have not been standardized. Testing has historically been driven by clinical factors, patient preference, and insurance coverage, but the process is prone to bias and relies on subjective provider assessment. This study characterizes the clinicodemographic features of EO-GEPNEN patients who underwent testing versus those who did not.

METHODS

In this IRB-approved study, we identified 252 EO-GEPNEN patients (age 18–49 at diagnosis, any stage/grade) from 2011–2023. Group differences in categorical and continuous variables were assessed using the Chi-squared and Wilcoxon tests.

RESULTS

Of 252 patients with EO-GEPNENs, 109 (43%) underwent germline testing. Among them, 29 (27%) had a PGM. Tested patients had a median age of 42 years at diagnosis, 55% female, 47% locoregional disease, and 92% well-differentiated tumors. Additional clinicodemographic features are in Table 1:

Characteristic	Not Tested (n=143, 56.7%)	Tested (n=109, 43.3%)	P Value
Age (median [IQR])	42.00 [36.00, 46.00]	43.00 [35.00, 47.00]	0.914
Sex Female Male	 78 (54.5) 65 (45.5)	 60 (55.0) 49 (45.0)	1
Race White Non-White	 86 (66.7) 43 (33.3)	 82 (78.1) 23 (21.9)	0.074
Suspected genetic syndrome	10 (9.2)	21 (19.3)	0.052
Other cancers besides NEN	14 (10.3)	18 (17.1)	0.173

Primary Tumor Site GI Pancreas	 70 (49.0) 73 (51.0)	 50 (45.9) 59 (54.1)	0.721
Grade at Diagnosis G1/G2 NET G3 NET G3 NEC Unknown	 108 (75.5) 3 (2.1) 8 (5.6) 24 (16.7)	 82 (75.2) 12 (11) 6 (5.5) 9 (8.3)	0.036
Metastatic Disease	79 (56.4)	82 (75.2)	0.003

CONCLUSIONS

EO-GEPNEN incidence is rising, but its association with PGMs is unclear. At UCSF, 43.3% of patients underwent germline testing, with 26.6% harboring a PGM. The tested population was enriched for G3 and stage IV disease, with no significant differences in age, sex, site, second cancers, or race, though our data suggest more suspected genetic syndromes in tested patients and more non-White patients in the non-tested group. Clinicodemographic features by PGM status will be presented. Further work is needed to define testing indications and assess downstream implications.

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