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Recurrence of Locoregional Small Bowel Neuroendocrine Tumors: Developing a Risk Prediction Nomogram

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BACKGROUND

Locoregional small bowel neuroendocrine tumors (sbNETs) are typically managed with curative-intent resection. Despite their generally indolent biology, recurrence rates of up to 50% have been reported. Evidence guiding individualized follow-up strategies remains limited. We aimed to develop a nomogram to predict recurrence risk after resection.

METHODS

Retrospective review was performed of adults undergoing surgical resection of stage I – III ileal and jejunal NETs from 2000 – 2023 at a quaternary referral center. Patients with unresectable disease or other abdominal malignancies at the time of surgery were excluded. Ki67 was missing for 131 patients with re-review underway. Kaplan Meier estimates and Cox proportional hazards regression were performed. LASSO regression was utilized for nomogram variable selection.

RESULTS

Patients meeting inclusion criteria (n=378) were a median age of 63.1 years [IQR 54.3, 72.3] at the time of surgery. 42.1% were female, 93.1% were white, and 41% had multifocal disease. Ki67 was less than 3% for 51.4% of patients, 3% - 20% for 47.8%, and >20% for 0.8%. Median lymph node retrieval was 13 [6, 23]. 85% had stage 3 disease, 10.2% were stage 2, and 4.8% were stage 1. With a median follow-up of 94 months, 55 patients had recurrence. 34.5% had locoregional-only recurrence, whereas 38.2% developed peritoneal disease and 41.8% had distant hematogenous (liver, lung, bone, pancreas) recurrence. Median time to recurrence was 59.7 months, with 29.1% undergoing subsequent resection. Kaplan-Meier estimate of 5-year recurrence free survival was 91.4% overall, 97.8% for stage I or 2 disease, and 90.8% for stage 3 (p=0.012). On multivariable analysis, risk of recurrence was associated with primary tumor size, multifocal disease, and perineural invasion (Table 1). Although pathologic N2 disease was not significant on multivariable regression, it was identified as an important predictor on LASSO regression and therefore included in the nomogram. The corrected c-index was 0.71.

Table 1: variables included in nomogram based on LASSO regression.

Variable	Level	HR (95% CI)	p-value
Primary Tumor Size	Per 5 mm	1.23 (1.10, 1.38)	0.0004
Multifocal	Yes	2.59 (1.45, 4.61)	0.0012
Perineural Invasion	Yes	3.05 (1.58, 5.90)	0.0009
Pathologic N2	Yes	1.71 (0.94, 3.13)	0.0807

CONCLUSIONS

Our model is well-calibrated to predict recurrence of locoregional small bowel neuroendocrine tumors on the basis of tumor size, multifocality, perineural invasion, and nodal status. A risk-prediction nomogram may help guide patient counseling and inform the frequency and duration of postoperative surveillance. A multi-center validation cohort has been established with data collection underway.

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