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Timing of Primary Tumor Resection & Long-Term Survival in Stage IV Small Bowel Neuroendocrine Tumors: A National Analysis

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BACKGROUND

In stage IV small bowel neuroendocrine tumors (SB-NETs), primary tumor resection (PTR) is frequently performed for symptom control or prevention of complications. The impact of operative timing on outcomes remains unclear.

METHODS

Using the National Cancer Database, we identified patients with stage IV well-differentiated SB-NETs undergoing PTR. Patients were stratified as urgent (≤30 days from diagnosis) or delayed (>30 days) resection. Clinicopathologic and perioperative variables were compared. Overall survival (OS) was evaluated using Kaplan–Meier methods and Cox regression. Timing of surgery was modeled as a time-dependent exposure to minimize immortal time bias, with additional analyses comparing alternative modeling approaches.

RESULTS

Among 5,161 patients, 2,688 (52.1%) underwent urgent resection. On unadjusted analysis, urgent surgery was associated with worse survival. In adjusted analyses, delayed surgery was not associated with improved survival at 5 years (HR 0.91, 95% CI 0.79–1.04; p=0.15), 10 years (HR 0.91, 95% CI 0.79–1.04; p=0.15), or 15 years (HR 0.92, 95% CI 0.82–1.03; p=0.13). Adequate lymph node evaluation (≥8 nodes) was independently associated with improved survival, whereas microscopic and macroscopic residual disease were independently associated with worse survival. Adequate lymph node retrieval & rates of R0 resection were improved in the delayed surgery group.

CONCLUSIONS

After accounting for confounding and immortal time bias, operative timing was not independently associated with long-term survival among patients with stage IV SB-NETs undergoing PTR. In contrast, oncologic quality measures, including adequate lymph

node evaluation and margin-negative resection remained independently associated with improved outcomes & were higher in the delayed surgery group. When surgery is pursued in stage IV disease, resection in a planned and optimized setting may improve oncologic quality.

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