Identification of Recurrence Predictors in Stage I-III Midgut NETs After Curative Surgery

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Background: Surgery represents the only curative treatment for stage I-III midgut neuroendocrine tumors (NETs). There is very little data on post-operative recurrence risk and therefore few evidence-based guidelines for long-term surveillance. This study is aimed at evaluating risk of recurrence and identifying predictors of recurrence which will facilitate generation of risk-based surveillance guidelines.

Methods: 150 patients with stage I-III midgut NET who underwent R0-R1 surgical resection between 1985 and 2011 were retrospectively evaluated for relapse and survival outcomes. Demographic (sex, age), clinical (NET primary site, tumor size, uni- or multifocality, presence of symptoms at diagnosis, type of surgery) and pathological features (tumor grading, differentiation, presence or absence of perineural or angiolymphatic invasion, degree of parietal invasion, presence of nodal metastases, margin clearance) were assessed as potential predictors of recurrence. Disease-free survival (DFS) was calculated using the Kaplan-Meier method.

Results: After a median follow-up of 82 months (range 1-325), 61/150 patients (41%) relapsed. The median DFS was 125 months (95% CI, 87-139 months). Amongst patients who recurred, the rate of relapse was stable after second year and the median time to recurrence was 61 months (95% CI, 51-73 months). Liver (64%), mesentery (23%) and pelvic lymph nodes (13%) were the most common sites of recurrence. No relapse was observed amongst patients (n=5) with stage I midgut NET. Tumor size predicted recurrence ($p<0.05$), while a borderline increased risk of relapse was observed in tumors with perineural invasion ($p=0.07$).

Conclusion: The risk of relapse is substantial in patients with resected local and locally advanced midgut NETs, with the possible exception of stage I disease. Given the long median relapse-free survival, guidelines should recommend long term (beyond 5 year) surveillance; however frequent scans may not be necessary.

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