

Prognostic Significance of the Extent of Lymph Node Metastases in Small Intestinal Neuroendocrine Tumors

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Background: Current staging guidelines for small intestinal neuroendocrine tumors (SI-NETs) only differentiate between the presence (N1) and absence (N0) of lymph node (LN) metastases. However, the prognostic significance of the extent of LN involvement remains unknown. In this study, we used data from a national population-based cancer registry to examine whether involvement of a higher number of LNs is associated with worse survival.

Methods: We used the Surveillance, Epidemiology and End Results (SEER) database to identify patients with histologically confirmed, surgically resected SI-NETS diagnosed between 1988 and 2010. Patients were classified into three groups by the lymph node ratio (number of positive lymph nodes/number of total lymph nodes examined, LNR): ≤ 0.20 , $>0.20-0.5$, and >0.5 . We used the Kaplan Meier method to assess NET cancer-specific survival differences (up to 10 years from diagnosis) according to LNR status. We constructed Cox models to evaluate differences in prognosis after controlling for potential confounders.

Results: We identified 2,984 surgically resected patients with N1, non-metastatic SI-NETS with detailed LN data. More than half of NETs were located in the ileum. Higher LNR was significantly associated with worse NET cancer-specific survival (Figure 1, $p < 0.0001$). Ten-year NET-specific survival was 85%, 77%, and 74% for patients in the ≤ 0.2 , $>0.2-0.5$, and >0.5 LNR groups, respectively. In stratified analyses, higher LNR groups experienced worse survival only in early tumor (T1, T2) disease ($p < 0.0001$). There were no differences in survival across LNR groups in patients with late tumor (T3, T4) status (T3, $p = 0.24$; T4, $p = 0.40$). Cox analysis confirmed a differential effect of LNR on NET-specific survival according to tumor category.

Conclusions: Extent of LN involvement provides independent prognostic information in patients with LN positive SI-NETS. This information may be used to identify patients at high risk of recurrence and inform decisions about use of adjuvant therapy.

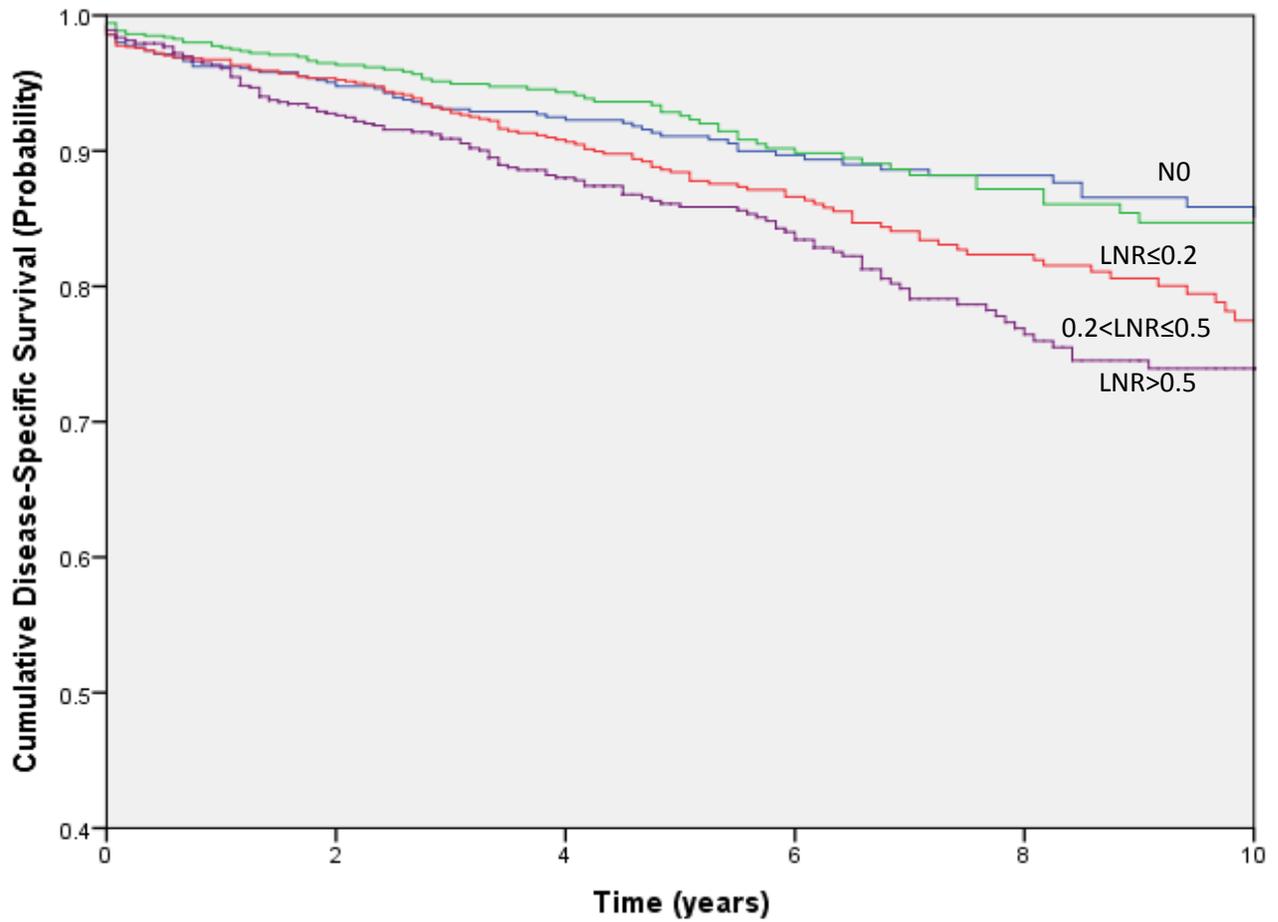


Figure 1. Disease-specific survival stratified by lymph node ratio (LNR) status. Disease-specific survival was progressively worse with increasing LNR ($p < 0.0001$). There was overlap of survival in patients with NO and lowest LNR status.