



Lymph node ratio in resected pancreatic head cancers: time for a broader clinical implementation?

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Lymph node ratio (LNR) has emerged as a promising predictor for survival outcome after surgery in different tumor types (1,2). The concept of evaluating LNR as a prognostic factor also after pancreatic surgery has been described in several publications (3,4). Most of the previous reports on LNR in this setting are single-center studies with rather small cohorts and/or mixed histological tumor types, possibly limiting the generalizability of the results. Even if the role of LNR in pancreatic cancer has been acknowledged, it is still regarded as having mostly academical implications when comparing results from different studies and is probably rarely being used as a tool in clinical decision-making world-wide.

Therefore, we read with interest the article by Joliat *et al.* about the prognostic importance of LNR in resected pancreatic head cancers published last year (5). In this international multicenter observational study collected data from six renowned Western high-volume institutions for hepatopancreatobiliary surgery was presented. The study cohort consists of 1,327 patients operated with a pancreatoduodenectomy for pancreatic cancer from 2000–2017, making it both larger and more homogenous than previous reports. Regarding the main findings, not only did LNR represent a strong predictor of overall survival in the whole cohort, but in the lymph node (LN) positive patients it could stratify subgroups with different survival outcome (especially for the N2 positive patients

with >4 metastatic glands). As mentioned, the present study is stronger than most previously published within this field, although residual bias due to the retrospective nature can of course still be harbored in the results.

The authors prudently recommend integrating LNR as an additional element to the tumor, node, metastasis (TNM)-grading system, as a significant step forward in the quest for an appropriate complement. Before widespread adoption, it is however essential to carefully examine and fine-tune specific aspects, including determining the optimal quantity and anatomical distribution of harvested LN, along with exploring the most favorable LNR cut-off level.

Previous reports indicate that a harvest of fewer than 15 LN correlate with compromised survival, irrespective of the count of positive LN (6). Such instances could represent an oncologically suboptimal resection, predisposing to residual disease in the form of cancer-invaded LN. In the context of modern pancreatoduodenectomy, the procedure nowadays entails the removal of a significantly greater number of LN, with some authorities reporting a retrieval that not seldom encompasses more than 25 nodes (7). Augmented LN retrieval not only enhances the likelihood of eliminating potentially affected regional LN, but also extends to non-regional LN, improving staging further (8). Consequently, a heightened LN harvest denotes a more oncologically radical resection, improves staging, and mathematically results in a lower LNR. However, the pursuit of a high LN harvest

coupled with a concurrently low LNR may not be devoid of risks. Extended lymphadenectomy may increase post-operative complications and possibly jeopardizing adjuvant chemotherapy. The primary objective of pancreatic surgery is the achievement of a margin-free resection accompanied by a judicious regional lymphadenectomy, all while minimizing post-operative morbidity to facilitate subsequent adjuvant chemotherapy. Current insights suggest that more extensive surgical interventions may contribute to an elevated risk of morbidity and a deterioration in quality of life.

Although the implementation of a staging complement, such as LNR, is needed, it is vital in the next steps to delineate the optimal quantity of harvested LN and exploring the most favorable LNR cut-off levels. With this publication the authors propose the clinical use of LNR when tailoring adjuvant chemotherapy regimens to the individual patient depending on postoperative pathology. We believe these results to be of importance in the contribution of evidence, adding to the likelihood of LNR being broadly implemented in clinical practice in the future.

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