Editorial Commentary



# Revisiting the role of lymph node dissection in renal cell carcinoma

**Alice Yu, Dimitar V. Zlatev, Michael L. Blute Sr**

Department of Urology, Massachusetts General Hospital, Boston, MA, USA

*Correspondence to:* Michael L. Blute Sr, MD. Chief of Department of Urology, Massachusetts General Hospital, Boston, MA, USA; Walter S. Kerr Jr, Professor of Surgery, Harvard Medical School, 55 Fruit St, GRB 1100, Boston, MA 02114, USA. Email: mblute@mgh.harvard.edu.

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Lymph node dissection (LND) in renal cell carcinoma (RCC) is accepted as the most accurate and reliable staging procedure. Yet, in recent years, there has been a gradual decline in use of LND across Europe and the United States (1,2). This is likely due to its limited therapeutic benefit as LND has not been shown to improve overall survival (OS) or progression-free survival (PFS) (3). Currently, guidelines recommend LND only in patients with palpable or enlarged lymph nodes detected on preoperative imaging (4). Additionally, the extent of LND remains controversial. Few urologists in the United States (6.6%) remove more than 5 lymph nodes during radical nephrectomy (2). The negative predictive value of a limited LND is not well defined.

Recently, Rieken and colleagues attempted to address this issue by developing a pathological nodal staging score (pNSS) for patients with clear cell RCC and clinically node-negative status (5). The aim of the score was to identify the probability that a node-negative status at surgery represented true absence of lymph node metastases (LNM). Since it is impossible to determine the true nodal status of the population, data from node-positive patients were used to interpret data for node-negative patients (5,6).

The model was developed using a multi-institutional database and validated using the Surveillance, Epidemiology and End Results (SEER) registry data. The authors found that the number of lymph nodes needed for correct nodal staging depends on pathologic tumor stage and Fuhrman grade. In patients with low-grade cancer (Fuhrman I/II), only 1 node was needed to achieve 95% certainty of absence of LNM in pT1-2 tumors. Similarly, only 3 nodes were needed for low-grade pT3-4 tumors. For high-grade cancer (Fuhrman III/IV tumors), significant differences between the development and validation cohorts limited prediction of the number of nodes needed for absence of LNM. However, it is clear that the number of nodes needed for correct staging is higher for Fuhrman III/IV tumors.

Despite the study's limitations, the authors should be congratulated on this original research. It adds to the body of literature showing that extended LND is needed to obtain adequate staging, particularly in high-risk patients (7). More importantly, one needs to be cautious of a false negative finding when only limited number of lymph nodes are removed.

LNM is associated with poor outcomes. Cancer-specific survival at 5 years following radical nephrectomy is only 21–38% in those with nodal metastasis (8,9). The role of adjuvant therapy, even in those with pN1 disease, remains controversial. Several phase III trials in the targeted therapy era failed to show that adjuvant treatment reduced the risk of relapse after nephrectomy (10,11). The S-TRAC trial showed a benefit in disease-free survival with adjuvant sunitinib in high-risk patients (12), however the absence of OS benefit has limited its widespread use.

The paradigm of systemic treatment in metastatic and advanced RCC is changing rapidly with the introduction of immunotherapy agents (13-15). As these agents have shown improvement in objective response rates and OS for advanced disease states, the exploration of their utilization in earlier stages is imminent. Indeed, there are several ongoing clinical trials evaluating the use of PD-1 and

PD-L1 inhibitors in the adjuvant setting (16,17). An appropriate understanding of the correct LND status is crucial for both postoperative surveillance and clinical trial eligibility in patients undergoing nephrectomy for kidney cancer.

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## Footnote

*Conflicts of interest*: The authors have no conflicts of interest to declare.

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