



Pelvic lymphadenectomy for muscle invasive urothelial carcinoma: extended morbidity for limited benefit?

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Lymph node dissection (LND) in muscle invasive urothelial carcinoma in the bladder provides staging and prognostic information to guide further treatment options. It may have a therapeutic role in treating early metastatic disease (1). The anatomical extent of LND is controversial, with contradictory data reported from large retrospective cohorts, while international guidelines and systematic reviews have failed to definitively outline the optimal proximal extent for LND (2-4).

Gschwend and colleagues in Germany reported on the first prospective randomized trial to compare limited versus extended LND in patients with high grade T1 to locally advanced T4 urothelial carcinoma planned for radical cystectomy between 2006 and 2010 (5). Use of neoadjuvant chemotherapy, cT4b or metastatic disease were exclusion criteria, while adjuvant chemotherapy was optional and given at the discretion of the treating physician for locally advanced (pT3/4) or lymph node positive (pN+) disease. At a median follow-up of 43.0 mo, no significant difference was demonstrated for the primary end-point of recurrence free survival, [5-yr recurrence-free survival (RFS) 65% *vs.* 59%, P=0.36] or secondary endpoints, including cancer specific survival [5-yr cancer-specific survival (CSS) 76% *vs.* 65%; P=0.10], and overall survival [5-yr overall survival (OS) 59% *vs.* 50%; P=0.12].

A clear difference in lymph node yield was observed for limited (median =19) and extended groups (median

=31), greater than conventional yields of 10 lymph nodes recommended by the EAU guidelines (1,2). While the differences observed in survival estimates were not statistically significant, these are likely to be clinically significant, given that similarly small, yet statistically significant benefits are used to support the use of neoadjuvant chemotherapy prior to cystectomy. A greater lymph node yield translated to a greater lymphocoele drainage rate for extended compared to limited (8.6% *vs.* 3.4%; P=0.04) without significant difference in mortality at 30 (2.5% *vs.* 2.0%) or 90 days (4.0% *vs.* 3.4%) or major complication (Clavien-Dindo grade ≥ 3). The additional operative time to perform an extended LND compared to limited was not discussed, which may contribute to major complications, as our experience is that a more extensive LND takes significantly longer time than a limited template.

Similar to other international series, 25% of patients had positive nodes confirming the importance of LND in accurate staging (6). Interestingly, the authors reported that an extended LND may find metastatic deposits not identified on a limited template in 2% of cases. Improved staging for these cases is likely to influence decisions regarding adjunctive chemotherapy and may convey a survival benefit. The authors reported that the administration of adjuvant chemotherapy conveyed a greater survival benefit than the extent of LND in this

study. Adjuvant therapy was used in 14% (extended) and 15% (limited) overall, despite a higher prevalence of pN+ (22% and 28%) and pT3/4 (40.1% and 49%) disease. However, those with pT3/4 or pN+ disease that receiving adjuvant chemotherapy (28%) demonstrated improved RFS (HR 0.56, 95% CI: 0.38–0.83, P=0.004) compared to those not receiving chemotherapy, equating to an overall median RFS of 35.4 vs. 11.5 mo, respectively.

The relevance of this study to contemporary practice will be questioned given a variably widespread adoption of neoadjuvant chemotherapy as recommended in modern international guidelines (2,7). In this study, no patients received neo-adjuvant chemotherapy as a predefined exclusion criterion. The bias inherent in selection of patients receiving adjuvant chemotherapy clouds the true benefit of adjuvant chemotherapy, a factor that has plagued previous adjuvant chemotherapy trials.

This study reassures urologists that a limited template remains a reasonable approach for lymphadenectomy during radical cystectomy, however those wishing to extend their template may detect additional metastases for minimal additional complications. Currently, the Southwest Oncology Group has recently finished accrual for their randomized control trial comparing extended and limited LND, including patients who have had neo-adjuvant chemotherapy. This trial may provide further answers to guide extent of lymphadenectomy in modern urological practice.

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Footnote

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

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