

Rethinking lymph node metastasis and cytoreductive nephrectomy

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Cite as: *Can Urol Assoc J* 2016;10(11-12):396-7. <http://dx.doi.org/10.5489/cuaj.4252>

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Cytoreductive nephrectomy (CN) is a difficult surgery under difficult circumstances. Early studies in the immunotherapy era cemented the survival advantage of CN, though modern prospective data has not yet emerged from the CARMENA and SURTIME trials.¹ Less certain is the extent to which all regional disease should be resected at the time of CN, that is, whether lymphadenectomy (LND) should feature routinely during surgery. Patel and colleagues have pitched in to address this issue using Surveillance, Epidemiology, and End Results (SEER) registry data in this issue of *CUAJ*, and found no therapeutic advantage.²

The paper covers significant ground while weaving between the metastatic, CN, LND, and node-positive cohorts. Several key findings crystallize. Median survival in newly diagnosed M1 patients remains less than a year, but has improved over time. CN is associated with longer survival, selection bias in administrative data notwithstanding. A “true” node dissection (the surrogates here are ≥ 3 and ≥ 8 nodes removed) does not impact survival (in fact, any LND was associated with decreased overall and disease-specific survival), and those CN patients who had nodes removed had worse survival than those with CN alone. Node-positive patients did much worse than node-negative (8–10 months vs 22 months survival), and the number of positive nodes worsened prognosis further.

These data sit well with other studies in this space, and doubt is cast on the use of LND at the time of CN. Trinh et al also queried SEER for CN patients and found nodal disease worsened survival, with similar incremental declines with increased node burden.³ Mayo Clinic researchers analyzed 305 CN patients, 188 (62%) of whom had a LND.⁴ They found no benefit to LND, even in clinically node-positive patients, and used the cohort alone, as well as propensity-score groupings to find no advantage to LND in cN0 patients at high risk for occult node metastasis. The authors advocate

against the use of LND at CN, and in fact, double down to suggest that omitting it may afford more minimally invasive CN (with earlier time to systemic therapy).

It may seem intuitive that once the incision is made, regional disease ought to be resected along with the affected kidney, and it is clear that the best outcomes from CN are for those patients in whom $\geq 90\%$ of the disease burden is removed with surgery.^{5,6} It is not clear, however, whether resection of positive nodes contributes to this percent-debulking, or whether the amount of tumour beyond the kidney has already mapped prognosis. Gershman and colleagues note that the pathology of the primary tumour was worse in patients with regional lymphadenopathy, suggesting a different and more aggressive phenotype that allows for lymphatic instead of hematogenous spread.⁴

It should be noted that specific harms have not been identified in those undergoing LND. Certainly the risk of intraoperative grief is higher with the addition of dissection around the great vessels, but the decreased survival in patients in the present study who underwent LND is probably a marker of more aggressive or advanced disease and not of surgical morbidity. The Mayo group looked as well at perioperative morbidity after CN, and found that although LND had hazard ratios (HR) of 1.76 and 1.65 for 30-day complication and increased length of stay (LOS) respectively, neither of these was significant.⁷ Removal of ≥ 13 nodes was close to significance for prolonging LOS (HR 2.01; $p=0.06$) in their series.

So should surgeons steel themselves to tackle the retroperitoneum in patients undergoing CN? It seems clear that clinically node-negative patients don't stand to benefit. Patients with high-volume metastases or those with numerous adverse prognostic factors likely should be spared LND as well (and for many, even CN).⁸ Patients with a large burden of regional node metastases seem unlikely to benefit from an aggressive approach; they have shown poor outcomes in this and other studies and have likely declared themselves as having particularly hostile cancers.^{2-4,7} Navigating the setting of small-volume, easily resectable node metastasis is trickier. There is likely little harm from excising paracaval or para-

aortic nodes in concert with the hilar dissection, but the benefits are backed by intuition rather than data (in fact, cN+ patients specifically have shown no benefit).⁴ On one side, leaving accessible disease behind feels unpalatable, and some with limited metastatic burden beyond the retroperitoneum may survive far beyond the median; it would seem unfair to leave cancer behind. On the other hand, node involvement betrays adverse biology that may evade any therapeutic efforts, and the data available do not bear out an advantage. Robust prospective data to answer this question is unlikely forthcoming. Patients facing CN are in peril and we want to do something to help. Studies like this help to resolve where our efforts are best laid and when more isn't actually more.

Competing interests: Dr. Leveridge has been an advisor for Astellas.

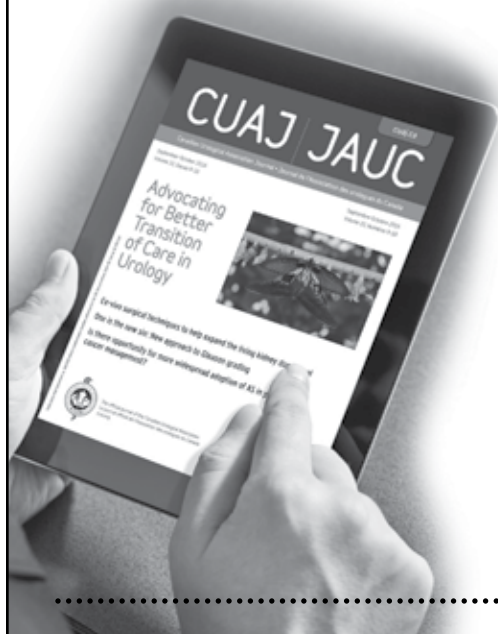
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