KIDNEY CANCER

Lymphadenectomy for RCC—how many nodes?

The role of lymph node resection at the time of surgery for renal cell carcinoma (RCC) is controversial. In an expert editorial for the American Society of Clinical Oncology, published online in February last year, Scott Delacroix Jr and Christopher Wood identified three of the main challenges associated with lymphadenectomy in this setting. First, how should patients at high risk of harbouring nodal metastasis be identified? Second, what is the optimum number and location of lymph nodes that should be removed? And finally, is there adequate evidence that lymphadenectomy has a durable therapeutic effect?

Umberto Capitanio and colleagues at San Raffaele Hospital in Milan, Italy, have tackled the second question in their study recently published in *BJU International*. As the title of their paper suggests, they believe that staging lymphadenectomy should be extended according to their finding that removal of at least 15 lymph nodes is required for the accurate prediction of lymph node metastasis.

From an initial cohort of 1,849 patients who underwent nephrectomy (radical or partial) for RCC at a single tertiary centre between 1987 and 2011, researchers identified 850 individuals who also underwent lymph node dissection. The majority of these patients received a regional (hilar) lymphadenectomy; an extended template was used in 23.9% of the study population (according to surgeon preference).

Capitanio and his team used receiver operator characteristic analysis to calculate the probability of a patient having one or more metastatic lymph nodes based on the number of lymph nodes removed. The resulting graph showed that 15–19 lymph nodes would need to be removed to achieve a 90–95% probability of detecting at least one metastatic lymph node. Subgroup stratification revealed that a more extended dissection was indicated in patients with unfavourable clinical or pathological characteristics (such as

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clinical node metastasis, evidence of distant metastasis or higher pathological T stage). “You might suspect that the removal of a high number of nodes would result in a plateau effect, after which removing additional nodes will contribute little to the diagnostic ability,” says Capitanio. “Indeed, this effect was seen in our study, where removing >20 lymph nodes resulted in practically no gain.”

Despite the authors’ bold conclusion that lymphadenectomy must be extended, there are some limitations to this study that should be considered. Marc Smaldone, a renal cancer specialist at Fox Chase Cancer Center in Philadelphia, who was not involved in the study, told *Nature Reviews Urology* that the patient sample might not be representative of most patients with RCC. “Less than 50% of patients in the original cohort underwent node dissection, suggesting that they might have been selected because they had characteristics (palpable nodes intraoperatively or subtle nodal enlargement on imaging) indicating increased clinical suspicion of regional disease,” he points out.

Another possible restraint is that only 24% of patients had an extended template dissection. Not only might positive nodes outside a standard template have been missed in the remaining 76%, but the median number of lymph nodes removed per patient was six, making it difficult to determine how far to extend dissection to achieve the advised 15-node yield. “I anticipate that the minimum yield would be different if all comers were evaluated or if the entire population underwent standardized node dissections,” Smaldone suggests.

Perhaps, then, the more pertinent issue for patients with RCC is whether lymphadenectomy should be performed in the first place. Certainly there is reason to believe that lymph node resection should not be performed for staging purposes only. Of the 666 patients in Capitanio’s study who were clinically node-negative on preoperative imaging, only 30 patients (<5%) were found to have positive nodes on final pathology. In other words, an unnecessary node dissection, which adds increased risk of morbidity, was performed in 95% of patients. This observation fits with the results of the EORTC 30881, which also demonstrated that dissection is not warranted in patients with clinically node-negative RCC.

Future research efforts might be better focused on the identification of patients at high risk of harbouring occult nodal metastasis who are most likely to gain a therapeutic advantage from node removal. “This paper supports the idea that if there is a clinical indication to perform node dissection in the first place, it may be wise to do the most thorough resection possible to maximize nodal yield and optimize staging,” says Smaldone.

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Original article Capitanio, U. et al. Staging lymphadenectomy in renal cell carcinoma must be extended: a sensitivity curve analysis. *BJU Int.* doi:10.1111/j.1464-410X.2012.11313.x.