Lymph Node Dissection for Small Renal Masses

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KEYWORDS

• Renal cell carcinoma (RCC) • Lymph node dissection (LND) • Small renal mass (SRM)

KEY POINTS

- Lymph node dissection (LND) for renal cell carcinoma (RCC) is not required for clinically localized disease; it does not afford a survival benefit.
- In patients with high-risk features, use of LND may provide important staging information.
- If performed, an LND template should be based on the known lymphatic drainage of the kidneys.

INTRODUCTION

The presentation of a patient with a small renal mass (SRM), with a maximum diameter of less than 4 cm, can represent a diagnostic and treatment dilemma for the urologic surgeon. Removal of a small benign mass may not be necessary, whereas surgery for a malignant tumor with aggressive features may prevent locally advanced disease or distant metastases. The proper surgical approach (partial vs radical nephrectomy) for SRMs with regard to optimizing survival rate and renal functional outcomes has been debated recently.[1,2] One aspect of surgical management that has not been extensively addressed is the role of regional lymph node dissection (LND) for SRMs at the time of nephrectomy. Given the low stage and low potential metastatic risk, the survival advantage conferred by LND with a clinically localized SRM is unclear. Herein, we address the usefulness of an LND in the setting of an SRM, clinical and pathologic predictors of regional lymph node metastasis, and appropriate dissection templates if an LND is performed.

PREDICTORS OF LYMPH NODE METASTASES IN RENAL CELL CARCINOMA

Although the natural history of SRMs is heterogeneous, the majority of tumors can be classified as benign or as malignant with low rates of metastatic progression.[3] The low rate of metastatic progression of SRMs is demonstrated with the low rates of disease progression after nephrectomy.[4] Such excellent cancer-specific outcomes have led to the adoption of less invasive treatments, such as thermal ablation and active surveillance, which have also demonstrated low rates of progression to metastatic disease in patients with SRMs. However, there is a subset of SRMs of greater malignant potential and possibly a greater risk of metastatic progression to regional lymph nodes. SRMs believed to have a greater metastatic potential are typically classified based on certain high-risk pathologic features. These high-risk pathologic features, if present, may predict lymph node involvement and consequently affect disease progression and cancer-specific survival.[5] This potential relationship between high-risk features noted in the primary tumor and an increase risk of metastasis to regional lymph nodes may prove valuable as lymph node positive disease portends poorer outcomes.[6] Thus, the identification these high-risk features may help to provide important information to help a clinician determine if and when an LND should be performed for a patient presenting with an SRM. Additionally, these high-risk features may also predict the risk for future disease recurrence and need for adjuvant therapy.

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Tumor size has been studied as a predictor for disease aggressiveness and has been linked to metastatic spread, even when considering SRMs.[7–9] In a systematic literature review on the behavior of SRMs undergoing active surveillance, Smaldone and colleagues[8] identified 18 of 880 patients (2%) who subsequently developed metastatic cancer including regional lymph node involvement. Although progression to metastatic disease occurred only in a small percentage of patients, after a pooled analysis, variables significant for predicting metastases included initial tumor size or diameter (4.1 ± 2.1 cm vs 2.3 ± 1.3 cm; $P<.0001$), initial tumor volume ($P<.0001$), and growth rates.

Further supporting the relationship between tumor size and metastatic potential, Lee and colleagues[10] reviewed their data from 1913 patients who received radical or partial nephrectomy for a T1a renal masses. Multivariate analysis revealed that tumor size was associated independently with an higher risk of metastatic potential: the risk of metastases according to size for T1a masses was found to be 1.1% (1.1–2.0 cm), 3.3% (2.1–3.0 cm), and 6% (3.1–4.0 cm). Additionally, their survival analysis demonstrated significant differences in metastasis-free survival between size groups ($P<.001$).[10] This highlights that, although the rate of metastatic recurrence after partial or radical nephrectomy may indeed be low, patients with larger tumors may have a nonnegligible metastatic potential. The relationship of SRM size and risk of metastatic potential has also been outlined using Surveillance, Epidemiology, and End Results data registry in an analysis of 22,000 patients with stage T1 renal cell carcinoma (RCC).[11] For tumors with a maximum diameter of 2 to 3 cm the metastatic rate was 4.9%, compared with tumors with a maximum diameter of 3 to 4 cm in which the rate of metastatic disease was 7.1%.

These studies reflect the small, albeit nontrivial, potential for stage T1a RCC to present with metastatic disease. Taken together, these studies show that tumor size may predict lymph node involvement and that a proportion of SRMs, particularly those 3 to 4 cm, that demonstrate significant growth over short periods may have increased metastatic potential. Performing an LND in these patients at the time of surgery may provide important staging information and may confer a potential survival benefit as lymphadenectomy may capture locally advanced stages of RCC in this select group of patients presenting with an SRM.

In addition to tumor size, there are other high-risk features of SRMs that may indicate possible lymph node metastasis including tumor grade, histologic subtype, and aggressive components, such as sarcomatoid or rhabdoid features (**Box 1**).[12] While assessing pathologic tumor characteristics for stage T1 RCC, Lau and colleagues[5] identified histologic subtype, grade, and size as independent predictors for metastases free survival rates. Of 682 patients with clear cell RCC, those more likely to experience metastatic disease demonstrated Fuhrman grade 3 or 4 (hazard ratio, 4.18; 95% confidence interval, 2.56–6.81) and larger tumor size (5 cm; hazard ratio, 1.5, 95% confidence interval, 1.26–1.79) on final pathology. In a similar study, Blute and colleagues[12] reviewed more than 1600 patients who underwent radical nephrectomy and identified 887 patients who had a concomitant LND. After multivariate analysis, 5 clinicopathologic predictors of lymph node metastasis in clear cell RCC were identified including nuclear grade 3 or 4 ($P<.001$), presence of sarcomatoid component ($P<.001$), tumor size 10 cm or greater ($P = .005$), tumor stage pT3 or pT4 ($P = .017$), and histologic tumor necrosis ($P = .051$).[12] In patients with at least 2 of the features 10% had regional lymph node metastasis compared with 53% in patients with all 5 adverse features present.

It should be noted that identifying these adverse features would require frozen section analysis of tumors intraoperatively, which may not be available and routine at all centers. Additionally, the median tumor size in the series by Blute and colleagues[12] was 6 cm and there is a known association with increasing tumor size and the remaining adverse pathologic features. The relationship between tumor size and other adverse pathologic features makes the likelihood of discovering 3 or more of the features in a patient undergoing surgery for an SRM very low. For these reasons, the authors' proposed protocol should not be applied to patients undergoing surgery in patients undergoing for an SRM until additional evidence supporting its use is available in this patient population. However, as more evidence becomes available in the future, these studies suggest that the evaluation of high-risk features may help to identify which patients are at greatest risk for metastatic disease and may potentially benefit from an LND to improve pathologic staging and regional disease control.

Box 1
Predictors of lymph node metastasis

- Large tumor size (>5 cm)
- Fuhrman nuclear grade 3 or 4
- Histologic tumor necrosis
- Presence of sarcomatoid or rhabdoid features
- Stage T3/T4 disease