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Perioperative Morbidity of Lymph Node Dissection for Renal Cell Carcinoma: A Propensity Score–based Analysis

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Abstract

Background: There are little data regarding the morbidity of lymph node dissection (LND) for renal cell carcinoma (RCC) to assess its risk–benefit ratio.
Objective: To evaluate the association of LND with 30-d complications among patients undergoing radical nephrectomy (RN) for RCC.
Design, setting, and participants: A total of 2066 patients underwent RN for M0 or M1 RCC between 1990 and 2010, of whom 774 (37%) underwent LND.
Intervention: RN with or without LND.
Outcome measurements and statistical analysis: Associations of LND with 30-d complications were examined using logistic regression with several propensity score techniques. Extended LND, defined as removal of ≥13 lymph nodes, was examined in a sensitivity analysis.
Results and limitations: A total of 184 (9%) patients were pN1 and 302 (15%) were M1. Thirty-day complications occurred in 194 (9%) patients, including Clavien grade ≥3 complications in 81 (4%) patients. Clinicopathologic features were well balanced after propensity score adjustment. In the overall cohort, LND was not statistically significantly associated with Clavien grade ≥3 complications, although there was an approximately 40% increased risk of any Clavien grade complication that did not reach statistical significance. Likewise, LND was not significantly associated with any Clavien grade or Clavien grade ≥3 complications when separately evaluated among M0 or M1 patients. Extended LND was not significantly associated with any Clavien grade or Clavien grade ≥3 complications. LND was not associated with length of stay or estimated blood loss. Limitations include a retrospective design.
Conclusions: LND is not significantly associated with an increased risk of Clavien grade ≥3 complications, although it may be associated with a modestly increased risk of minor complications. In the absence of increased morbidity, LND may be justified in a predominantly staging role in the management of RCC.
Patient summary: Lymph node dissection for renal cell carcinoma is not associated with increased rates of major complications.

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1. Introduction

The role of lymph node dissection (LND) in the surgical management of renal cell carcinoma (RCC) remains uncertain. Although there are little data to support an oncologic benefit to LND at the time of radical nephrectomy (RN) for RCC, it provides pathologic assessment of nodal stage [1–7]. This may provide valuable prognostic information given the association of lymph node metastasis with survival [6,8–10], and it may identify candidates for consideration of adjuvant therapies [11]. In this context, proponents have argued that LND may have a role in the surgical management of RCC by providing valuable staging information, and guidelines have recommended LND in the setting of radiographic lymphadenopathy [1,12,13]. Moreover, it has been suggested that LND may provide a survival benefit to a small subset of patients with lymph node metastases [14–17].

An accurate assessment of the risks of LND is critical to determine its risk–benefit ratio. Yet despite numerous studies examining a therapeutic benefit to LND, there is a paucity of data regarding its morbidity [2,3,6,18,19]. We, therefore, examined the perioperative morbidity of LND among patients undergoing RN for RCC. Specifically, in this study, we characterized 30-d complications among patients undergoing RN with or without LND, and we evaluated the associations of LND with 30-d complications using a propensity score–based approach to adjust for nonrandom treatment allocation.

2. Patients and methods

2.1. Patient population

After obtaining Institutional Review Board approval, we identified 2103 patients treated with RN for sporadic, unilateral, M0 or M1 RCC between 1990 and 2010. Thirty-seven patients lacked data regarding complications within 30 d of surgery and were excluded. The final cohort included 2066 patients for study, of whom 774 (37%) underwent LND. LND was performed at the surgeon's discretion, and a standardized template was not utilized.

2.2. Clinicopathologic features

The clinicopathologic and radiographic features in Table 1 were assessed as described in the Supplementary Material. All pathologic features were reviewed by one urologic pathologist (J.C.C.) without knowledge of patient outcome. Indicator variables were employed to denote missing data for the radiographic features studied.

Complications within 30 d of RN were assessed by a trained nurse abstractor using standardized definitions and graded according to the Clavien classification [20]. Complication categories included bleeding (requiring reoperation or angioembolization) or hematoma (on cross-sectional imaging), deep vein thrombosis (DVT), pulmonary embolism (PE), myocardial infarction (MI), wound infection (requiring antibiotics or drainage) or dehiscence (partial or complete), abscess, sepsis (bacteremia with hypotension or requiring admission to intensive care unit), acute renal failure with or without dialysis, pneumothorax, any other complication not specified above, and death. Patients were typically evaluated at 3 mo after surgery and then according to the recommended surveillance protocol based on surgical pathology.

2.3. Statistical methods

Clinicopathologic and radiographic features were summarized with medians and interquartile ranges (IQRs) or frequency counts and percentages, and were compared for patients with and without LND using Wilcoxon rank sum, chi-square, and Fisher exact tests. Propensity scores (PSs) for treatment with LND were estimated using a logistic regression model with LND as the outcome and the features listed in Table 1 as covariates, except body mass index (BMI), estimated blood loss (EBL), and length of stay. BMI was excluded because of the amount of missing data and its lack of a statistically significant association with LND. Year of surgery and age at surgery were categorized into four groups of approximately equal patient numbers since there was evidence that the associations of these features with LND were not linear. Forty-nine patients missing covariate data (16 with and 33 without LND) were excluded from the PS analytic cohort, as were 91 patients with a PS that did not fall within the common range (50 with and 41 without LND). A total of 1926 patients formed the cohort for PS analyses, including 708 (37%) who underwent LND and 1218 (63%) who did not.

The associations of LND with any complication or a Clavien grade $\geq$3 complication were evaluated with logistic regression models using several PS techniques, and summarized with odds ratios (ORs) and 95% confidence intervals (CIs) [21]. Patients with LND were matched 1:1 to patients without LND using the caliper method based on the logit of the PS and a caliper width of 0.2 times the standard deviation of the logit [22]. Using this approach, 457 patients with LND were matched to 457 patients without LND. To incorporate all 1926 patients in the analyses, we conducted PS analyses reweighting by stabilized inverse probability weights (IPWs). Additional PS techniques were employed including adjustment for PS quintile and stratification by PS quintile (Supplementary Material). ORs for the stratified analyses were obtained by pooling estimates obtained within each PS quintile. ORs for the subset of 457 matched pairs were obtained by stratifying on the matched sets. Stabilized IPWs were truncated by setting weights below the first percentile to the value of the first percentile, and weights above the 99th percentile to the value of the 99th percentile [23]. Models were further separately adjusted for surgeon and BMI with similar results. We further examined the association of LND with 30-d complications among M0 and M1 patients by constructing logistic regression models that included an indicator variable for performance of LND, an indicator for M1 status, and the interaction between the two.

Given heterogeneity in the extent of LND, we conducted a sensitivity analysis to examine associations of extended LND, defined as removal of $\geq$13 LNs [24] (vs no LND or LND with <13 LNs removed), with complications. PSs for treatment with extended LND were obtained using a logistic regression model, and associations of extended LND with any complication or a Clavien $\geq$3 complication were evaluated using the PS techniques described above.

Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA) and R version 3.1.1 (R Foundation for Statistical Computing, Vienna, Austria). All tests were two sided, and $p < 0.05$ was considered statistically significant.

3. Results

A total of 2066 patients formed the study cohort, including 774 (37%) who underwent LND. Overall, 184 (9%) patients were pN1 and 302 (15%) had distant metastases at the time of RN. The median number of LNs removed during LND was 6 (IQR 2–13). Clinicopathologic and radiographic features stratified, by performance of LND, are summarized in Table 1. Patients who underwent LND had more advanced disease and more aggressive pathologic characteristics,

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