

Surgical Management of Local Retroperitoneal Recurrence of Renal Cell Carcinoma after Radical Nephrectomy

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Abbreviations and Acronyms

CSS = cancer specific survival
CT = computerized tomography
MRI = magnetic resonance imaging
NED = no evidence of disease
RCC = renal cell carcinoma
RFS = recurrence-free survival
RN = radical nephrectomy
RPR = retroperitoneal recurrence

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For other articles on related topics see pages 532 and 539.

Editor's Note: This article is the second of 5 published in this issue for which category 1 CME credits can be earned. Instructions for obtaining credits are given with the questions on pages 602 and 603.

Purpose: Isolated local retroperitoneal recurrence after radical nephrectomy for renal cell carcinoma poses a therapeutic challenge. We investigated outcomes in patients with localized retroperitoneal recurrence treated with surgical resection.

Materials and Methods: This was a retrospective, single institutional study of 102 patients with retroperitoneal recurrence treated with surgery from 1990 to 2014. Demographics, clinical and pathological features, location of retroperitoneal recurrence and perioperative complications are reported using descriptive statistics. We studied recurrence-free and cancer specific survival using univariate and multivariate analyses.

Results: Median age at retroperitoneal recurrence diagnosis was 55 years (IQR 49–64). Cancer was pT3-4 in 62 patients (60.8%) and pN1 in 20 (19.6%). No patients had distant metastatic disease at retroperitoneal recurrence surgery. Median time from nephrectomy to retroperitoneal recurrence diagnosis was 19 months (IQR 5–38.8). The median size of the resected retroperitoneal recurrence was 4.5 cm (IQR 2.7–7). Median followup after recurrence surgery was 32 months (IQR 16–57). Metastatic progression was observed in 60 patients (58.8%) postoperatively. Neoadjuvant and salvage systemic therapy was administered in 46 (45.1%) and 48 patients (47.1%), respectively. On multivariate analysis pathological nodal stage at original nephrectomy and maximum diameter of retroperitoneal recurrence were identified as independent risk factors for cancer specific death.

Conclusions: Clinicopathological factors at nephrectomy as well as retroperitoneal recurrence surgery are important prognosticators. Aggressive surgical resection offers potential cure in a substantial number of patients with retroperitoneal recurrence with acceptable complications and still has a dominant role in the management of isolated locally recurrent RCC.

Key Words: kidney; carcinoma, renal cell; neoplasm recurrence, local; nephrectomy; lymph nodes

RENAL cell carcinoma is an increasingly common malignancy. Even with curative RN metastatic disease develops in 20% to 40% of patients.^{1–5} Of these patients those who are untreated have a poor 5-year survival

rate of less than 20% with a median survival of 6 to 12 months.¹ Localized RPR for RCC is a rare event that develops in 1% to 3% of patients after RN.⁶ Treatment of RPR represents a significant surgical and therapeutic

challenge as patients are at high risk for overt metastatic disease and overall prognosis could be poor.²

Data on the natural history, patient outcomes and prognostic factors associated with RPR are limited and to date there is no standard management strategy. In earlier series small subsets of patients had relatively long-term survival but such surgery is associated with significant morbidity and mortality.^{7–10} In the era of targeted therapy for locally advanced and metastatic RCC, treatment paradigms using combinations of medical and surgical therapies in patients diagnosed with localized recurrence after nephrectomy are paramount to maximize the oncologic outcome.⁹

Our study objective was to assess the surgical and oncologic outcomes of patients undergoing surgical resection of RPR and identify prognostic factors for survival after surgical resection.

PATIENTS AND METHODS

The University of Texas MD Anderson Cancer Center institutional review board approved the current study. From 1990 to 2014 we identified 102 patients who underwent prior RN for RCC and had subsequent isolated RPR that was managed by surgical resection. We defined RPR as pathologically proven RCC in the soft tissue/renal fossa, including the psoas muscle, ipsilateral adrenal gland or ipsilateral retroperitoneal lymph nodes. Patients with nonRCC pathology or detectable distant metastatic disease at RPR surgery were excluded from the study. Patients treated with partial nephrectomy or ablative therapies were also excluded.

We assessed patient demographics, Charlson comorbidity index,¹¹ tumor pathology, time to local and/or distant progression, location of RPR, perioperative complications using the Clavien-Dindo system¹² and outcomes. Recurrence after RPR surgery was defined as any radiological evidence of local and/or distant metastatic disease. Systemic therapy before or after RPR surgery was also recorded. We defined neoadjuvant systemic therapy as therapy given between the time of RN and RPR surgery, and salvage systemic therapy as therapy given after recurrence following RPR surgery. Adjuvant therapy was not done in this study. RCC stage was assigned using the AJCC (American Joint Committee on Cancer) 2010 classification.¹³

Initial diagnosis of RPR was based on CT or MRI performed in the context of regular followup or due to local and/or systemic symptoms. Restaging at the time of suspected progression included comprehensive physical and laboratory evaluation, chest CT, abdomen and pelvis CT or MRI and nuclear bone imaging. MRI of the brain was done as clinically indicated. Followup consisted of history, physical examination, serum chemistry and liver function tests. Radiological evaluation with CT of the chest and CT or MRI of the abdomen and pelvis was performed in all patients every 3 to 6 months for the first 2 years after RPR surgery and every 6 to 12 months thereafter.

At RPR surgery retroperitoneal lymph node dissection was performed in isolation or with adrenalectomy and/or soft tissue resection depending on the recurrence pattern in the retroperitoneum and at surgeon discretion. Retroperitoneal lymph node dissection involved removal of at least the para-aortic nodal tissue from the crus of the diaphragm to the bifurcation of the aorta for left tumors, and the paracaval and interaortocaval lymph nodes from the diaphragmatic crus to the bifurcation of the great vessels for right tumors as well as removal of any other suspicious lymph nodes.

RFS was defined as time from RPR surgery to a diagnosis of local or distant recurrence, or last followup. Patients who were alive with NED at their last followup were censored on that date. CSS was defined as time from RPR surgery to death from RCC or last followup. The 2 patients who died postoperatively were counted as cancer specific deaths. Patients who were alive at their last followup were censored on that date. The Kaplan-Meier method¹⁴ was used to estimate RFS and CSS. Survival differences were assessed with the log rank statistic. Univariate and multivariate survival analyses were performed using the Cox proportional hazard regression model. Statistical significance in this study was considered at $p \leq 0.05$. All analyses were performed with SPSS®, version 22.

RESULTS

Analysis

At RN. A total of 102 patients were identified as having a RPR of RCC after RN and were surgically treated between 1990 and 2014. Of the patients 86 (84.3%) underwent RN elsewhere and were subsequently referred to our institution for RPR surgery. Median time from nephrectomy to RPR diagnosis was 19 months (IQR 5–38.8). At nephrectomy 62 cases (60.8%) were pT3-4 and 20 (19.6%) were pN1. Supplementary table 1 (<http://jurology.com/>) shows other patient demographics and pathological features after RN.

At RPR Surgery. Supplementary table 2 (<http://jurology.com/>) shows patient demographics and pathological features after RPR surgery. Of the 102 RPRs 49 were in soft tissue/renal fossa, 41 were in ipsilateral lymph nodes and 12 were in the ipsilateral adrenal gland. All patients underwent complete extirpation of the RPR with grossly negative margins. Median size of resected RPRs was 4.5 cm (IQR 2.7–7). In RPR specimens surgical margins were microscopically positive in 12 patients (11.8%) and predominantly occurred in soft tissue recurrence in the renal fossa (8 of 12 or 66.6%). Of the 20 patients with pN1 disease at RN 14, 4 and 2 had recurrence in the retroperitoneal lymph nodes, soft tissue and the ipsilateral adrenal gland, respectively. Median followup after RPR surgery was 32 months (IQR 16–57). Table 1 shows intraoperative details and postoperative outcomes,

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