



Original article

Surgical resection of locally recurrent renal cell carcinoma after nephrectomy: Oncological outcome and predictors of survival

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Abstract

Objective: To describe the course of disease of patients surgically treated for locally recurrent renal cell carcinoma (LRRCC) after nephrectomy and to identify potential predictive factors for long-term survival.

Patients and methods: We, retrospectively, identified 54 patients who underwent surgical resection of LRRCC after open nephrectomy for localized kidney cancer. The median age at time of surgery for LRRCC was 65 years. Survival rates were determined with the Kaplan-Meier method. Mantel-Haenszel hazard ratios were calculated. Comparisons were made with the log-rank test. Cox proportional hazard models were used to analyze combined effects of variables.

Results: Median time to local recurrence after nephrectomy was 36 months (5–242 months). Median follow-up after surgery for LRRCC was 39 months. At time of analysis 18 patients (33%) were alive without any evidence of disease, 8 patients (15%) were alive with disease, 20 patients (37%) died of renal cell carcinoma, and 8 patients (15%) died of other causes. A 5-year overall survival (OS) was 60% (95% CI: 0.44–0.73) and 10-year OS was 32% (95% CI: 0.15–0.51). The median survival after surgery for LRRCC was 79 months. In univariate analysis OS differed significantly by the time period between primary surgery and occurrence of LRRCC (<2 years vs. ≥2 years: 10-year OS rate 31% (95% CI: 10.2–55.0) vs. 45% (95% CI: 21.5–65.8; hazard ratio = 0.26; $P = 0.0034$). In multivariate analysis sarcomatoid features in the primary nephrectomy specimen, positive surgical margins of the LRRCC specimen and a Charlson score of ≥2 were associated with a significantly worse prognosis in this cohort.

Conclusion: In patients with a disease-free interval of more than 2 years after surgery for the primary tumor, surgical removal of LRRCC may achieve long-term survival in most patients. In those with a shorter disease-free interval, long-term survival is unlikely. © 2017 Elsevier Inc. All rights reserved.

Keywords: Kidney neoplasms; Renal cell carcinoma; Local recurrence; Prognosis

1. Introduction

Up to 30% of patients who undergo surgical therapy of renal cell carcinoma (RCC) with curative intent will

develop metastasis and about one-third of all patients with RCC have systemic disease at presentation [1]. The aim of postoperative surveillance after surgery for localized RCC is to detect local recurrence or metastatic disease while the patient is still surgically curable [2]. Isolated local recurrence of RCC is rare and occurs in about 3% after radical nephrectomy [3,4]. Most patients with local recurrence of RCC are diagnosed by either computed tomography (CT) or magnetic resonance imaging scans as part of the

Study type: Therapy (case series), Level of Evidence 4.

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postoperative surveillance regimen after nephrectomy for RCC. However, some patients with LRRCC have single or multiple distant metastases at time of diagnosis of LRRCC. Targeted therapy is effective in stabilizing metastatic disease in approximately 70% to 80% of patients in the first-line setting and prolonging overall survival (OS) in a significant proportion of patients with metastatic RCC. Nevertheless, complete responses are reported in only 1% to 3% of these patients [5,6]. Therefore, the primary curative option for oligometastatic patients remains the surgical removal of all evident metastasis if feasible.

Disease data from retrospective series suggest that with a surgical approach to local recurrence long-term tumor control and longer OS can be achieved in a significant proportion of patients without evidence of systemic disease [3,4,7–12]. In this study we, retrospectively, examined the natural history of locally recurrent RCC in patients with isolated local recurrence. We also analyzed our data for factors that may potentially predict long-term survival after surgery for LRRCC.

2. Patients and methods

We, retrospectively, identified 54 consecutive patients who underwent surgical resection for suspected locally recurrent RCC between 1992 and 2014 at 2 academic institutions. The study was approved by the institution's ethics committee. All patients had undergone radical nephrectomy for localized RCC. Postoperative follow-up after nephrectomy was done by the outpatient office urologists according to their discretion, usually consisting of physical examination, blood chemistry and imaging according to the guidelines of the European Association of Urology [2]. LRRCC after nephrectomy was defined according to Margulis et al. [9] as a contrast-enhancing retroperitoneal tumor either in the renal fossa, the ipsilateral adrenal gland or ipsilateral lymph nodes after nephrectomy. All patients that underwent surgery for contrast-enhancing lesions at the aforementioned loci with histologically proven local recurrence of RCC were included in the final analysis. Also, all patients underwent extensive staging before surgical resection of LRRCC, which consisted generally of a physical examination, blood chemistry, abdominal and chest CT, and a nuclear bone scan. Histological RCC subtype was classified according to the current WHO classification [13]. Tumor grade was assessed according to the Fuhrman's system [14]. Follow-up after LRRCC resection was again up to the discretion of the office urologist but generally consisted of chest and abdominal CT every 6 months for the first 2 years after LRRCC surgery and then at least annually. To assess the current health status and follow up of the patients we contacted the office urologists, general practitioners, the local cancer registries and health authorities. Overall

survival rates were determined with the Kaplan-Meier method. Mantel-Haenszel hazard ratio (HRs) were calculated. Comparisons were made with the log-rank test. Cox proportional hazard models were used to analyze combined effects of variables. All tests were done using the Statistical Analysis Systems v9.4 statistical package (SAS Institute, Cary, NC).

3. Results

3.1. Patient and tumor baseline characteristics

A total of 62 patients underwent surgery for contrast-enhancing lesions suspicious of LRRCC according to the definition of Margulis et al. [9] at our 2 academic centers. In all, 8 patients had to be excluded from the analysis with 4 patients having concomitant lung metastasis and 4 patients having a benign histology. All of the remaining 54 patients included in the final analysis had histologically proven RCC recurrence. The median age was 59 years at time of nephrectomy (range: 30–75 years). The clinical and pathological characteristics at time of nephrectomy are summarized in Table 1. Totally, 59% of patients had organ-confined disease at nephrectomy (\leq pT2). Clear cell RCC constituted 80% of the nephrectomy specimens. Out of 54, 4 patients (7%) had positive lymph nodes and 3 patients (6%) had microscopically positive surgical margins at initial nephrectomy.

3.2. Characteristics of LRRCC

The study cohort consisted of 39 male (72%) and 15 female patients (28%). The median age at surgery for LRRCC was 65 years (range: 39–77 years). The median time between radical nephrectomy and surgery for LRRCC was 36 months (range: 5–242 months). A total of 47 patients (87%) had LRRCC in the renal fossa, 6 patients in the ipsilateral lymph nodes, and 1 patient had a combined recurrence in the ipsilateral lymph nodes and the renal fossa. At LRRCC diagnosis 7 patients were symptomatic. Patients suffered from weight loss, fatigue, or flank pain.

All 54 patients had isolated LRRCC without evidence of metastatic disease. Clinical and pathological characteristics of the patients at time of LRRCC are summarized in Table 2. Median follow-up was 48 months (range: 19–226 months) for the whole study cohort.

3.3. Surgical aspects

Open surgery for LRRCC was performed in all cases. Median surgical time was 163 minutes (range: 44–485 minute). Median size of local recurrence was 42 mm (range: 10–170 mm). In 8 patients the resection of an adjacent organ was necessary (splenectomy in three cases, partial liver resection in 2 cases, resection of colon in 2 cases and

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