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The natural history of large renal masses followed on observation

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Abstract

Purpose: The safety and feasibility of active surveillance in comorbid patients with renal masses ≥4.0 cm is uncertain. The aim of this study is to describe our institutional experience with the observation of large renal masses.

Materials and methods: One hundred patients were identified with renal masses ≥ 4.0 cm that were followed on observation for at least 6 months without surgical intervention between 1994 and 2016. Linear regression was conducted to determine predictors for renal mass growth and competing risk methods were used to estimate the probability of progression in the setting of death from other causes.

Results: Median age at diagnosis was 73 years and 73% of patients had a Charlson Comorbidity index ≥ 4. At presentation, the median mass size was 4.9 cm. The median growth rate was 0.4 cm/y and there were no significant predictors of growth. Surveillance was discontinued in 34 patients who underwent delayed intervention. Median follow up for metastasis-free survivors was 4 years. In total, 10 patients developed metastatic disease, 3 died from kidney cancer and 30 patients died from other causes. The 5-year probability of other cause mortality was 22% (95% CI: 14%–32%) compared to 6% (95% CI: 2%–13%) for metastatic progression of kidney cancer.

Conclusion: In highly comorbid patients, the observation of large renal masses has low likelihood for metastatic progression relative to the risk of nonkidney cancer related death. This data supports the use of surveillance as an acceptable strategy for highly selected patients with competing risks from other serious illnesses.

Keywords: Large renal mass; Observation; Surveillance; Growth rate; Renal cell carcinoma

1. Introduction

Over 67,000 new cases of kidney cancer are diagnosed each year in the United States, with the greatest incidence in men and women over the age of 70 [1]. The majority are incidental small renal masses; although large renal masses (LRM) ≥ 4 cm make up a significant portion of cases and can present unique challenges in elderly and highly comorbid populations. Historical data indicate an increased risk of high-grade malignancy and potential for disease progression with each 1 cm increase in tumor size,[2] supporting the use of surgical extirpation as the standard treatment for LRM. Despite these oncologic concerns, many patients with competing risks from multiple comorbidities may not be suitable candidates for immediate operative intervention. Previous works assessing overall survival in patients with localized renal cell carcinoma (RCC) have questioned the benefits of surgery in individuals with multiple comorbidities [3–5].

Active surveillance (AS) is an acceptable alternative to surgery for selected patients whose medical comorbidities increase the risk associated with intervention. The American Society of Clinical Oncology has endorsed the practice of AS for kidney tumors, linking slow tumor growth rates with low potential for progression, albeit limited to patients with small renal masses < 4 cm [6]. No guidelines or management recommendations exist for the observation of LRM in patients with poor performance status. The safety and feasibility of AS for LRM in this population is therefore unclear with a paucity of data on the natural history of these

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untreated tumors. The aim of this study is to describe a single institutional experience with the observation and expectant management of renal masses ≥ 4 cm including the growth rate of LRM under surveillance, factors associated with growth rate, and overall clincal outcomes.

2. Materials and methods

2.1. Study cohort

Following Institutional Review Board approval, the Memorial Sloan Kettering Cancer Center patient registry was used to identify patients with LRM undergoing surveillance from 1994 until 2016. Surveillance initiation date was defined as the first diagnostic image identifying the renal mass. Patients were included with renal masses ≥4 cm and if they had been followed with serial imaging for at least 6 months without surgical intervention. The date of surveillance discontinuation was defined as the first event of surgical intervention (partial or radical nephrectomy) or the diagnosis of RCC metastasis. Imaging was conducted by surgeon discretion at 3 to 6 month intervals after the initial diagnosis. Patients were excluded from if they had Bosniak class 1 and 2 renal cysts, benign renal masses such as angiomyolipomas, upper tract urothelial cell carcinoma, or evidence of RCC metastases at the time of diagnosis.

2.2. Outcome measurement

The maximal cross-sectional diameter for each mass was obtained from imaging studies interpreted and measured by a radiologist at the time of the original study. All measurements from serial imaging were utilized to determine the annual growth rate of the LRMs, expressed as centimeters per year. Computerized tomography (CT), magnetic resonance imaging (MRI), and ultrasonography were used interchangeably for follow-up. The development of RCC metastasis during the surveillance period was identified from clinical records that indicated the histologic confirmation of RCC metastasis or radiographic evidence of distant metastatic disease. Clinical endpoints such as RCC-related mortality and all cause mortality were also captured from institutional records.

2.3. Statistical analysis

Linear regression was used to calculate LRM growth rate (cm/yr) for each patient based on maximal diameter. Univariate linear regression was used to assess whether growth rate was associated with factors such as initial renal mass size, cystic renal mass versus solid, tumor location, age, body mass index, Charlson Comorbidity Index (CCI), smoking status, history of another malignancy, gender, and race. Univariate Cox regression was used to assess whether any clinical or renal mass characteristics were associated with the time until surgical intervention in our cohort. Additionally, competing risk methods were used to estimate the probability of developing RCC metastasis in the setting of death from other causes. All statistical analyses were completed with Stata version 13.0 (StataCorp, College Station, TX).

3. Results

3.1. Patient population

A total of 401 patients with renal masses managed by AS were identified, 100 met the study inclusion criteria. Eighty-one patients were initially diagnosed with LRM ≥ 4 cm while an additional 19 patients on AS were identified that had been initially diagnosed with renal masses smaller than 4 cm, but had progressed to 4.0 cm or greater within a 12-month time frame. These patients were also included as part of the analysis and the duration of surveillance was defined from the date of initial renal mass diagnosis. As it could be argued that there may be a potential lead time bias in patients with renal masses smaller than 4 cm, we ran a sensitivity analysis defining surveillance from the date in which the renal masses were ≥4 cm. One patient was excluded from the sensitivity analysis as there were no additional scans following the date in which the renal mass was ≥4 cm. Overall, the results from the sensitivity analysis were nearly identical to the results reported below, therefore all patients were included in the final analysis using data from the time of initial diagnosis. The overall median renal mass size at time of discovery was approximately 4.9 cm (IQR: 4.0–6.6). Median size at diagnosis for masses initially less than 4.0 cm was 3.3 cm (IQR: 2.8–3.5) and 5.2 cm (IQR: 4.3–7.1) for masses greater than 4 cm at diagnosis. Only 18% had Bosniak class 3 and 4 lesions (Table 1). The median age at diagnosis was 73 years (IQR: 64–80) and 73% of patients had a Charlson Comorbidity Index ≥ 4 immediately before the diagnosis of the renal mass. At the time of LRM diagnosis, 32% of patients had a history of another nonrenal malignancy. In total, 19% of the cohort was diagnosed with non-RCC metastatic disease from another malignancy during the surveillance period.

3.2. Growth rate

The median renal mass growth rate was 0.4 (IQR: 0.1–0.8) cm/yr (Fig. 1). Seventeen patients (17%) were found to have renal masses with stable or negative growth throughout the follow-up period. There were no significant associations between growth rate and any of the clinical variables tested (Supplemental Table 1).

3.3. Delayed intervention and outcomes

Surveillance was discontinued for 34 patients who underwent delayed surgical intervention (Table 2). The