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Original article

Patients with anatomically "simple" renal masses are more likely to be placed on active surveillance than those with anatomically "complex" lesions

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Abstract

Objective: To determine if radiographically less complex renal lesions are deemed clinically less "worrisome" and therefore are more likely to be considered for active surveillance (AS).

Methods: We examined our prospective institutional database to identify and compare patients with localized renal cell carcinoma undergoing an initial period of AS or immediate surgery. Multivariate logistic regression was used to examine covariates associated with receipt of AS.

Results: Of 1,059 patients with available anatomic complexity data, 195 underwent an initial period of AS (median duration of AS 25.6 mo [interquartile range: 11.8–52.8 mo]). Compared with patients undergoing immediate surgical treatment, patients selected for AS had lower overall nephrometry scores (NS) with tumors that were smaller, further from the sinus or urothelium, more often polar, and less often hilar ($P < 0.0015$ all comparisons). After adjustment for age, largest tumor size, individual components of NS, total NS, and Charlson comorbidity index, total NS (odds ratio [OR] = 1.9 [CI: 1.4–2.5]), "R" score of 1 (OR = 5.2 [CI: 1.8–15.2]), "N" score of 1 (OR = 2.3 [CI: 1.5–3.6]), "L" score of 1 (OR = 1.4 [CI: 0.84–2.2]), and nonhilar tumor location (OR = 2.7 [CI: 1.2–5.8]) increased the probability of being selected for AS compared with immediate surgery. Findings remained significant in a subanalysis of T1a renal masses.

Conclusions: Lower tumor anatomic complexity was strongly associated with the decision to proceed with AS in patients with stage I renal mass. Not only may these data afford new insights into renal mass treatment trends, but the findings may also prove useful in the development of objective protocols to most appropriately select patients for AS.

Keywords: Renal cell carcinoma; Active surveillance; Nephrometry score; Radiographic imaging

1. Introduction

Increased use of abdominal imaging over the past 3 decades has led to a rise in the incidental detection of asymptomatic small renal masses (SRMs), typically defined as tumors 4 cm or less in diameter [1]. In fact, SRMs now account for nearly 50% of all newly diagnosed kidney tumors, with the greatest number of cases found in patients older than 70 years. As such, increased detection at earlier stages in elderly patients has led to a significant stage migration with a concurrent increase in the median age at diagnosis of renal cell carcinoma (RCC) [2,3].

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Although nephron-sparing surgery is currently the reference standard treatment for healthy patients with clinically localized T1a renal tumors, meaningful effect of active treatment on overall survival in elderly patients with SRM is yet to be demonstrated [1,4,5]. For patient populations that are either unfit or unwilling to undergo surgery, including the elderly and infirmed, recent emphasis has been placed on the role of initial active surveillance (AS) [6] with delayed intervention as necessary in management of SRMs [7].

The subjective nature of clinical decision making for treatment of SRMs, which is likely influenced by surgeon and institutional biases, is recognized and thus reflected by the intentional ambiguity of international treatment guidelines [8–12]. In fact, the peer-reviewed literature regarding which masses are appropriate for AS nearly exclusively focuses on tumor size [7,10–12]. We hypothesized that tumor characteristics beyond tumor size likely influence critical decision making regarding immediate intervention, as anatomically "simple" renal masses may be more likely to be deemed clinically less "worrisome." To test the hypothesis, we compared patients who underwent an initial course of AS with those who proceeded to immediate surgery regarding tumor anatomic complexity at diagnosis, as quantified by the R.E.N.A.L. nephrometry score (NS), in our large prospectively maintained institutional cohort adjusting for patient age and comorbidity.

2. Material and methods

After institutional review board approval, our prospectively maintained kidney tumor database was examined to identify all patients undergoing AS, radical nephrectomy, or partial nephrectomy for clinical stage I renal tumors from 2007 to 2012 with available NS data. AS or surgery was offered to patients at each surgeon's (R.G.U., R.V., D.Y.C., R.E.G., and A.K.) discretion. Clinical variables evaluated included variables such as age, gender, Eastern Cooperative Oncology Group [ECOG] performance status, and body mass index. Disease-related variables included R.E.N.A.L. NS, and its components including the hilar designation, solitary kidney status, tumor size, and laterality. For multifocal tumors, tumor size indicated diameter of the largest tumor. Treatment variables included use of AS and its duration, year of surgery, and surgery type. Comorbidity status was quantified using the Charlson comorbidity index (CCI). Patients were stratified into low (NS: 4–6), intermediate (NS: 7–9), and high (NS: 10–12) anatomic complexity groups. Tumor staging was designated according to the TNM classification based on the 2010 American Joint Committee on Cancer/International Union Against Cancer classification system.

Duration of AS was defined from the time of diagnosis to an outcome or to last clinical examination for those who did not reach a specified outcome. Patients who withdrew or were lost to follow-up were censored at the time of their last visit and those who died were censored at time of death. Active patients were censored at the time of their last surveillance visit. Patients undergoing an initial period of AS were compared with those who went directly to surgery using tumor anatomic attributes as quantified by nephrometry (size, endophycity/exophycity, nearness to sinus/urothelium, anterior/posterior, location relative to polar line, and hilar structures) total NS, age, largest tumor size, CCI, and modified total NS (removal of the "R" component to minimize the influence of tumor size on outcome). To avoid simultaneous inclusion of collinear variables, separate multivariable models including either individual NS components or total NS were created. A subgroup analysis of patients with T1a tumors was also performed. Patient and tumor characteristics were compared using Fisher Exact and Wilcoxon rank sum tests. The associations between AS and tumor anatomic characteristics were assessed using multivariate logistic regression models, using patients undergoing surgery as the reference group. Covariates meeting a $P < 0.10$ level of significance were included for model development, and our final model was adjusted for age, tumor size, total NS, modified NS, individual NS components, and CCI. All analyses were performed using Stata, version 10 (StataCorp, College Station, TX); all hypothesis tests were 2 sided, and the criterion for statistical significance was $P < 0.05$.

3. Results

A total of 1,059 patients (mean age 65 ± 13 y, 64.4% males, 81% white, and mean CCI 1.8 ± 1.8) with clinical stage Ia (77.5%) or Ib (22.5%) renal tumors (mean tumor size 3.1 ± 1.6 cm and mean NS sum 6 ± 1.8) met the final inclusion criteria. There were 30 (2.9%) patients who had a solitary kidney and 127 (12.0%) patients with multifocal tumors. As quantified by NS, 30.6%, 49.5%, and 19.8% of patients had low-, medium-, and high-complexity lesions, respectively.

Overall, 195 patients (mean age 75 ± 13 y, 60% male, and 79% white) underwent an initial period of AS (median duration of AS 25.6 mo [interquartile range: 11.8–52.8 mo]). NS was available in all patients included for final analysis. Comparing patients placed on initial AS and those who underwent immediate surgical treatment ($n = 864$), significant differences in age (75 ± 13 vs. 63 ± 12 y, $P < 0.001$), tumor diameter (2.5 ± 1.2 vs. 3.2 ± 1.7 cm, $P < 0.001$), modified NS (5.5 ± 1.8 vs. 6.1 ± 1.8), CCI (3.1 ± 1.5 vs. 1.4 ± 1.7, $P < 0.001$), body mass index and NS complexity grouping (44.1% vs. 50.9% intermediate complexity, $P < 0.001$; 7.8% vs. 21.8% high complexity, $P = 0.013$), were observed, whereas no differences were seen in gender, race, ECOG performance status, tumor location, and laterality. When compared with patients who underwent immediate surgical treatment, lesions