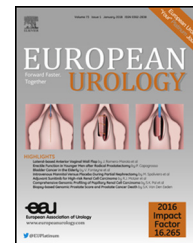


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## Platinum Priority – Kidney Cancer

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# Active Surveillance for Localized Renal Masses: Tumor Growth, Delayed Intervention Rates, and >5-yr Clinical Outcomes

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### Abstract

**Background:** Active surveillance (AS) has gained acceptance as a management strategy for localized renal masses.

**Objective:** To review our large single-center experience with AS.

**Design, setting, and participants:** From 2000 to 2016, we identified 457 patients with 544 lesions managed with AS from our prospectively maintained kidney cancer database. A subset analysis was performed for patients with  $\geq 5$ -yr follow-up without delayed intervention (DI).

**Outcome measurements and statistical analysis:** Linear growth rates (LGRs) were estimated using linear regression for the initial LGR (iLGR) AS interval and the entire AS period. Overall survival (OS) and cumulative incidence of DI were estimated with Kaplan-Meier methods utilizing iLGR groups, adjusting for covariates. DI was evaluated for association with OS in Cox models.

**Results and limitations:** Median follow-up was 67 mo (interquartile range [IQR] 41–94 mo) for surviving patients. Cumulative incidence of DI ( $n = 153$ ) after 1, 2, 3, 4, and 5 yr was 9%, 22%, 29%, 35%, and 42%, respectively. Median initial maximum tumor dimension was 2.1 cm (IQR 1.5–3.1 cm). Median iLGR and overall LGR were 1.9 (IQR 0–7) and 1.9 (IQR 0.3–4.2) mm/yr, respectively. Compared with the no growth group, low iLGR (hazard ratio [HR] 1.25, 95% cumulative incidence [CI] 0.82–1.91), moderate iLGR (HR 2.1, 95% CI 1.31–3.36), and high iLGR (HR 1.87, 95% CI 1.23–2.84) were associated with DI ( $p = 0.003$ ). The iLGR was not associated with OS ( $p = 0.8$ ). DI was not associated with OS (HR 1.34, 95% CI 0.79–2.29,  $p = 0.3$ ). Five-year cancer-specific mortality (CSM) was 1.2% (95% CI 0.4–2.8%). Of 99 patients on AS without DI for  $> 5$  yr, one patient metastasized.

**Conclusions:** At  $> 5$  yr, AS  $\pm$  DI is a successful strategy in carefully managed patients. DI often occurs in the first 2–3 yr, becoming less likely over time. Rare metastasis and low CSM rates should reassure physicians that AS is safe in the intermediate to long term.

**Patient summary:** In this report, we looked at the outcomes of patients with kidney masses who elected to enroll in active surveillance rather than immediate surgery. We found that patients who need surgery are often identified early and those who remain on active surveillance become less likely to need surgery over time. We concluded that active surveillance with or without delayed surgery is a safe practice and that, when properly managed and followed, patients are unlikely to metastasize or die from kidney cancer.

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**1. Introduction**

Renal cancers are projected to comprise an estimated 63 990 new cancer diagnoses in 2017 [1]. The incidence of incidentally discovered localized renal masses has risen due in part to increased utilization of ultrasound and cross-sectional imaging [2]. Using tumor registry data, a paradoxical rise in mortality from renal cell carcinoma (RCC) over time has been described, despite increased detection and intervention [2]. Explanations for this phenomenon—termed “treatment disconnect”—have been proposed, and when one examines cancer-specific survival (CSS) in all comers over time, rates have remained relatively stable [3].

Active surveillance (AS) has emerged as an initial management option to address the variable clinical significance [4,5] and potential overtreatment of localized renal masses [6–8]. The paradigm of AS is to identify patients with potentially low-risk renal masses contextualized by their competing risks of death during an initial observation period [9]. This period allows the triage of patients into continued AS or delayed intervention (DI), a decision most often made on the basis of radiographic tumor growth kinetics, evolving and competing risks, and/or patient preference [10,11].

Published AS cohorts offer encouraging early results, albeit limited by relatively short lengths of follow-up [12–14]. Despite these limitations, AS has been incorporated into recent

American Society of Clinical Oncology [15], European Association of Urology [7], and American Urological Association [8] guidelines. We reviewed our large single-center experience with AS for renal masses with a median of >5 yr of follow-up. We evaluated patterns and associations in tumor growth kinetics, rates of crossover to and predictors of DI, and clinical outcomes including overall survival (OS), cancer-specific mortality (CSM), and progression to metastasis. Further, we analyzed outcomes for a subset of patients who remained on AS for >5 yr without DI.

**2. Patients and methods**

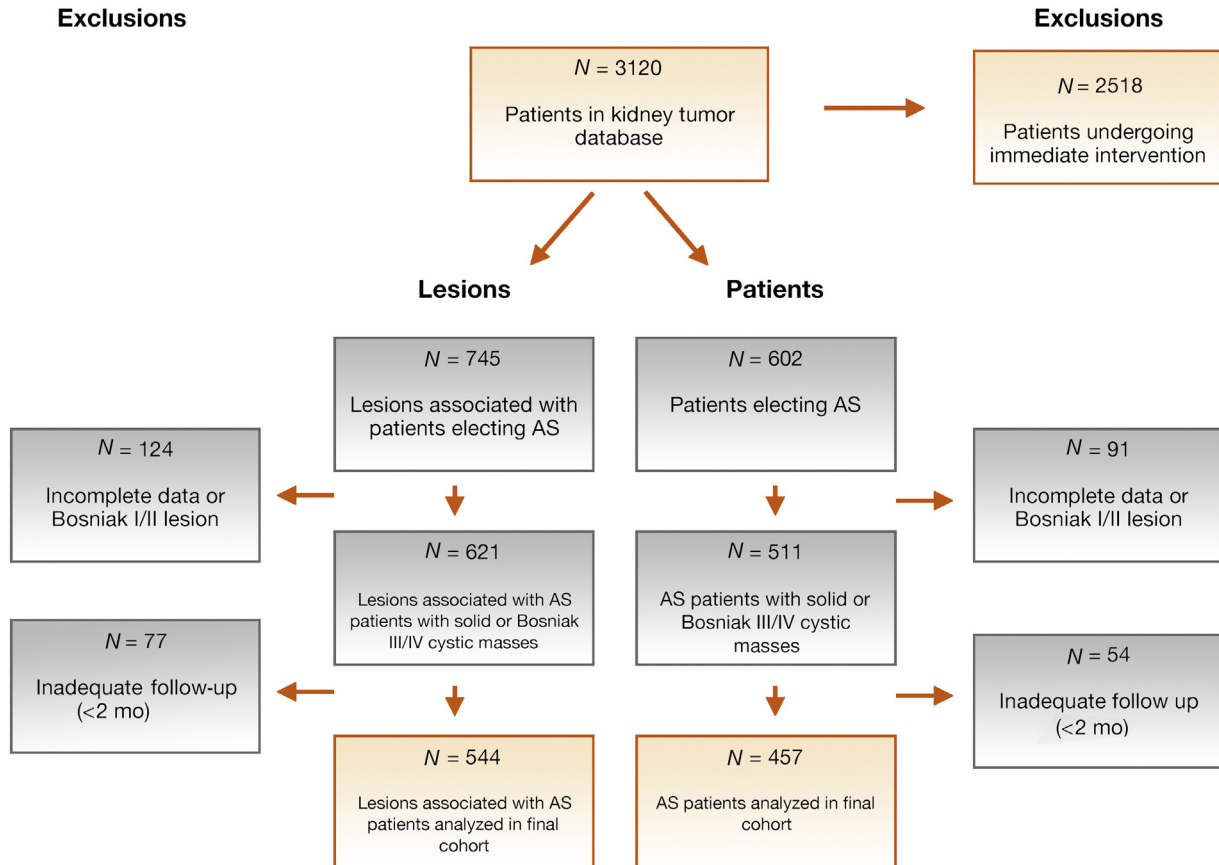
**2.1. Patient selection**

Our institutional review board–approved renal cancer database (n = 3120) was reviewed for masses or enhancing cystic lesions (Bosniak III and IV) managed by AS from January 2000 through July 2016 (Fig. 1).

Lesions were localized (cT1-2N0M0) based on established radiographic staging protocols. Variables examined included patient and tumor characteristics, duration of AS, tumor growth (linear), crossover to DI, and rates of metastasis and death. Patients were followed for oncologic outcomes after DI. There were no predefined selection criteria for AS.

**2.2. Imaging and tumor growth kinetics**

Radiographic surveillance was performed at a median interval of 6.7 mo (interquartile range [IQR] 4.6–12 mo) across 2667 abdominal images



**Fig. 1 – Flow diagram for patient selection and exclusions from Fox Chase Cancer Center kidney tumor database. AS = active surveillance.**

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