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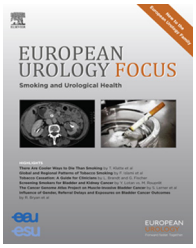

Review – Renal Disease

Active Surveillance for Small Renal Masses: When Less is More

Benjamin T. Ristau *, *Alexander Kutikov, Robert G. Uzzo, Marc C. Smaldone*

Division of Urologic Oncology, Fox Chase Cancer Center, Philadelphia, PA, USA

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Abstract

Context: A marked increase in incidentally detected small renal masses (SRMs) has occurred over the past decade. Active surveillance (AS) has emerged as an initial management option for these patients.
Objective: (1) To determine selection criteria, assess appropriate imaging modalities and surveillance frequencies, and define triggers for delayed intervention (DI) for patients on AS. (2) To describe oncologic outcomes for patients on AS protocols.
Evidence acquisition: The PubMed database was queried for English language articles using the keywords "surveillance" and "renal mass" or "renal cell carcinoma" or "kidney cancer." The level of evidence, sample size, study design, and relevance to the review were considered as inclusion criteria.
Evidence synthesis: A total of 69 manuscripts were included in the review. Selection criteria at initial evaluation for patients interested in AS include patient-related factors (eg, age, baseline renal function, other comorbidities), tumor-related factors (size, complexity, history of growth, possible renal mass biopsy), and patient preferences (illness uncertainty, quality of life). Cross-sectional imaging is the preferred initial imaging modality. Surveillance imaging should be performed at frequent intervals (3–4 mo) up front; intervals can be reduced over time if favorable growth kinetics are demonstrated. Delayed intervention (DI) should be considered for rapid tumor growth (eg, > 0.5 cm/yr), an increase in maximum tumor diameter >3–4 cm, malignant renal mass biopsy results, development of symptoms, or patient preferences. Oncologic outcomes in well-controlled studies demonstrate a metastatic rate of 1–2%. Most patients who undergo DI remain eligible for nephron-sparing approaches; oncologic outcomes are not compromised by DI strategies.
Conclusions: A period of initial AS is safe for most patients with SRMs. Management decisions should focus on a thorough assessment of risk-benefit trade-offs, judiciously integrating patient-related factors, tumor-related factors, and patient preferences.
Patient summary: A period of initial active surveillance for kidney masses of ≤4 cm in diameter is safe in most patients. Frequent imaging and follow-up are necessary to determine if the tumor grows. If delayed intervention becomes necessary, cancer outcomes are not compromised by the initial choice of active surveillance when patients adhere to close follow-up regimens.

* Corresponding author. Division of Urologic Oncology, Fox Chase Cancer Center, 333 Cottman Avenue, Philadelphia, PA 19111, USA. Tel. +1 215 7282548; Fax: +1 215 2141734.
E-mail address: benristaumd@gmail.com (B.T. Ristau).

1. Introduction

The incidence of renal cell carcinoma (RCC) in Europe and the USA was 136 509 in 2012 and accounted for 44 833 deaths [1,2]. Owing in part to increased use of cross-sectional imaging, the incidence over time has risen and a migration to lower-stage tumors has occurred [3,4]. In fact, detection of small renal masses (SRMs), defined as enhancing renal tumors of ≤4 cm in maximum diameter, has accounted for most of this rise in incidence [4].

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Paradoxically, increased detection has not led to a reduction in kidney cancer–specific mortality, a phenomenon termed treatment disconnect [5]. Treatment disconnect implies that detection and immediate treatment of SRMs may not be the most effective strategy to optimize survival outcomes.

The heterogeneity of SRM biology offers some insight to help better understand treatment disconnect. At the extremes, SRMs are benign in 15–20% and potentially aggressive in 10% of cases; however, while the majority of masses are malignant, many exhibit indolent biologic behavior [6–9]. Given the substantial proportion of benign masses in this patient population and the fact that metastatic progression is associated with larger tumor size [10], better matching of biological behavior to treatment intensity is desired.

For these reasons, a shift in the management paradigm for patients with SRMs has occurred with increasing enthusiasm for the role of an initial period of active surveillance (AS) in select patients. This manuscript evaluates the exiting evidence for AS and reviews modern management strategies. Clinical decision points such as appropriate patient selection, consideration of patient-reported quality of life (QOL) metrics, and a judicious balance between continued AS and delayed intervention as time from the initial SRM diagnosis passes are discussed.

2. Evidence acquisition

The present review was conducted using the PubMed database to search for English language articles pertaining to renal masses and surveillance from January 1980 to March 2017. The query search terms “surveillance” and “renal mass” or “renal cell carcinoma” or “kidney cancer” yielded 1398 abstracts. All the abstracts were reviewed in their entirety. Duplicates and irrelevant abstracts were removed. From the 1398 abstracts, 57 manuscripts were selected and read completely by two authors (B.R. and M.S.). Bibliographic review of the selected manuscripts and pertinent prior reviews provided an additional 12 articles for inclusion. The full text of each article was reviewed. The level of evidence, sample size, study design, and relevance to the review were considered as inclusion criteria. A total of 69 manuscripts were included.

3. Evidence synthesis

3.1. Deliverables and outcomes for AS

AS is an acceptable initial management strategy in the majority of patients with SRMs. First and foremost, AS allows patients who are uniformly asymptomatic to avoid the risks inherent to invasive intervention. This benefit is particularly relevant to older, frailer patients with significant comorbidities, since they generally have the greatest risk of non–kidney cancer–related mortality and are least likely to benefit from active treatment [11]. Second, AS allows patients to safely delay treatment until it is necessary and perhaps more convenient. In fact, the risk of metastasis with short-term follow up on rigorous AS programs is 1–2% [12,13], and an initial period of AS does not preclude future nephron-sparing surgical treatment in most cases [54]. Third, AS results in maximum preservation of renal function relative to intervention. Thus, there is a strong rationale for including AS in the armamentarium of management options for SRMs.

3.2. Selecting patients for initial AS

At present, no standardized criteria exist to guide patient selection for a period of initial AS. Variables that are commonly integrated into thoughtful clinical decision-making can be divided into patient-related factors and tumor-related factors.

3.2.1. Patient-related factors: age and comorbidity

The age at which patients with SRMs present is increasing [14], and incidental kidney masses are most often diagnosed after the seventh decade of life [15]. Since the correlation between older age and the risk of comorbid illness or other-cause mortality is a biological reality [16], it is imperative to consider age and comorbidity status when counseling patients with SRMs.

Observational study designs have been used to quantify the chance of death from non-cancer causes relative to kidney cancer death [11,17,18]. A Surveillance, Epidemiology, and End Results (SEER)–Medicare based analysis of 6655 patients aged ≥66 yr compared post-treatment kidney cancer–specific mortality to the risk of death from competing causes in patients undergoing surgery for pathologically node-negative RCC. Even after adjustment for comorbidities captured by the Charlson comorbidity index (CCI), other-cause mortality exceeded the risk of kidney cancer death at 3 yr (10.9% vs 4.7%), 5 yr (20.1% vs 7.5%), and 10 yr (44.0% vs 11.9%). Only patients with no comorbidities and a tumor >7 cm received a cancer-specific survival benefit from surgical intervention. Similarly, a SEER analysis including 26 618 patients with surgically treated RCC stratified by clinical tumor size demonstrated 5-yr cancer-specific survival of 94.7% [18]. By contrast, 5-yr overall survival for patients older than 70 yr was 71.8%. In fact, 5-yr survival depended more on competing risks than cancer-specific causes for patients aged >60 yr with SRMs. Although these findings are limited by the fact that risk estimation is based on post-treatment survival assessments, they underscore the long natural history of disease progression in patients whose renal tumors may have become micrometastatic before treatment.

A retrospective institutional analysis considered 537 patients aged ≥75 yr with clinical stage T1, node-negative renal masses [17]. Most underwent a surgical intervention (53% nephron-sparing surgery, 27% radical nephrectomy), while a minority (20%) were observed. Overall mortality was higher than cancer-specific mortality in all management groups (19.9% vs 4.0% for nephron-sparing surgery; 23.2% vs 9.3% for radical nephrectomy; 33.3% vs 5.8% for observation). This suggests that the additional risks