Active Surveillance for the Small Renal Mass

Growth Kinetics and Oncologic Outcomes

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KEYWORDS

• Active surveillance • Small renal mass • Kidney cancer • Growth kinetics • Outcomes

KEY POINTS

- A period of initial active surveillance to determine tumor growth kinetics in patients with small renal masses and significant competing risks is safe.
- Tumor growth rate is the primary driver for delayed intervention in patients managed initially with active surveillance.
- Competing risks to mortality should be considered when determining the appropriate initial management strategy for patients presenting with a newly diagnosed small renal mass.
- The risk of metastasis for carefully followed, adherent patients on active surveillance for SRMs is 1% to 2% at a median of 2 years follow-up.

INTRODUCTION

Renal cell carcinoma (RCC) is among the 10 most common cancers in women and men with an estimated 62,700 new cases and 14,240 deaths expected in 2016.[1] Due in part to increasing utilization of cross-sectional imaging, the incidence of small renal masses (SRMs; defined as maximum tumor diameter less than 4 cm) is increasing.[2] SRMs represent a range of histologic entities from benign to malignant; approximately 15% to 20% are benign and 20% to 25% are considered to be potentially biologically aggressive. Most, however, are of intermediate risk; that is, they are histologically malignant but are of uncertain clinical risk.[3–5] Given this uncertainty, active surveillance (AS) has been proposed as an initial management strategy in appropriately selected patients who either prefer a noninterventional strategy or for whom intervention is prohibitive because of competing risks.[6–8] In this review, we summarize the published literature examining the AS of SRMs with an emphasis on tumor growth kinetics, oncologic outcomes in patients managed expectantly, analysis of competing risks to mortality, and existing prospective AS strategies.

GROWTH KINETICS OF SMALL RENAL MASSES MANAGED EXPECTANTLY

The most easily measured and well-studied indicator of aggressive malignant potential in renal masses is tumor size. There is a direct relationship between maximal tumor diameter (MTD) and malignant features at surgery including presence of high-grade disease,[4,9] clear-cell histology,[5] and metastatic disease at presentation.[10] The natural history of untreated SRMs has been explored over the past decade[6] and can be categorized based on growth rates (positive growth, net zero growth, and masses that decrease in size over

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time). Although anecdotes of the disappearing renal mass exist,[11] these represent a very small proportion of the overall growth kinetics of observed renal masses. Instead, most renal tumors under observation either demonstrate zero net growth or increase slowly in size over time (Table 1).[6,12]

The proportion of tumors under observation that demonstrate zero net growth ranges from 5% to 73% in small series.[13,14] A large meta-analysis of 18 series including 880 patients and 936 SRMs demonstrated a total zero net growth rate of 23% (65 masses).[12] Importantly, no tumor demonstrating zero net growth in this meta-analysis metastasized with intermediate follow-up (mean 34 months). In the largest retrospective institutional series of 173 tumors managed with AS, Crispen and colleagues[15] reported a negative or no net growth rate of 26%. The Delayed Intervention and Surveillance for Small Renal Masses (DISSRM) registry is the lone cohort with prospectively established criteria for AS that has documented the proportion of patients with SRMs demonstrating zero net growth.[16] With a median follow-up of 8.3 months, 16 patients (10%) experienced zero net growth. Thus, although the proportion of patients who experience zero net growth varies by population studied and length of time under observation, it represents a clinically significant proportion of SRMs managed expectantly (approximately 10%–25%).

Positive tumor growth has been defined in several different ways. Most commonly, the change in MTD over time can be reported as a linear growth rate (LGR). This measure makes the

Table 1
Growth kinetics of small renal masses managed initially with a period of observation

Study	n	Mean Age (y)	Mean MTD at Diagnosis (cm)	Mean LGR (cm/y)	Proportion with Zero or Negative Net Growth (%)	Median Follow-up (mo)
Abou Youssif et al,[23] 2007	44	71.8	2.2	0.15	NR	47.6
Abouassaly et al,[28] 2008	110	81.0[a]	2.5[a]	0.26	43.0	24.0
Beisland et al,[24] 2009	65	76.6	4.3	0.66 (0.37 for SRMs)	5.0 (decreased size on AS)	33.0
Bosniak et al,[13] 1995	40	65.1	1.73	0.4	5.0	43.9
Crispen et al,[15] 2009	173	69.0	2.45	0.29	26.0	31.0
Dorin et al,[19] 2014	131	69.1	2.1	0.07	37.4	48.0
Fernando et al,[50] 2007	13	80.4	5.02	0.17	NR	38.4
Hwang et al,[51] 2010	58	64.3	2.1	0.21	NR	22.0
Kato et al,[52] 2004	18	55.1	1.98	0.42	0 (all had surgery)	27.0
Kouba et al,[26] 2007	46	67.0	2.92	0.7	26.0	35.8
Lamb et al,[53] 2004	36	76.1	7.2	0.39	55.0	27.7
Li et al,[54] 2012	32	52.2	2.14	0.8	0 (all had surgery)	46.0
Matsuzaki et al,[14] 2007	15	67.0	2.2	0.06	73.0	38.0
Organ et al,[21] 2014	207	72.5	2.15	0.12	NR	20.1
Pierorazio et al,[16] 2015	158	70.6[a]	1.9[a]	0.11[a]	10.0	8.3
Rosales et al,[55] 2010	223	71.0[a]	2.8[a]	0.34[a]	0	35.0
Schiavina et al,[29] 2015	72	76.0	2.1	0.5	2.7	61.0
Siu et al,[56] 2007	47	68.0	2.0	0.27	45.0	29.5
Sowery et al,[20] 2004	22	77.0[a]	4.08	0.86	NR	26.0
Volpe et al,[18] 2004	32	71.0[a]	2.48	0.1	12.0	35.3
Wehle et al,[57] 2004	29	70.5	1.83	0.12	52.0	32.0

Abbreviation: NR, not reported.
[a] Value represents a median.