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Alessandro Volpe, M.D.

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The role of active surveillance of small renal masses

Alessandro Volpe, M.D.

Division of Urology
Department of Translational Medicine
University of Eastern Piedmont
Maggiore della Carità Hospital, Novara, Italy

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Corrispondence to:

Alessandro Volpe, MD

Division of Urology, Department of Translational Medicine,

University of Eastern Piedmont

Maggiore della Carità Hospital

Corso Mazzini, 18

28100, Novara, Italy

Tel: +39- 0321- 373417/201

Fax: +39-0321-3733763

E-mail: alessandro.volpe@med.uniupo.it

ABSTRACT

Introduction. The use of modern abdominal imaging modalities have led in recent years to an increased incidental diagnosis of small renal masses (SRMs), especially in elderly patients. The natural history of SRMs has been historically poorly understood because most have been traditionally surgically removed soon after diagnosis. However, several studies of active surveillance (AS) of SRMs have been published in the last decade.

Methods. A review of English-language publications on AS of SRMs was performed from 1995 to 2015 using the Medline, Embase and Web of Science databases. Fifty-six articles were selected based on their scientific relevance and critically analysed.

Results. When followed conservatively with serial imaging, SRMs have variable growth rates with an average of 0.31 cm/year in the largest multicenter analysis. A significant number of SRMs have a slow growth and some have zero growth under surveillance. The risk of progression to metastatic disease during AS is rare (1-2%). Population-based analyses in older patient populations (> 75 years) fail to show a benefit in cancer-specific mortality for surgical treatment of SRMs.

Discussion. The standard of care for localized renal tumors is surgery. In elderly or unfit patients with decreased life expectancy, it is reasonable to propose an initial period of AS, with delayed intervention for those tumors which exhibit a fast growth during follow-up. At present AS is not recommended in younger and fit patients and for masses >4 cm at diagnosis outside clinical trials. Percutaneous needle biopsies of renal tumors have the potential to characterize histologically SRMs at diagnosis, thereby providing useful information for the selection of the best suited patients for AS.

Conclusions. Most SRMs are benign tumors or RCCs with a relatively indolent clinical behaviour. AS can be offered to patients with SRMs and decreased life expectancy. Prospective series of AS of histologically confirmed RCCs are needed to confirm the long term safety of this conservative approach.

1. INTRODUCTION

The incidence of renal cell carcinoma (RCC) has been steadily growing in the last decades, largely due to a wider use of modern and accurate abdominal imaging modalities.⁽¹⁾ The increase in incidence is mainly due to the increased diagnosis of localized renal tumors.⁽²⁾ In fact, most RCCs are today discovered incidentally as small renal masses (SRMs) in asymptomatic patients. The lesions discovered incidentally are on average smaller and of lower stage compared to those detected in symptomatic patients.⁽³⁾ In addition, a significant number of small, asymptomatic tumors appears to be benign. Frank et al. have reviewed the histology of 2,935 renal tumors operated at Mayo Clinic, observing a significant increase in the probability of benign histology with decreasing tumor size. Overall, 30% of tumors <4 cm were histologically benign and more than 87% of clear cell RCC tumors were low grade.⁽⁴⁾ Many authors have also shown that small, incidental tumors are characterized by a better survival.^(3, 5) The first evidence of an association between tumor size and prognosis was provided by Bell, who noticed an increased incidence of metastases in patients in whom a RCC > 3 cm was found at autopsy.⁽⁶⁾

2. METHODS

A literature review was performed from 1995 to 2015 on the Medline, Embase and Web of Science databases using the terms “active surveillance” (AS) combined with “renal cell carcinoma”, “small renal mass”, “renal tumors”. We limited our search to English language articles. In addition, cited references from the selected articles and from previous review articles on this topic were assessed to identify significant manuscripts that were not previously included. Based on level of evidence provided, sample size, study design and relevance of each study with regard to the topic of the review, 56 articles were selected and critically analysed.

3. RESULTS

3.1 NATURAL HISTORY OF SMALL RENAL TUMORS

SRMs are traditionally surgically removed soon after diagnosis. For this reason, their natural history has been better defined only in recent years. In 1995 Bosniak et al. retrospectively examined the imaging of 40 incidental renal masses <3.5 cm in size which had been followed without active treatment for an average of 3.2 years. Twenty-six tumors were eventually removed after an average of 3.8 years and 84.6% of them were histologically RCCs. Variable tumor growth behaviors were observed and

the overall mean linear growth rate was 0.36 cm/year (0-1.1 cm/year).

Nineteen tumors grew less than 0.35 cm/year and no patient developed metastatic disease.⁽⁷⁾ It is important to note that these patients were reviewed at the time of surgery so that there may have been a bias towards faster growth.

The first prospective study of observation of SRMs was conducted at the University Health Network in Toronto. The authors followed over time with serial abdominal imaging 32 incidentally diagnosed, <4 cm renal masses in patients who were elderly or unfit for surgery. Twenty- six tumors were solid and 7 were complex cysts (4 Bosniak III and 3 Bosniak IV). The patients were prospectively followed with serial abdominal imaging for a mean of 27.9 months (5.3-143) and each mass had at least 3 follow-up measurements. Tumor volume in addition to single and bidimensional diameters was calculated from each follow-up image or report. Nine masses in 8 patients were surgically removed after an average of 38 months of follow-up because of surgeon's concern or patient's anxiety that the tumor was enlarging. All tumors were clear cell RCCs except one, which was an oncocytoma. The overall average growth rate, considered the cube root of the volume, was 0.1 cm/year and was not associated with either initial size ($p=0.28$) or mass type ($p=0.41$). (Figure 1) Seven masses

(22%) reached 4 cm in diameter after 12-85 months of follow-up. Eight (25%) doubled their volumes within 12 months. Overall, eleven (34%) fulfilled one of these two criteria of rapid growth. No patient progressed to metastatic disease, while two patients died of unrelated causes.⁽⁸⁾

Several other series of AS of SRMs have been subsequently published, showing similar results.⁽⁷⁻²³⁾ (Table 1-2)

A meta-analysis published in 2006 included 234 renal masses followed with AS in 8 institutions in North America and Japan. The average tumor diameter was 2.6 cm and the mean follow-up 34 months. The average tumor growth rate was 0.28 cm/year. Histological confirmation was available in 46% of cases and 92% of these SRMs were found to be RCCs. This meta-analysis indicated that size at diagnosis does not correlate with tumor growth rate ($p = 0.46$).⁽²⁴⁾

Another pooled analysis of studies of AS has recently included 18 series with a total of 880 patients and 936 renal masses with an average diameter of 2.3 cm at diagnosis. With a mean follow-up of 33.5 months, the average growth rate was 0.31 cm / year. When histological characterization was obtained, 88% of renal masses were found to be RCCs. Sixty-five tumors (23%) showed no growth during the surveillance period.⁽¹⁷⁾

The evidence resulting from these studies clearly indicates that progression to metastatic disease is rare during AS (1-2% of cases).^(17, 24) Smaldone et al. observed that the probability of progression to metastatic disease is significantly higher for tumors with greater diameter at diagnosis (4.1 ± 2.1 cm vs. 2.3 ± 1.3 cm, $p < 0.001$) and with a faster growth rate during surveillance (0.8 ± 0.7 cm/yr vs. 0.3 ± 0.4 cm/yr, $p < 0.001$).⁽¹⁷⁾

Most available studies of AS are retrospective, have a relatively short follow-up and include a relatively small number of patients.

However, the results of two large, prospective and multi-institutional clinical trials have been recently published. These studies confirmed the safety and good oncological outcomes of AS of SRMs with short to intermediate-term follow-up.^(18, 23)

The first results of a prospective phase II study including 209 SRMs in 178 elderly or ill patients from 8 Canadian academic centres were reported by Jewett et al in 2011. At a mean follow-up of 22 months, the tumor growth rate was on average 0.13 cm/year, and 37% of SRMs showed no growth during follow-up. Percutaneous biopsy was proposed at diagnosis, and was eventually performed in 101 cases (48.3%). The growth rate of histologically confirmed malignant lesions was not statistically faster compared to the growth rate of histologically confirmed benign tumors.

Very importantly, progression to metastatic disease was observed in only 2 cases (1.1%).⁽¹⁸⁾ A further analysis on this cohort of patients revealed that patient age, symptoms at diagnosis, tumour pattern and maximum diameter were not predictors of the growth of SRMs.⁽²⁵⁾

Finally, Pierorazio et al. recently reported the results of a multicentre clinical trial based on the DISSRM registry (Delayed Intervention and Surveillance for Small Renal Masses). This study included 497 patients with SRMs, of which 223 (45%) were followed with AS and the remaining underwent active treatment. The study was prospective, but not randomized and the median follow-up was 2.1 years. In the AS group, a rapid growth rate led to the indication of a deferred surgical or ablative treatment in only 36 cases (16.1%). No patients developed metastases during AS (cancer-specific survival 100%), while the overall survival in this group of patients was respectively 96% and 75% at 2 and 5 years compared to 98% and 96% in the active intervention group.⁽²³⁾

Further analysis based on the DISSRM registry has recently shown that patients on active surveillance have a better preservation of renal function assessed by eGFR compared to patients who undergo radical nephrectomy, but not to those who underwent partial nephrectomy.⁽²⁶⁾

3.2 NATURAL HISTORY OF cT1b-cT2 RENAL TUMORS

The results of few series of AS for larger renal masses have also been reported. (Table 3-4) Lamb et al. assessed the natural history of 36 renal tumors with a median tumor size of 6.0 cm (range 3.5-20 cm) in elderly patients with severe comorbidities or high risk of postoperative dialysis. The mean patient age was 76.1 years, and the median follow-up was 24 months. Thirteen patients (36.1%) died of other causes after an average of 9 months from diagnosis of their renal tumor, and no cancer-specific death was observed. Only one patient developed metastatic disease after 132 months from diagnosis, and was still alive at 136 months. The mean tumor size was roughly unchanged in most patients during the follow-up period.⁽²⁷⁾ More recently, Mues et al. reported the outcomes of AS in 36 patients with 42 localized renal tumors larger than 4 cm. 52.8% of these patients had severe comorbidities with a CCI (Charlson comorbidity index) ≥ 3 , while only 25% of them were symptomatic at diagnosis. The mean patient age was 73.8 years, the mean tumor size was 7.13 cm and the median linear growth rate was 0.57 cm/year. Percutaneous renal biopsies were performed in 12 patients and pathology revealed 10 clear cell RCC, one chromophobe RCC and one undifferentiated tumor. Three patients with a fast tumor growth rate were treated with delayed laparoscopic radical

nephrectomy. Pathology showed clear cell RCC in all cases. Overall, only 2 patients (5.6%) progressed to metastases, and no cancer-related deaths were observed.⁽²⁸⁾

Another recent report from the United States assessed a cohort of 68 patients with 72 contrast enhancing cT1b-cT2 renal tumors. The patients were managed expectantly with AS for at least 6 months from diagnosis. The mean patients' age was 69 years, the median CCI was 3 and the mean tumor size at presentation was 4.9 cm. The mean linear growth rate was 0.44 cm/year. The mean R.E.N.A.L. nephrometry score was 8.7 ± 1.6 , suggesting anatomically intermediate to complex renal tumors. Renal tumor biopsies were performed in 21 patients (31%). At a mean follow-up of 39 months, 45 patients remained on surveillance, while 23 underwent delayed surgical intervention because of fast tumor growth, development of tumor-related symptoms, patient or physician choice. Patients who stayed on AS were older (77 vs. 60 years, $p=0.0002$) and had slower linear growth rate (0.37 cm/yr vs. 0.73 cm/yr, $p=0.02$) compared to those who underwent delayed intervention. Conversely, no significant differences in term of mean R.E.N.A.L. score or CCI were found among the two groups.⁽²⁹⁾

3.3 ROLE AND MODALITIES OF ACTIVE SURVEILLANCE OF SMALL RENAL TUMORS

Surgical removal is the treatment of choice for SRMs. Nephron-sparing surgery is currently the gold standard for these lesions, since it was shown to achieve similar oncological outcomes of radical nephrectomy with less impact on renal function.⁽³⁰⁻³³⁾ Overall, the outcomes of surgery for <4 cm (pT1a) RCCs are excellent. In an international multicenter study including 1,454 patients, Patard et al. observed a cancer specific survival at 5 years close to 97% after nephron-sparing surgery.⁽³⁴⁾

Surgical complications of nephrectomy have decreased with the improvement of surgical techniques, but are still significant especially in the elderly population.⁽³⁵⁾ This is clinically important since an increasing number of incidental renal tumors are diagnosed in elderly patients who undergo radiological examinations for other medical problems. These patients often have significant comorbidities and therefore a higher risk of postoperative morbidity and mortality.

Despite the increased incidence of low-grade neoplasms and the excellent results of surgical treatment of SRMs, mortality from RCC has not decreased in recent years.⁽³⁶⁾ This suggests a potential overtreatment of a proportion of small renal tumors with a long natural history and a limited

risk of progression. This concept is also supported by autopsy studies.

Hellsten et al. showed that 67-74% of RCCs used to remain unnoticed until death before the diffusion of modern imaging techniques. Moreover, only 9-20% of all diagnosed RCCs were in fact responsible for the patient's death.⁽³⁷⁾

Based on these observations and on the analysis of data that are gradually emerging about the natural history of SRMs, it is necessary to review the indications of immediate surgery for all small renal tumors. In fact, many incidentally discovered SRMs are not histologically malignant or have an indolent clinical behavior and therefore do not represent an immediate threat to the patient's life. This is especially true for elderly patients or patients with significant comorbidities.

In fact, non-RCC related mortality after surgical treatment for SRMs is significant and correlates with age and the presence of other medical conditions. A population-based analysis of 26,618 patients who were surgically treated for loco-regional kidney cancer between 1983 and 2002 showed that about 40% of patients who were >70 years old and had a kidney tumor <4 cm died from unrelated causes in the 5 years following the surgical removal of their tumor.⁽³⁸⁾ In a retrospective review of 192 patients with clear cell RCC, Arrontes et al, observed that a CCI >2 was significantly

associated with a worse overall survival after surgical treatment
($p < 0.001$).⁽³⁹⁾

Finally, an interesting study from the Cleveland Clinic reported the oncological outcomes of a series of 537 patients with < 4 cm renal tumors who were either surgically treated or followed with AS. Only age and comorbidities were found to be independent predictors of overall survival in this series, while surgical removal did not provide any significant survival advantage.⁽⁴⁰⁾ No statistically significant difference in overall and cancer-specific survival were observed in another study of radical nephrectomy vs. partial nephrectomy vs. AS for T1a renal masses with a follow-up of 34 months.⁽⁴¹⁾

Population-based studies also compared the oncological outcomes of surgical and non-surgical management for tumours < 4 cm. The analyses showed a significantly lower cancer-specific mortality for patients treated with surgery.^(42, 43) However, the patients assigned to the surveillance arm were older and likely to be more frail and less suitable candidates for surgery. Other cause mortality rates in the non-surgical group significantly exceeded that of the surgical group.⁽⁴²⁾ Population-based analyses in older patient populations (> 75 years) failed to show the same benefit in cancer-specific mortality for surgical treatment.⁽⁴⁴⁾

Therefore, a limited life expectancy and the presence of concomitant medical comorbidities may significantly reduce the survival advantage provided by surgical extirpation of renal tumors.⁽⁴⁵⁾ An estimate of the risk of competing cause mortality can be useful in order to decide the most appropriate treatment for patients with renal cancer. This can be easily obtained with the use of specific nomograms.^(46, 47)

In patients with SRMs who are elderly or have significant comorbidities, and life expectancy is likely less than the time the cancer will take to progress, AS can be therefore proposed as a reasonable option.^(30, 33, 48)

Minimally invasive ablative techniques such as radiofrequency and cryoablation can be also offered to this population of patients according to the current major urological guidelines.⁽³⁰⁾ However, an interesting cost-utility analysis of the available treatment modalities for SRMs have shown that AS with delayed percutaneous cryoablation, if needed, may be a safe and cost-effective alternative to immediate ablation.⁽⁴⁹⁾

AS may also be an option for younger and fit patients in order to potentially reduce overtreatment and/or delay active treatment, but the evidence to support expectant management in this population is currently lacking.

The concept of AS implies an initial period of observation of the growth rate and clinical behaviour of a SRM with serial abdominal imaging, with a

delayed active treatment reserved only for those tumors which show a fast growth or clinical progression during follow-up.⁽⁵⁰⁾ In fact, it was observed that tumors that will eventually metastasize during surveillance have a significantly greater growth rate compared to those who will not.^(17, 51) A recent study also showed that a faster linear and volume growth rate and a shorter volume doubling time significantly correlates with a higher grade histology for clear cell RCCs under AS.⁽⁵²⁾

No standardized criteria to indicate delayed intervention during AS have been yet defined. However, reaching a diameter of 3-4 cm or a tumor volume doubling time <12 months under surveillance are generally used to identify renal masses at greatest risk of progression which should be conveyed to an active treatment.⁽⁴⁸⁾ Further studies are needed to define precise and evidence-based criteria to indicate delayed intervention.

Different criteria may be recommended for renal masses with different tumor size at diagnosis.

With a careful use of surgical treatment for tumors with fast growth, the risk of progression to metastatic disease during surveillance appears very limited. Crispen et al. analyzed the outcomes of 87 patients treated with delayed intervention after AS for a median period of 14 months (>24 months in 33% of cases) at the Fox Chase Cancer Center in Philadelphia.

In this series, delayed treatment was not shown to limit or complicate the possible treatment options, including nephron sparing surgery or minimally invasive surgical approaches. Tumor progression to pT3a disease was observed only in one case, while no case of metastatic progression was observed during follow-up.⁽⁵³⁾

The optimal follow-up schedule for patients on AS has yet to be defined. Based on the experience of the largest reported series, it is generally recommended to perform a triphasic abdominal scan every 3 months in the first year, then every 6 months up to 3 years, and every year thereafter in case of little or no growth of the SRM.⁽⁵⁰⁾ CT scan can be sometimes alternated to ultrasound - possibly with contrast enhancement – when there is dimensional stability and good visibility of the renal mass at ultrasound assessment. This approach can decrease radiation exposure for the patient and treatment costs. Chest imaging should be also performed every 6 months in the first 3 years and annually thereafter to exclude metastatic progression to the lungs.

When the patient's clinical conditions contraindicate a delayed treatment, the follow-up schedule should be less intensive and imaging should be mainly performed in the presence of signs of symptoms indicating clinical progression.

Overall, AS requires an adequate and thorough patient counselling, a precise follow-up schedule and a good compliance of the patient to undergo the examinations required by the protocols.

All published series of AS include a large proportion of patients with unknown tumor histology. This represents a bias in the interpretation of the oncological outcomes. Results from multicenter studies with long follow-up and histological confirmation of the disease with a percutaneous biopsy at diagnosis is needed to confirm the safety of AS in the management of patients with histologically confirmed RCC. Renal tumor biopsy is useful to select patients who are eligible for a conservative treatment. In fact, AS is a reasonable option for tumors with low-grade histology and therefore limited risk of progression, while surgery should be always advocated – whenever possible – for tumors with aggressive histology. Furthermore, information from RTBs can be of help to plan the intensity of follow-up in patients in AS. In fact, benign tumors at biopsy can be followed with a less stringent follow-up schedule, thereby reducing the risks of radiation exposure and the costs for the healthcare system.⁽⁵⁴⁾

In the absence of a curative treatment for metastatic disease, AS should not be recommended for young patients with low surgical risk outside clinical studies. AS for larger, T1b tumors should also be considered only

for highly selected and well informed patients, since the promising outcomes reported to date must be carefully interpreted, mainly because of the relatively short follow-up.

4. CONCLUSIONS

The majority of SRMs are benign tumors or low-grade RCCs with a relatively indolent clinical behaviour. Most SRMs have a slow growth rate and some have zero growth during observation. A judicious AS protocol implying serial follow-up imaging of a SRM and delayed intervention for those masses that show a rapid growth or cause symptoms appears to be safe with a limited risk of progression to metastatic disease at short-mid term follow-up. Based on the current evidence, AS can be offered to elderly or unfit patients with SRMs and decreased life expectancy. Percutaneous biopsy to characterize tumor histology at diagnosis can support the selection of the best suited candidates for AS and can help to tailor follow-up intensity for each individual patient.

Prospective series of AS of histologically confirmed RCCs with longer follow-up are expected to confirm the long-term safety of this conservative approach.

ACCEPTED MANUSCRIPT

FIGURE LEGENDS

Figure 1. Growth pattern of 32 small renal masses in active surveillance (grey dotted lines). The black line represents the average growth rate. (from Volpe et al.⁽⁸⁾)

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Table 1. Mean growth rate and progression to metastatic disease in the largest series of active surveillance of SRMs.

	Cases	Study design	Mean tumor size (cm)	Mean follow-up (mos)	Mean growth rate (cm/year)	Progression to metastasis (%)
Bosniak <i>et al.</i> <i>Semin Urol Oncol</i> 1995 ⁽⁷⁾	40	Retrospect. Mono	1.73	39	0.36 (0-1.1)	NA
Volpe <i>et al.</i> <i>Cancer</i> 2004 ⁽⁸⁾	32	Prospect. Mono	2.48	27.9	0.1 (NA)	0
Kassouf <i>et al.</i> <i>J Urol</i> 2004 ⁽⁹⁾	24	Retrospect. Mono	3.27	31.6	0.09 (0-1.2)	0
Kato <i>et al.</i> <i>J Urol</i> 2004 ⁽¹⁰⁾	18	Retrospect. Mono	1.98	22.5	0.42 (0.08-1.6)	NA
Wehle <i>et al.</i> <i>Urology</i> 2004 ⁽¹¹⁾	29	Retrospect. Mono	1.83	32	0.12 (NA)	0
Kouba <i>et al.</i> <i>J Urol</i> 2007 ⁽¹²⁾	46	Retrospect. Mono	2.92	35.8	0.39 (0-3.51)	0
Abouassaly <i>et al.</i> <i>J Urol</i> 2008 ⁽¹³⁾	110	Retrospect. Mono	2.5	24	0.26 (0-3.26)	0
Crispen <i>et al.</i> <i>Cancer</i> 2009 ⁽¹⁴⁾	173	Retrospect. Mono	2.5	31	0.28 (-1.4-2.47)	2 (1.3%)
Rosales <i>et al.</i> <i>J Urol</i> 2010 ⁽¹⁵⁾	223	Retrospect. Mono	2.8	35	0.34 (0.29-2.3)	1 (0.5%)

Haramis et al. Urology 2011 ⁽¹⁶⁾	44	Retrospect. Mono	2.67	77.1	0.15 (0-1.73)	0
Smaldone et al. Cancer 2012 ⁽¹⁷⁾	880	Pooled analysis	2.3	33.5	0.31 (-1.4 – 2.5)	18 (2%)
Jewett et al. Eur Urol 2011 ⁽¹⁸⁾	178	Prosp Multi	2.1	28	0.13 (NA)	2 (1.1%)
Mason et al. Eur Urol 2011 ⁽¹⁹⁾	82	Prosp Multi	2.3	36	0.25 (-1.1 – 2.86)	1 (1.2%)
Schiavina et al. Clin Genitourin Cancer 2015 ⁽²⁰⁾	70	Retrospect Mono	2.1	92.7	0.5 (NA)	2 (2.8%)
Bahouth et al. Adv Urol 2015 ⁽²¹⁾	70	Retrospect Mono	1.87	34	0.17 (-0.29 – 0.88)	0
Dorin et al. Int Braz J Urol 2014 ⁽²²⁾	114	Retrospect Mono	2.1	50.4	0.07 (NA)	1 (0.9%)
Pierorazio et al. Eur Urol 2015 ⁽²³⁾	223	Prosp Multi	1.9	24	0.11 (-1.1-0.41)	0

Legend: Retrospect.= Retrospective study, Prosp.= Prospective study, Multi= Multi-institutional study. Mono= Single institutional study, NA=Not available

Table 2. Pathology of SRMs in the largest series of active surveillance.

	Cases	Available pathology (%)	RCC at pathology (%)
Bosniak <i>et al.</i> <i>Semin Urol Oncol</i> 1995 ⁽⁵⁵⁾	40	26 (65%)	22 (85%)
Volpe <i>et al.</i> <i>Cancer</i> 2004 ⁽⁸⁾	32	9 (28%)	8 (89%)
Kassouf <i>et al.</i> <i>J Urol</i> 2004 ⁽⁹⁾	24	4 (15%)	4 (100%)
Kato <i>et al.</i> <i>J Urol</i> 2004 ⁽¹⁰⁾	18	18 (100%)	18 (100%)
Wehle <i>et al.</i> <i>Urology</i> 2004 ⁽¹¹⁾	29	4 (14%)	3 (75%)
Kouba <i>et al.</i> <i>J Urol</i> 2007 ⁽¹²⁾	46	14 (30.4%)	12 (87%)
Abou Youssif <i>et al.</i> <i>Cancer</i> 2007 ⁽⁵⁶⁾	44	8 (23%)	6 (75%)
Abouassaly <i>et al.</i> <i>J Urol</i> 2008 ⁽¹³⁾	110	9 (8%)	3 (33%)
Crispen <i>et al.</i> <i>Cancer</i> 2010 ⁽¹⁴⁾	173	68 (39%)	57 (84%)
Rosales <i>et al.</i> <i>J Urol</i> 2010 ⁽¹⁵⁾	223	40 (18%)	37 (92.5%)
Haramis <i>et al.</i> <i>Urology</i> 2011 ⁽¹⁶⁾	44	17 (38.6%)	17 (100%)

Jewett et al. Eur Urol 2011 ⁽¹⁸⁾	178	101 (48.3%)	56 (55%)
Mason et al. Eur Urol 2011 ⁽¹⁹⁾	82	14 (17.1%)	14 (100%)
Schiavina et al. Clin Genitourin Cancer 2015 ⁽²⁰⁾	70	44 (62.9%)	35 (79.5%)
Bahouth et al. Adv Urol 2015 ⁽²¹⁾	80	10 (12.5%)	7 (70%)
Dorin et al. Int Braz J Urol 2014 ⁽²²⁾	114	13 (11.4%)	12 (92.3%)
Pierorazio et al. Eur Urol 2015 ⁽²³⁾	223	32 (14.3%)	13 (41%)

Legend: NA= Not available

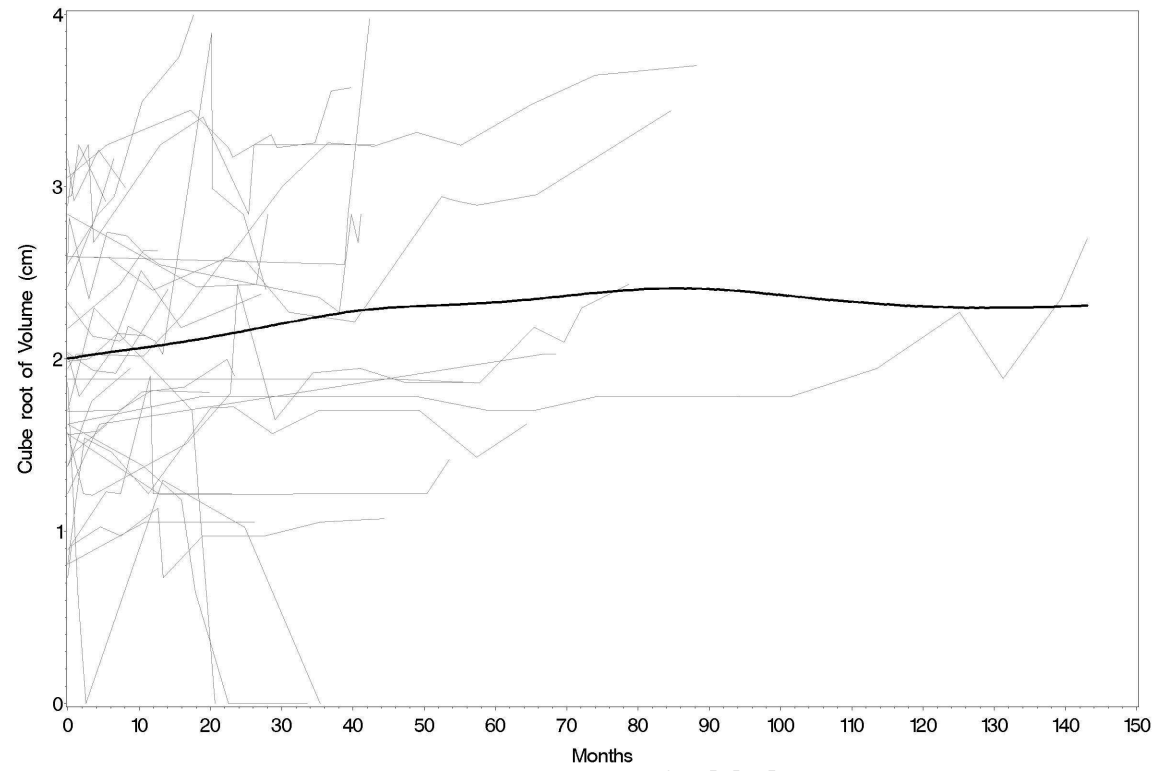
Table 3. Mean growth rate and progression to metastatic disease in the largest series of active surveillance of cT1b-T2 renal tumors.

	Cases	Study design	Mean tumor size (cm)	Mean follow-up (mos)	Mean growth rate (cm/year)	Progression to metastasis (%)
Lamb <i>et al.</i> <i>Urology</i> 2004 ⁽²⁷⁾	36	Retrospect. Mono	6.0	24	0.39 (0-1.76)	2.8
Mues <i>et al.</i> <i>Urology</i> 2010 ⁽²⁸⁾	36 (42 masses)	Retrospect. Mono	7.13	36	0.57 (0-5.9)	4.7
Mehrazin <i>et al.</i> <i>Urol Oncol</i> 2015 ⁽²⁹⁾	68 (72 masses)	Retrospect. Mono	4.9	32	0.44 (0-1.48)	0

Legend: Retrospect.= Retrospective study, Mono= Single institutional study

Table 4. Pathology in the largest series of active surveillance of cT1b-T2 renal tumors.

	Cases	Available pathology (%)	RCC at pathology (%)
Lamb <i>et al.</i> <i>Urology</i> 2004 ⁽²⁷⁾	36	24 (66.7%)	23 (96%)
Mues <i>et al.</i> <i>Urology</i> 2010 ⁽²⁸⁾	36 (42 masses)	3 (7.2%)	3 (100%)
Mehrazin <i>et al.</i> <i>Urol Oncol</i> 2015 ⁽²⁹⁾	68 (72 masses)	44 (64.7%)	31 (70%)



HIGHLIGHTS

- The incidental diagnosis of SRMs has been increasing significantly.
- Most SRMs have a slow growth rate when followed conservatively with serial imaging.
- The risk of progression to metastatic disease during active surveillance is rare (1-2%).
- Active surveillance can be offered to elderly or unfit patients with SRMs, with delayed active intervention for those tumors with fast growth during follow-up.
- Histological characterization of SRMs by percutaneous biopsy is useful for the selection of patients for active surveillance.