The Role of Active Surveillance for Small Renal Masses

5

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Abbreviations

CCI	Charlson comorbidity index
CT	Computed tomography
FNA	Fine needle aspiration
RCC	Renal cell carcinoma
SRM	Small renal mass

Key Messages

- Increases in the incidence of renal cell carcinoma have been mainly due to increased diagnosis of small renal masses (SRMs).
- Recent data show that the risk of progression to metastatic disease and cancer-related mortality in SRM is low.
- For patients with significant comorbidities or limited life expectancy, active surveillance can be proposed as a reasonable treatment option.
- Active surveillance uses serial abdominal imaging to monitor the growth rate and clinical behaviour of a SRM with delayed active treatment reserved only for those tumours which show a fast growth or clinical progression.
- Active surveillance requires an adequate and thorough patient counselling, a precise organization of follow-up and a good patient compliance.
- In experienced centres, percutaneous renal tumour biopsies of SRM have been shown to be safe with a good detection rate and can provide important information for treatment decisions.

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5.1 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. The increase in incidence is mainly due to the increased diagnosis of localized renal tumours [1]. 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 a lower stage compared to those detected in symptomatic patients [2]. In addition, a significant number of small, asymptomatic tumours appear to be benign. Frank et al. have reviewed the histology of 2935 renal tumours operated at Mayo Clinic, observing a significant increase in the probability of benign histology with decreasing tumour size. Overall, 30% of tumours <4 cm were histologically benign, and more than 87% of clear cell RCC tumours were low grade [3]. Many authors have also shown that small, incidental tumours are characterized by a better survival [2, 4]. The first evidence of an association between tumour 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 [5].

5.2 Natural History of Small Renal Tumours

SRMs are generally surgically removed soon after diagnosis. For this reason, their natural history has only recently been better defined. In 1995 Bosniak et al. retrospectively examined the imaging of 40 incidental renal masses (<3.5 cm) which had been followed without active treatment for an average of 3.2 years. Twenty-six tumours were eventually removed after an average of 3.8 years, and 84.6% of them were histologically RCCs. Variable tumour growth behaviours were observed, and the overall mean linear growth rate was 0.36 cm/year (0–1.1 cm/year). Nineteen tumours grew less than 0.35 cm/year, and no patient developed metastatic disease [6]. 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-five tumours were solid and seven complex cystic (four Bosniak III and three Bosniak IV). The patients were prospectively followed with serial abdominal imaging for a mean of 27.9 months (range 5.3–143 months), and each mass had at least three follow-up measurements. Tumour volume in addition to single and bi-dimensional diameters was calculated from each follow-up image or report. Nine masses in eight patients were surgically removed after an average of 38 months of follow-up because of the surgeon's concern or the patient's anxiety that the tumour was enlarging. All tumours were clear cell RCCs except one, which was an oncocytoma. Overall average growth rate was 0.1 cm/year and was not associated with either initial size ($p = 0.28$) or mass type ($p = 0.41$) (Fig. 5.1). Seven masses (22%) reached 4 cm in diameter after 12–85 months of follow-up. Eight (25%) doubled their volumes within 12 months. Overall, 11 (34%) fulfilled one of these two criteria of rapid growth. No patient progressed to metastatic disease, while two patients died of unrelated causes [7]. Several other series of active surveillance of SRMs have been subsequently published, showing similar results (Tables 5.1 and 5.2).

A meta-analysis published in 2006 included 234 renal masses followed with active surveillance in eight institutions in North America and Japan. The average tumour diameter was 2.6 cm and the mean follow-up 34 months. The average tumour 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 tumour growth rate ($p = 0.46$) [9].

Another pooled analysis of studies of active surveillance 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

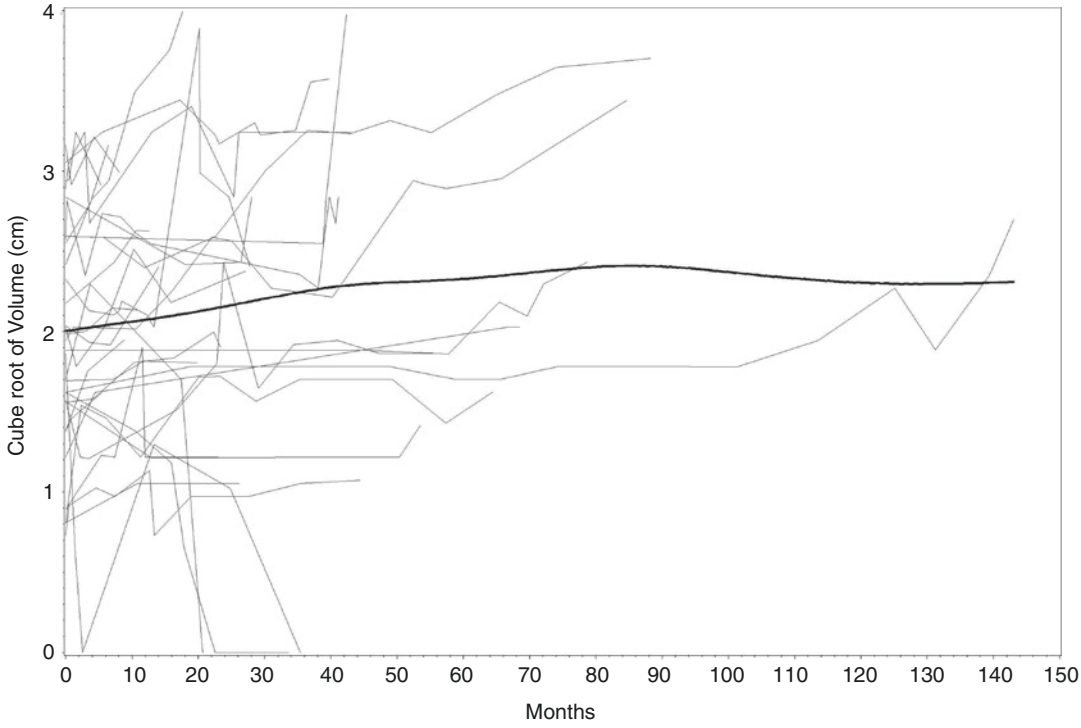

Fig. 5.1 Growth pattern of 32 small renal masses in active surveillance (*grey dotted lines*). The *black line* represents the average growth rate (from Volpe et al. [7])

characterization was obtained, 88% of renal masses were found to be RCCs. Sixty-five tumours (23%) showed no growth during the surveillance period [10].

The evidence resulting from these studies clearly indicates that progression to metastatic disease is rare during active surveillance (1–2% of cases) [9, 10]. Smaldone et al. observed that the probability of progression to metastatic disease is significantly higher for tumours 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/year vs. 0.3 ± 0.4 cm/year, $p < 0.001$) [10].

Most available studies of active surveillance 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 active surveillance of SRMs with short- to intermediate-term follow-up [13, 14].

The first results of a prospective phase II study including 209 SRMs in 178 elderly or infirm patients from eight Canadian academic centres were reported by Jewett et al. in 2011. At a mean follow-up of 22 months, the tumour 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 tumours. Very importantly, progression to metastatic disease was observed in only two cases (1.1%) [13]. 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 [15].

Finally, Pierorazio et al. recently reported the results of a multicentre clinical trial based on the DISSRM (Delayed Intervention and Surveillance for Small Renal Masses) registry. This study

Table 5.1 Mean growth rate and progression to metastatic disease in the largest series of active surveillance of SRMs

	Cases	Study design	Mean tumour size (cm)	Mean follow-up (mos)	Mean growth rate (cm/year)	Progression to metastasis (%)
Bosniak et al., Semin Urol Oncol (1995)	40	Retrosp. Mono	1.73	39	0.36 (0–1.1)	NA
Volpe et al., Cancer (2004)	32	Prosp. Mono	2.48	27.9	0.1 (NA)	0
Kassouf et al., J Urol (2004)	24	Retrosp. Mono	3.27	31.6	0.09 (0–1.2)	0
Kato et al., J Urol (2004)	18	Retrosp. Mono	1.98	22.5	0.42 (0.08–1.6)	NA
Wehle et al., Urology (2004)	29	Retrosp. Mono	1.83	32	0.12 (NA)	0
Kouba et al., J Urol (2007)	46	Retrosp. Mono	2.92	35.8	0.39 (0–3.51)	0
Abouassaly et al., J Urol (2008)	110	Retrosp. Mono	2.5	24	0.26 (0–3.26)	0
Crispen et al., Cancer (2010)	173	Retrosp. Mono	2.5	31	0.28 (−1.4–2.47)	2 (1.3)
Rosales et al., J Urol (2010)	223	Retrosp. Mono	2.8	35	0.34 (0.29–2.3)	1 (0.5)
Haramis et al., Urology (2011)	44	Retrosp. Mono	2.67	77.1	0.15 (0–1.73)	0
Smaldone et al., Cancer (2012)	880	Pooled analysis	2.3	33.5	0.31 (−1.4–2.5)	18 (2)
Jewett et al., Eur Urol (2011)	178	Prosp. Multi	2.1	28	0.13 (NA)	2 (1.1)
Pierorazio et al., Eur Urol (2015)	223	Prosp. Multi	1.9	24	0.11 (−1.1–0.41)	0

Retrosp. retrospective study, *Prosp.* prospective study, *Multi* multi-institutional study, *Mono* single institutional study, *NA* not available

included 497 patients with SRMs, of which 223 (45%) were followed with active surveillance and the remaining underwent active treatment. The study was prospective, but not randomized, and the median follow-up was 2.1 years. In the active surveillance group, a rapid growth rate led to the indication of a deferred surgical or ablative treatment in only 36 cases (16.1%). No patient developed metastases during active surveillance (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 [14]. Further analysis based on the DISSRM registry has recently shown that patients on active surveillance present better preservation of renal function assessed by eGFR compared to patients who underwent radical nephrectomy, but not to those who underwent partial nephrectomy [16].

5.3 Natural History of cT1b-cT2 Renal Tumours

The results of few series of active surveillance for larger renal masses have also been reported. Lamb et al. assessed the natural history of 36 renal tumours with a median tumour 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

Table 5.2 Pathology of SRMs in the largest series of active surveillance

	Cases	Available pathology (%)	RCC at pathology (%)
Bosniak et al., Semin Urol Oncol (1995)	40	26 (65)	22 (85)
Volpe et al., Cancer (2004)	32	9 (28)	8 (89)
Kassouf et al., J Urol (2004)	24	4 (15)	4 (100)
Kato et al. J Urol (2004)	18	18 (100)	18 (100)
Wehle et al., Urology (2004)	29	4 (14)	3 (75)
Kouba et al., J Urol (2007)	46	14 (30.4)	12 (87)
Abou Youssif et al., Cancer (2007)	44	8 (23)	6 (75)
Abouassal yet al., J Urol (2008)	110	9 (8)	3 (33)
Crispen et al., Cancer (2010)	173	68 (39)	57 (84)
Rosales et al., J Urol (2010)	223	40 (18)	37 (92.5)
Haramis et al., Urology (2011)	44	17 (38.6)	17 (100)
Jewett et al., Eur Urol (2011)	178	101 (48.3)	56 (55)
Pierorazio et al., Eur Urol (2015)	223	32 (14.3)	13 (41)

NA not available

their renal tumour, and no cancer-specific death was observed. Only one patient developed metastatic disease 132 months after diagnosis and was still alive at 136 months. The mean tumour size was roughly unchanged in most patients during the follow-up period [17]. More recently, Mues et al. reported the outcomes of active surveillance in 36 patients with 42 localized renal tumours larger than 4 cm. About 52.8% of these patients had severe comorbidities with a Charlson comorbidity index (CCI) ≥ 3, while only 25% of them were symptomatic at diagnosis. The mean patient age was 73.8 years, the mean tumour 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, 1 chromophobe RCC and 1 undifferentiated tumour. Three patients with a fast tumour growth rate were treated with delayed laparoscopic radical nephrectomy. Pathology showed clear cell RCC in all cases. Overall, only two patients (5.6%) progressed to metastases, and no cancer-related deaths were observed [18].

Another recent report from the United States assessed a cohort of 68 patients with 72 contrast-enhancing cT1b-cT2 renal tumours. The patients were managed expectantly with active surveillance for at least 6 months from diagnosis. The mean patients' age was 69 years, the median CCI was 3 and the mean tumour size at presentation was 5.3 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 tumours. Renal tumour 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 tumour growth, development of tumour-related symptoms, patient or physician choice. Patients who stayed on active surveillance were older (77 vs. 60 years, $p = 0.0002$) and had slower linear growth rate (0.37 cm/year vs. 0.73 cm/year, $p = 0.02$) 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 [19].

5.4 Role and Modalities of Active Surveillance of Small Renal Tumours

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 [20–22]. Overall, the outcomes of surgery for <4 cm (pT1a) RCCs are excellent. In an international multicentre study including 1454

patients, Patard et al. observed a cancer-specific survival at 5 years close to 97% after nephron-sparing surgery [23].

Surgical complications of nephrectomy have decreased with the improvement of surgical techniques but are still significant especially in the elderly population [24]. This is clinically important since an increasing number of incidental renal tumours 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 [25]. This suggests a potential overtreatment of a proportion of small renal tumours 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 [26].

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 tumours. In fact, many incidentally discovered SRMs are not histologically malignant or have an indolent clinical behaviour 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 are >70 years old and have a kidney tumour <4 cm died from unrelated causes in the 5 years following the surgical removal of their tumour [27]. 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 ($p < 0.001$) [28].

Finally, an interesting study from the Cleveland Clinic reported the oncological outcomes of a series of 537 patients with <4 cm renal tumours who were either surgically treated or followed with active surveillance. 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 [29]. No statistically significant differences in overall and cancer-specific survival were observed in another study of radical nephrectomy vs. partial nephrectomy vs. active surveillance for T1a renal masses with a follow-up of 34 months [30].

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 [31, 32]. 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 [31]. Population-based analyses in older patient populations (>75 years) failed to show the same benefit in cancer-specific mortality for surgical treatment [33].

Therefore, a limited life expectancy and the presence of concomitant medical comorbidities may significantly reduce the survival advantage provided by surgical extirpation of renal tumours [34]. 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 [35, 36]. In patients with SRMs who are elderly or have significant comorbidities, and life expectancy is less than the time the cancer will take to progress, active surveillance can be proposed as a reasonable option [37].

The concept of active surveillance implies an initial period of observation of the growth rate and clinical behaviour of a SRM with serial abdominal imaging, with a delayed active treat-

ment reserved only for those tumours which show a fast growth or clinical progression [8]. It has been observed that tumours that will eventually metastasize have a significantly greater growth rate during surveillance compared to those that will not [10, 38]. No standardized criteria for delayed intervention during active surveillance have been yet defined. However, a diameter of 3–4 cm or a tumour volume doubling time <12 months under surveillance is generally used to identify renal masses at greatest risk of progression which should prompt active treatment. Further studies are needed to define precise and evidence-based criteria to indicate delayed intervention. With a careful use of surgical treatment for tumours with fast growth, the risk of progression to metastatic disease during surveillance appears very limited. Crispen et al. analysed the outcomes of 87 patients treated with delayed intervention after active surveillance for a median period of 14 months (>24 months in 33% of cases) at the Fox Chase Cancer Centre, Philadelphia, USA. In this series, delayed treatment was not shown to preclude or complicate active treatment, including nephron-sparing surgery or minimally invasive surgical approaches. Tumour progression to pT3a disease was observed only in one case, and there were no cases of metastatic progression [39].

The optimal follow-up schedule for patients on active surveillance has yet to be defined. It is generally recommended to perform a triple phase abdominal scan every 3 months in the first year, then every 6 months up to 3 years, and every year thereafter in cases of little or no growth of the SRM [8]. Computed tomography (CT) scans may sometimes be replaced by ultrasound—possibly with contrast enhancement—when there is dimensional stability and good visibility of the renal mass on ultrasound. 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, active surveillance requires an adequate and thorough patient counselling, a precise organization of follow-up and a good patient compliance.

All published series of active surveillance include a large proportion of patients with unknown tumour histology. This represents a bias in the interpretation of the oncological outcomes. Results from multicentre studies with long follow-up and histological confirmation of the disease with a percutaneous biopsy at diagnosis are needed to confirm the safety of active surveillance in the management of patients with histologically confirmed RCC. In the absence of a curative treatment for metastatic disease, this conservative approach should not be recommended for young patients with low surgical risk outside clinical studies. Active surveillance for larger T1b tumours 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. Finally, information on histology and biological aggressiveness obtained with renal tumour biopsy (RTB) can have a very important role in treatment decision-making for SRMs and in particular for the selection of patients to include in active surveillance protocols.

5.5 The Role of Percutaneous Biopsy in the Management of Small Renal Masses

Percutaneous biopsy of renal neoplasms has historically been used for only limited indications, including the differential diagnosis of lymphoma, the diagnosis of renal metastatic disease in the presence of a known extrarenal malignancy and the histological characterization of surgically unresectable retroperitoneal tumours or of primary renal tumours in the setting of diffuse metastatic disease.

Beyond these clinical scenarios, biopsies of renal tumours have been rarely used given

uncertainty over their safety (perceived risk of tumour seeding along the needle tract and haemorrhagic complications), diagnostic rate and accuracy and their effectiveness in terms of impact on clinical decisions, due to the perception that all solid renal masses have a malignant potential and should be removed surgically. Many of these uncertainties have now been overcome due to the growing experience of urologists and interventional radiologists in performing biopsies, the growing experience of pathologists in interpreting specimens and the growing confidence of urologists to use information from biopsies to support clinical decisions.

From a practical standpoint, RTBs are generally performed on an outpatient basis under local anaesthesia and are generally well tolerated. Biopsies can be performed under ultrasound, CT or MRI guidance according to physician's preference, tumour location and size and patient's habitus. When possible, an ultrasound guidance is preferred, since it allows a puncture in real time, does not expose the patient to any radiation exposure and has low costs. However, CT guidance should be preferred in obese patients and for masses with poor ultrasound visibility and is more frequently used for renal masses located in the upper pole, at the anterior margin of the kidney or with a size <15 mm.

RTBs are generally performed with 18G Trucut needles. The use of full-core needles appears to provide better results both in terms of diagnostic yield and diagnostic accuracy. Smaller needles (≤21 G) are used for fine needle aspiration (FNA). However, a recent systematic review and meta-analysis have shown the superiority of core biopsies over FNA for the histological characterization of renal tumours [40]. The "coaxial" technique is mandatory to reduce the risk of dissemination along the needle tract. A guiding cannula is placed just inside the tumour. The stylet is then removed, and the biopsies are taken with an automatic biopsy gun through the guiding cannula. Multiple samples can be obtained through the cannula that is left in place and finely repositioned within the lesion to allow sampling of different areas without being extracted.

At least two good quality samples should be obtained in different regions of the tumour, avoiding areas of necrosis. Wunderlich et al. observed a lower diagnostic accuracy for central biopsies in tumours >4 cm, likely because of the more frequent presence of necrosis in the central portion of large renal tumours [41]. Based on these results, it is recommended to obtain a central and a peripheral biopsy in tumours <4 cm and two peripheral samples in tumours >4 cm.

Complications of RTBs are uncommon with the use of modern biopsy techniques and mainly comprise immediate or delayed bleeding, since kidney tumours are generally hypervascular. However, bleedings that require hospitalization and/or blood transfusion are rare in experienced centres (<1%) [42]. The risk of tumour seeding along the needle tract is anecdotal, with very few cases reported with the use of modern biopsy techniques [43].

In recent series from centres with experience, needle biopsy of solid renal tumours has a good detection rate (78–97%) and high specificity (98–100%) and sensitivity (86–100%) for the diagnosis of malignancy [42] (Table 5.3). A recent meta-analysis of 33 studies on RTBs with lower risk of bias has shown an overall diagnostic rate of 92% and a sensitivity and specificity of core biopsies for the diagnosis of malignancy of 99.1% and 99.7%, respectively [44]. The diagnostic accuracy of RTBs for the diagnosis of tumour histotype is also high (90.3% overall and 96% for SRMs in the reported systematic review and meta-analysis) [46]. Conversely, the accuracy for the assessment of Fuhrman grade (I–IV) is only fair (43–75%) but can be increased using a simplified grading system (high grade vs. low grade) [42, 46].

RTBs have lower diagnostic rates for cystic renal masses and should not be generally recommended for these lesions, except for Bosniak IV masses [45]. The combination of core biopsy and FNA can obtain complementary results in these patients [47].

The increased incidence of SRMs and the availability of alternative treatment options for these lesions in selected patients increased the awareness that pretreatment characterization of

Table 5.3 Diagnostic performance of renal tumour biopsies of renal tumours in the largest available series

	No.	Mean tumour size (cm)	Guidance	Needle size (G)	% diagnostic biopsies	Accuracy for malignancy	Accuracy for histotype (%)	Accuracy for grading (%)
Neuzillet et al., J Urol (2004)	88	2.8	CT	18	91	92%	92	69.8
Shannon et al., J Urol (2008)	235	2.9	CT/US	18	78	100%	98	NA
Schmidbauer et al., Eur Urol (2008)	78	4.0	CT	18	97	Sensitivity 93.5% Specificity 100%	91	76
Lebret et al., J Urol (2007)	119	3.3	CT/US	18	79	86%	86	46/74
Maturen et al. AJR (2007)	152	4.1	CT/US	18	96	Sensitivity 97.7% Specificity 100%	NR	NA
Volpe et al., J Urol (2008)	100	2.4	CT/US	18	84	100%	100	66.7/75
Wang et al., Urology (2009)	110	2.7	CT/US	18	90.9	100%	96.6	NA
Veltri et al., Eur Radiol (2011)	103	3.4	US	18	100	NR	93.2	NA
Leveridge et al., Eur Urol (2011)	345	2.5	CT/US	18	80.6	99.7%	88	63.5

NA not available

renal tumour histology is necessary to tailor the best-suited treatment to each individual patient, with a significant impact on clinical practice [42].

Pretreatment percutaneous biopsy can indeed reduce the number of unnecessary surgical indications for patients with benign renal tumours, especially in the elderly population with comorbidities. As previously mentioned, SRMs are in fact benign in a non-negligible proportion of cases, with a probability that significantly increases with decreasing tumour size [48–50]. Conventional radiology (CT scan, multiparametric MRI, contrast-enhanced ultrasound) does not allow a reliable diagnosis of oncocytoma. The typical appearance of this benign tumour as a homogeneous, hypervascular mass with a starry central scar is actually observed in a limited number of cases. Moreover, no other radiological CT or MR feature is sufficiently accurate for the diagnosis of this benign tumour [51, 52]. In addition, although most angiomyolipomas are easily diagnosed at CT for their characteristic fatty content, low-fat angiomyolipomas (leiomyoma-like and epithelioid variants) cannot be properly diagnosed by radiological investigations [53]. Overall, Remzi et al. observed that only 17% of benign tumours are correctly identified by preoperative CT scan [54].

Furthermore, percutaneous biopsy can support for choice of the best-suited treatment for all localized renal tumours, especially in patients with limited life expectancy and high surgical risk. Biopsy is particularly useful to select patients who are eligible for a conservative treatment. In fact, active surveillance is a reasonable option for tumours with low-grade histology and therefore limited risk of progression, while surgery should be always advocated—whenever possible—for tumours with aggressive histology. Information from RTBs can also be of help to plan the intensity of follow-up in patients in active surveillance. In fact, benign tumours 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.

Percutaneous biopsy may also be performed in selected cases of larger renal tumours (T1b-T2). In fact, although the decision to perform a radical or partial nephrectomy depends essentially on patient's characteristics and on tumour features at imaging, biopsy may favour the choice of radical nephrectomy for aggressive disease at pathology and conversely support the indication of nephron-sparing surgery in cases with high anatomical complexity in the presence of benign disease or tumours with indolent biological potential. In summary, percutaneous RTBs can provide important information for treatment decisions in patients with SRMs. Research studies are needed to determine the ideal pattern of biopsy (number and location of cores according to tumour size) in order to optimize the diagnostic results. The application of cytogenetics and molecular markers on biopsy specimens has the potential to provide further diagnostic and prognostic information, thereby further increasing the role of percutaneous biopsy in the management of renal neoplasms.

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