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Small Renal Masses: Contemporary Concepts in Diagnosis and Management

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Abstract | **Original Research Article**

Renal cell carcinoma (RCC) has shown a steady increase in incidence over the past three decades, largely attributed to the widespread use of cross-sectional imaging modalities such as computed tomography (CT) and magnetic resonance imaging (MRI). As a result, small renal masses (SRMs), defined as contrast-enhancing renal tumors ≤ 4 cm in diameter, are now detected with increasing frequency and represent up to two-thirds of newly diagnosed renal tumors. SRMs constitute a biologically heterogeneous group of lesions. While many are malignant, a substantial proportion are benign or indolent tumors with limited metastatic potential. This biological variability has significantly influenced management strategies, shifting the paradigm from routine radical nephrectomy to more individualized approaches including active surveillance, nephron-sparing surgery, and minimally invasive ablative therapies. This review aims to provide an updated overview of the epidemiology, pathology, natural history, diagnostic evaluation, and contemporary management strategies for small renal masses. A literature search was conducted using major medical databases including PubMed, Scopus, and Web of Science. Articles published in English focusing on small renal masses, their epidemiology, natural history, diagnostic evaluation, and management strategies were reviewed. Priority was given to recent systematic reviews, prospective studies, and current clinical guidelines.

Keywords: active surveillance, bosniak classification, partial nephrectomy, renal cell carcinoma, renal mass biopsy, small renal mass.

INTRODUCTION & BACKGROUND

Renal cell carcinoma (RCC) has been steadily increasing during the past three decades, which is mostly due to the increasing incidence of cross-sectional imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI). Small renal masses (SRMs) are defined as incidental, enhancing renal masses ≤ 4 cm in greatest dimension, corresponding to clinical T1a renal cell carcinoma. SRMs now account for 48-66% of all detected renal cell carcinomas [1-2]. This has dramatically changed the management of kidney cancer, as these masses are now being detected incidentally by imaging performed for unrelated reasons [1,3].

The significance of SRMs lies in their heterogeneous nature, where 80% of SRMs are malignant, while 20-30% of SRMs are benign [1-2,4]. Out of these malignant SRMs, 25% of patients have indolent histological variants with minimal metastatic potential, such as chromophobe and type 1 papillary RCC [1]. The good prognosis of small RCCs has changed management from aggressive surgical approaches to conservative management [5-6].

The management of SRMs also poses a series of challenges, as current imaging techniques cannot differentiate benign from malignant lesions, nor can they predict the aggressiveness of a tumor [1,3]. Moreover, the management of SRMs should take into account the possibility of the development of chronic kidney disease, with the associated cardiovascular consequences [4]. The current review offers a comprehensive overview of the current evidence regarding the epidemiology, pathology, natural course, diagnosis, and treatment of SRMs, with a focus on current management concepts.

An overview of the diagnostic and management pathway for small renal masses is illustrated in Figure *1*.

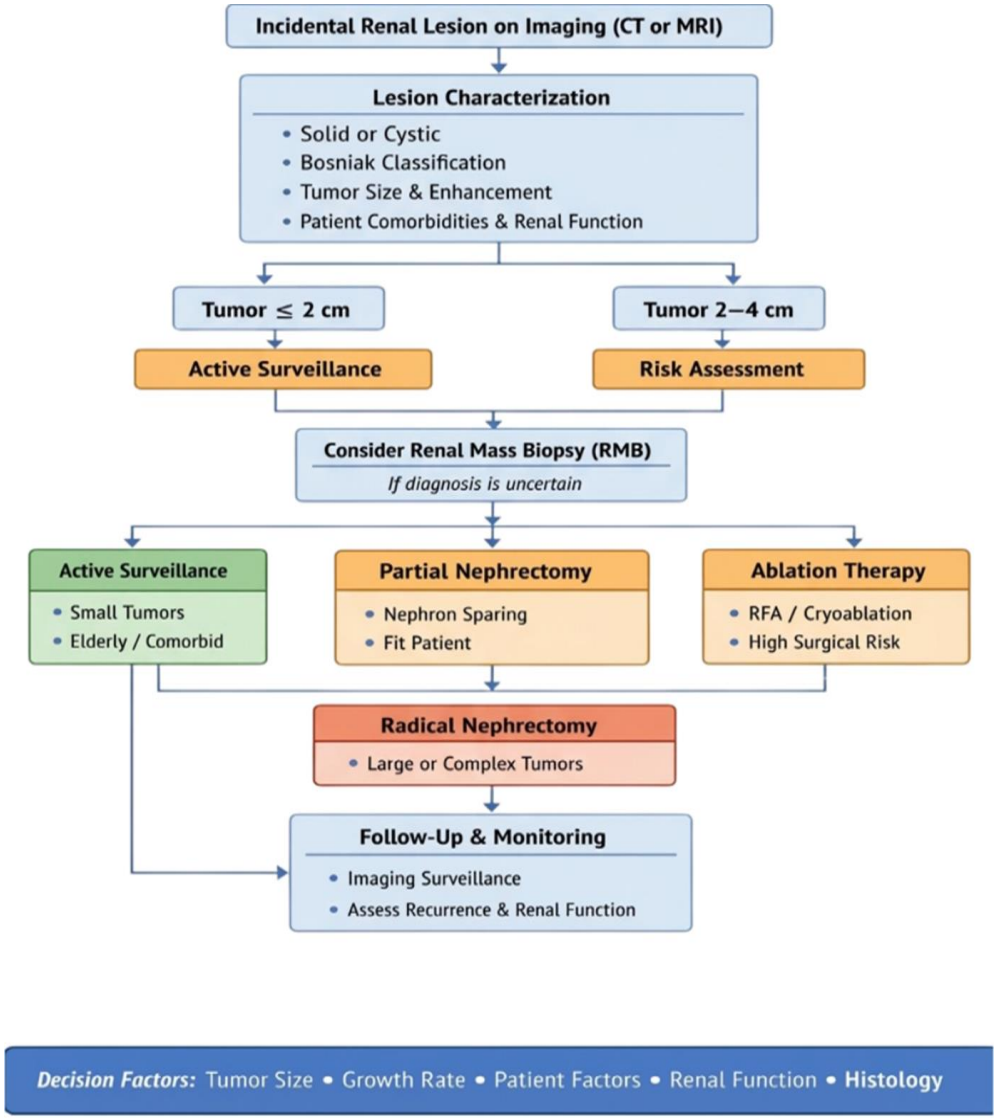

Figure 1: Diagnostic and management algorithm for small renal masses.

This schematic illustrates the clinical decision-making pathway including imaging evaluation, renal mass biopsy, and treatment options such as active surveillance, partial nephrectomy, radical nephrectomy, and ablative therapies. Created using BioRender.com by the authors. Adapted from previously published literature [1,5,7-8]

Review

Epidemiology and Pathology

Incidence and Detection

The incidence of SRMs has risen significantly, with 50% to 61% of all renal tumors now being detected incidentally [3]. About 13% to 27% of abdominal imaging studies detect a renal lesion, although most are simple benign cysts without need for any intervention [2]. The rising incidence of SRMs has not been accompanied by a corresponding decline in the incidence of advanced disease, suggesting that many detected SRMs are likely overdiagnosed clinically insignificant tumors [5].

Histologic Composition

Amongst resected SRMs, 80% are malignant and 20% are benign [2,4]. However, there is variation in their distribution based on tumor size. For SRMs with size ≤ 2 cm, benign tumors comprise 22.5% [9]. Clear cell RCC predominates over other malignancies, accounting for 69-72%, whereas papillary and chromophobe variants comprise 20-21% and 6-7%, respectively [9,10]. Multilocular cystic RCC constitutes 2% of all SRMs [10].

Significantly, it has been noted that amongst SRMs with small size, the grade distribution tends to be favorable. In T1a SRMs with size ranging from 0 to 2 cm, 85% show favorable histology with Fuhrman grade 1 and 2, whereas 14.5% SRMs show high-grade characteristics with Fuhrman grade 3 and 4, out of which 9.8% and 4.8% comprise clear cell and papillary variants, respectively. Advanced age and male sex are risk factors for high-grade SRMs [10].

METASTATIC POTENTIAL

The metastatic potential of SRMs is considered to be generally low but not insignificant. The rate of synchronous metastases for T1a tumors with sizes ranging from 0 to 2 cm is found to be approximately 0.4% [10]. However, it has been reported to range from 1% to 13%. A higher risk is found in tumors larger than 3 cm. Although tumors smaller than 2 cm may occasionally show aggressive characteristics, including synchronous metastases, it is not common, with an occurrence rate of 2.2% in surgical series. Size alone cannot be used to rule out aggressive characteristics, and decision-making should take into account tumor histology, grade, and radiologic characteristics [9].

Natural History and Growth Kinetics

Growth Rates

Knowledge of the natural history of SRMs is critical in the implementation of active surveillance (AS) strategies. The growth kinetics of SRMs have been extensively characterized in several prospective studies on AS. The mean linear growth rate of SRMs ranges from 0.09 to 0.28 cm/year, with most studies showing linear growth rates of 0.2-0.3 cm/year [1,4,11-12] The volumetric growth rate is around 6.15 cm^3/year [11].

Growth kinetics have shown considerable variability in SRM growth, both intertumor and intratumor. The growth kinetics are highly variable in the initial period of AS (first 6-12 months), with mean growth rates of 0.54 cm/year, reducing to 0.07 cm/year after more than 1 year of observation. The variability in growth kinetics is reduced with long periods of observation, indicating that initial growth kinetics may not accurately predict long-term growth kinetics [13].

Histology-Specific Growth Patterns

The rate of tumor growth also differs among different histological types. In a large cohort of patients with tumor biopsy results, clear cell RCCs showed a faster growth rate compared with papillary type 1 RCCs (mean 0.25 cm/year vs. 0.02 cm/year, $p = 0.0003$) [14]. Notably, growth rate is not always predictive of benign vs. malignant tumors because both can have similar growth rates or static growth [1,15] About 40% of SRMs show no significant growth after 3 years of follow-up [1].

Progression and Metastasis Risk

However, long-term surveillance studies have shown that the risk of progression to metastatic disease is low. In one prospective cohort study, the 1.9% developed metastatic disease, and 1.0% died from metastatic RCC in the cohort with a median follow-up of 55.5 months [11]. A large Canadian multicenter study showed a 0.67% 2-year cumulative incidence and 2.3% 5-year cumulative incidence of metastasis in patients with metastatic progression [16]. Metastatic progression is preceded by rapid local tumor growth measurable on imaging [1].

The incidence of tumor progression requiring intervention also varies depending on the study design and patient population. In the Canadian study, the 2-year and 5-year cumulative incidence of local treatment were 8.4% and 21%, respectively, and were primarily nephron-sparing procedures. In patients who developed metastatic disease, 23 out of 29 patients developed evidence of tumor progression before detection of metastatic disease [16].

Diagnostic Evaluation

Imaging Modalities

Computed Tomography

CT with and without the use of intravenous contrast continues to be the mainstay in the characterization of SRM [3]. The use of specific renal mass protocols with thin-slice cuts, such as 3-5 mm, is critical in the evaluation of enhancement, which is the hallmark in differentiating solid or complex cystic lesions from purely cystic ones. Enhancement is described as an increase in attenuation of more than 15 Hounsfield units (HU) following the administration of contrast [2].

CT is good in the evaluation of macroscopic fat, especially in the absence of calcification, in which case a diagnosis of angiomyolipoma, a benign lesion, can be made [1-2]. However, CT is limited in the evaluation of homogeneous hyperattenuating lesions with significant calcification, in which case MRI is preferred [17].

Magnetic Resonance Imaging

Several advantages of MRI over CT have been noted, such as better contrast resolution, functional imaging, no ionizing radiation, and use in patients with allergy to iodine contrast [3]. MRI is also useful in the evaluation of cystic renal masses, with specific features formally included in the Bosniak classification system version 2019 [18-19].

Certain features on MRI help in characterizing renal masses, such as masses that are homogeneously hyperintense on T1-weighted images, similar to cerebrospinal fluid, or markedly hyperintense on fat-suppressed T1-weighted images, more than two and a half times more intense than the surrounding parenchyma, which can be classified as Bosniak type II, thus suitable for observation. MRI is also recommended for renal masses with abundant thick or nodular calcifications on CT, masses that are homogeneous and hyperattenuating greater than or equal to 3 cm in size with no enhancement, or heterogeneous with no enhancement [17].

Key imaging characteristics used in differentiating renal masses are summarized in Table *1*.

Table 1: Imaging Characteristics of Small Renal Masses

Feature	CT Findings	MRI Findings	Clinical Relevance
Enhancement	>15 HU increase	Contrast enhancement	Suggests solid tumor
Fat content	Macroscopic fat	Signal drop on fat-suppression	Angiomyolipoma
Calcification	Detectable	Limited	May obscure diagnosis
Cystic features	Bosniak classification	Better characterization	Risk stratification

Imaging characteristics of small renal masses using CT and MRI modalities [2-3,17-19].

Bosniak Classification

The Bosniak classification system divides cystic renal masses according to their malignancy potential. The 2019 update of this classification system is a major modification, which now includes MRI, defines MRI terminology, and aims for better interobserver agreement and specificity [18-19].

In recent meta-analyses of Bosniak version 2019, malignancy rates were pooled at 9% for class II, 26% for class IIF, 80% for class III, and 88% for class IV lesions [20]. Compared with version 2005, this 2019 update shows better interobserver agreement (weighted kappa 0.64 vs 0.50) and higher specificity (83% vs 68%) without compromising sensitivity [21-22]. This modification causes a shift from class III to class IIF, which might reduce unnecessary procedures [23].

Renal Mass Biopsy

Indications and Utility

The utility of renal mass biopsy (RMB) has increased substantially in recent years. Current guidelines suggest performing RMB on a utility-based approach when it can impact management [7]. Indications include risk stratification in patients contemplating active surveillance, distinguishing unusual diagnoses like lymphoma or metastatic disease, aiding in decision-making in ablative therapies, and in oncologic risk stratification in cases where management decisions are equivocal [1,7,24].

The utility of RMB in the management of SRMs is also significant because of the high incidence of benign disease. In surgical series, 18 to 26% of surgically excised SRMs have been shown to be benign, which translates to "needless nephrectomy" [25]. In masses measuring 3 cm or less in size, the incidence of benign disease is as high as 30% [26-27].

Needless nephrectomy can be avoided in these patients while providing additional information in decision-making [4].

Diagnostic Performance

Currently, the diagnostic accuracy of RMB is high, with a sensitivity of 99.1% for malignancy detection, coupled with a specificity of 99.7%. The median concordance rate between biopsy results and final surgical pathology is as high as 90.3% [15]. The histological type is correctly identified in approximately 88%, while Fuhrman grade concordance is only 64% [28].

Incidence of nondiagnostic biopsies is between 10-20%, with a recent systematic review documenting a rate of 14% [4]. The results are significantly better for masses measuring 3-4 cm in size, with a yield of 93%, as opposed to masses measuring only 3 cm, where the yield is only 85% ($p = 0.01$) [26]. Multiple core biopsies, with 2-3 cores taken with a 16-18 gauge needle, are preferred over fine-needle aspiration (FNA) to maximize the yield [7].

Safety Profile

RMB is safe, and the complication rate is low. The overall complication rate in contemporary series ranges from 0.3% to 5.3% [28]. In a systematic review of 2979 patients who underwent 3113 biopsies, the complication rate was 5% for hematoma, 1% for pain, and 0.7% for bleeding that required embolization or nephrectomy [4,15]. Tumor seeding, historically a concern, is exceedingly rare with modern coaxial needle techniques [15].

It is noteworthy that RMB is not associated with any adverse effect on oncologic outcomes. RMB is not associated with an increased risk of tumor upstaging (OR 0.90, 95% CI 0.6-1.34) and cancer recurrence (OR 1.04, 95% CI 0.57-1.89) in comparison to those who did not undergo RMB and proceeded to surgery [4].

Management Strategies

Active Surveillance

Rationale and Patient Selection

Active surveillance (AS) has been recognized as a safe initial treatment for a select population of SRMs. The basis for AS is the indolent nature of SRMs, the high rate of benign histology, and the possibility that the morbidity of treatment may outweigh the benefits, especially in elderly patients with comorbid conditions [1,5,29].

Current recommendations for AS in the management of SRMs are for: renal masses ≤ 2 cm, with a high likelihood of benign histology and low metastatic potential; T1a renal masses with predominantly cystic components; and for patients with a high likelihood of mortality from treatment-related complications [24,8]. The oncological risks of renal masses ≤ 2 cm are low, with cancer-specific survival rates approaching 98-100% in most AS series during a follow-up period of 12-36 months [24].

Surgical Management

Partial Nephrectomy

Partial nephrectomy (PN) has emerged as the gold standard treatment for SRMs when technically possible [1,4,8]. The advantage of PN is the preservation of renal function, which reduces the risk of chronic kidney disease and cardiovascular disease [4,15]. The only randomized control trial comparing PN with RN for small renal masses of 5 cm size found similar cancer-specific survival with improved renal functional outcomes with PN [1]. In a retrospective cohort study of 662 patients, PN had a 80% chance of preserving renal function with an estimated glomerular filtration rate (eGFR) of 60 mL/min/1.73 m² at 3 years compared with 35% with RN ($p < 0.001$) [4].

The oncologic outcomes with PN are excellent. The 5-year cancer-specific survival rate is between 94-97% [4]. The Cochrane review found no significant difference between PN and RN with regards to cancer-specific survival and time to recurrence. However, PN was associated with reduced mortality from all causes (HR 1.50, 95% CI 1.03-2.18) compared with RN [30].

PN may be performed through an open, laparoscopic, and robotic approach with similar oncologic results [8]. The complication rate is higher in PN than in RN, particularly for the laparoscopic approach, although still acceptable. The effect of robotic assistance on complication rates is still being evaluated [1].

Radical Nephrectomy

Radical nephrectomy remains an option for certain SRMs, such as those with tumors not suitable for PN due to tumor characteristics or complexity, and for patients preferring a definitive treatment approach in a single surgical stage [8]. Nevertheless, RN results in compromised renal function and possible increased risk of other-cause mortality due to the development of CKD [15,31-32]

With respect to T1b-T2 SRMs (4-7 cm), RN results in substantially worse postoperative and 1-year function, with a higher incidence of acute kidney injury (58% vs 17%), less recovery of eGFR to > 90% of baseline (16% vs 51%), and a higher incidence of CKD progression (65% vs 38%) compared to PN. Every effort should be made to preserve nephrons for larger masses when technically and oncologically feasible [32].

Ablative Therapies

Thermal Ablation

Percutaneous thermal ablation, including radiofrequency ablation (RFA), cryoablation, and microwave ablation, provides an alternative to surgery for some patients. The best candidates for ablation are tumor sizes ≤ 3 cm, particularly in patients with co-morbidities and high risk for surgery [4,8].

The procedure can be done with or without prior RMB, although biopsy should be done to confirm malignancy and plan treatment [8].

The complication rates are favorable, including bleeding (2-4%), ureteral damage (2%), urine leak (0-4%), and urinary tract infections (2%) [4]. The procedure may be repeated to obtain results comparable to surgery [8].

Stereotactic Body Radiotherapy

Stereotactic body radiotherapy (SBRT) is a newer ablative treatment option for non-optimal candidates for surgery or ablation [4,8]. The current guidelines rate SBRT as a category 2A option for clinical stage T1a kidney cancer in non-optimal surgical candidates [8].

For a meta-analysis of 199 patients treated with SBRT for primary RCC, the 5-year rate of local recurrence was 5.5%, with a decrease in eGFR of 14 mL/min/1.73 m2, fatigue, nausea, and chest wall pain as adverse events [4]. Recent comparative studies indicate that SBRT may provide a favorable local control rate for larger tumors, with the highest rates for ablative techniques and low rates of severe complications [33].
A comparison of management strategies for small renal masses is presented in Table *2*.

Table 2: Management Options for Small Renal Masses

Strategy	Indications	Advantages	Limitations
Active Surveillance	Elderly, comorbid, ≤2 cm	Avoid overtreatment	Risk of progression
Partial Nephrectomy	Fit patients, T1a	Nephron-sparing	Surgical risks
Radical Nephrectomy	Complex tumors	Complete removal	CKD risk
Ablation	Poor surgical candidates	Minimally invasive	Recurrence risk
SBRT	Non-surgical candidates	Non-invasive	Limited long-term data

Summary of management strategies for small renal masses and their clinical considerations [4-5,8,24,33].

Special Considerations

Very Small Masses (≤ 2 cm)

These masses ≤ 2 cm should be considered carefully, especially because of their high rate of benign pathology (22.5%) and their extremely low metastatic potential [9,24]. In the context of T1a tumors, specifically for those with a size of 0-2 cm, the rate of synchronous metastasis is only 0.4%, with favorable biological behavior for most histologic types [10]. Active surveillance is especially appropriate for this size, with specific guidelines recommending AS as an option

because of the high rate of benign tumors and low metastatic potential [24,8].

Cystic Renal Masses

Cystic renal masses need to be evaluated with a specific system, the Bosniak classification system. The updated system in 2019 has improved the stratification of risk, with Bosniak IIF lesions showing a malignancy rate of 26%, Bosniak III lesions showing an 80% malignancy rate, and Bosniak IV lesions showing an 88% malignancy rate [20]. Notably, predominantly cystic T1a lesions have a very indolent course, with AS being recommended for management [8].

Verification bias in Bosniak IIF lesions results in a malignancy rate of 2% with imaging follow-up, as opposed to a malignancy rate of 41% with histopathology as a reference standard [20], indicating that a significant proportion of conservatively managed Bosniak IIF lesions may be benign or indolent in nature.

Chronic Kidney Disease

Patients with pre-existing CKD are a difficult group to manage. Patients with pre-existing CKD are likely to have benign or indolent disease, yet are at greatest risk for progression of their CKD with a nephrectomy procedure. RMB should be strongly considered in this population to aid in management decisions [7]. Should intervention be necessary, maximum preservation of nephrons with PN or ablation is crucial to prevent dialysis dependence [15,32].

Future Directions

Several areas need further research. The use of molecular biomarkers to assess the aggressiveness of a tumor and its metastatic potential could be a revolutionary tool, which might reduce overtreatment [15,34]. Radiomics techniques using machine learning algorithms hold promise for improving the characterization of renal masses and distinguishing between RCC histologies [3,6]. More prospective randomized trials on treatment strategies (AS vs. intervention, PN vs. ablation) need to be conducted to offer a higher level of evidence on treatment options for RCC [5-6,15].

The role of neoadjuvant systemic therapy for certain high-risk localized RCCs is being explored, which might allow for PN-sparing therapies when PN is not immediately possible [8]. Moreover, adjuvant pembrolizumab has been shown to be beneficial for high-risk clear cell RCC after nephrectomy, thus expanding the treatment options for aggressive RCC [8,35].

CONCLUSIONS

Small renal masses comprise a heterogeneous group of lesions that need to be individually managed depending on the characteristics of the tumor, patient-related factors, and associated health risks. The transformation from traditional radical nephrectomy to a risk-adapted strategy using active surveillance, partial surgical techniques, and ablative therapies has occurred due to a clear understanding of SRM tumor biology. Renal mass biopsies have assumed a vital role in the evaluation of small renal masses. This may potentially reduce overtreatment. Partial surgical techniques should be the primary surgical option for the treatment of SRMs, providing similar oncologic control with excellent functional outcomes. Active surveillance is a safe option for selected patients with SRMs. This includes small tumor size, significant comorbidity, and short life expectancy. Future advances in molecular biomarkers, radiomics, and personalized risk stratification may further refine the management of small renal masses and help avoid unnecessary treatment while maintaining optimal oncologic outcomes.

Declaration

Conflicts of Interest: The authors declare that they have no competing interests.

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Ethical Approval

Ethics approval has been obtained to proceed with the current study

Ethical approval for this study (Ethical Committee N009-24) was provided by the Ethical Committee Ibn University Hospitals, Rabat Morocco on 22 January 2024

GUARANTOR OF SUBMISSION

The corresponding author is the guarantor of submission.

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Availability of Data and Materials

Supporting material is available if further analysis is needed.

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