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Renal Mass and Localized Renal Cancer: Evaluation, Management, and Follow-up: AUA Guideline: Part II

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Purpose: This AUA Guideline focuses on active surveillance (AS) and follow-up after intervention for adult patients with clinically-localized renal masses suspicious for cancer, including solid enhancing tumors and Bosniak 3/4 complex cystic lesions.

Materials and Methods: In January 2021, the Renal Mass and Localized Renal Cancer guideline underwent additional amendment based on a current literature-search. This literature search retrieved additional studies published between July 2016 to October 2020 using the same Key Questions and search criteria from the Renal Mass and Localized Renal Cancer guideline. When sufficient evidence existed, the body of evidence was assigned strength-rating of A (high), B (moderate), or C (low) for support of Strong, Moderate, or Conditional Recommendations. In the absence of sufficient evidence, additional information is provided as Clinical Principles and Expert Opinions (table 1).

Results: AS with potential delayed intervention should be considered for patients with solid, enhancing renal masses <2cm or Bosniak 3-4 lesions that are predominantly-cystic. Shared decision-making about AS should consider risks of intervention/competing mortality versus the potential oncologic benefits of intervention. Recommendations for renal mass biopsy and considerations for periodic clinical/imaging-based surveillance are discussed. After intervention, risk-based surveillance protocols are defined incorporating clinical/laboratory evaluation and abdominal/chest imaging designed to detect local/systemic recurrences and possible treatment-related sequelae, such as progressive renal-insufficiency.

Conclusion: AS is a potential management strategy for some patients with clinically-localized renal masses that requires careful risk-assessment, shared decision-making and periodic-reassessment. Follow-up after intervention is designed to identify local/systemic recurrences and potential treatment-related sequelae. A risk-based approach should be prioritized with selective use of laboratory/imaging resources.

Abbreviations and Acronyms

AS = active surveillance
AUA = American Urological Association
CXR = chest x-ray
CT = computed tomography
HR = high risk
IR = intermediate risk
LR = low risk
MRI = magnetic resonance imaging
PN = partial nephrectomy
PET = positron emission tomography
PGC = Practice Guidelines Committee
RN = radical nephrectomy
RCC = renal cell carcinoma
RMB = renal mass biopsy
US = ultrasound
VHR = very high risk

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Key Words: kidney cancer, active surveillance, nephrectomy, thermal ablation, cancer surveillance

BACKGROUND

Objective and Methods

This AUA Guideline Part II focuses primarily on two aspects of the management of patients with localized renal masses: 1) active surveillance (AS) and expectant management of renal lesions suspicious for renal cell carcinoma (RCC); and 2) follow-up after surgical or ablative intervention for adult patients with clinically-localized renal masses suspicious for

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Table 1. *AUA Nomenclature Linking Statement Type to Level of Certainty, Magnitude of Benefit or Risk/Burden, and Body of Evidence Strength*

	Evidence Strength A (High Certainty)	Evidence Strength B (Moderate Certainty)	Evidence Strength C (Low Certainty)
Strong Recommendation (Net benefit or harm substantial)	Benefits >Risks/Burdens (or vice versa) Net benefit (or net harm) is substantial Applies to most patients in most circumstances and future research is unlikely to change confidence	Benefits >Risks/Burdens (or vice versa) Net benefit (or net harm) is substantial Applies to most patients in most circumstances but better evidence could change confidence	Benefits >Risks/Burdens (or vice versa) Net benefit (or net harm) appears substantial Applies to most patients in most circumstances but better evidence is likely to change confidence (rarely used to support a Strong Recommendation)
Moderate Recommendation (Net benefit or harm moderate)	Benefits >Risks/Burdens (or vice versa) Net benefit (or net harm) is moderate Applies to most patients in most circumstances and future research is unlikely to change confidence	Benefits >Risks/Burdens (or vice versa) Net benefit (or net harm) is moderate Applies to most patients in most circumstances but better evidence could change confidence	Benefits >Risks/Burdens (or vice versa) Net benefit (or net harm) appears moderate Applies to most patients in most circumstances but better evidence is likely to change confidence
Conditional Recommendation (No apparent net benefit or harm)	Benefits=Risks/Burdens Best action depends on individual patient circumstances Future research unlikely to change confidence	Benefits=Risks/Burdens Best action appears to depend on individual patient circumstances Better evidence could change confidence	Balance between Benefits & Risks/Burdens unclear Alternative strategies may be equally reasonable Better evidence likely to change confidence
Clinical Principle	A statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature		
Expert Opinion	A statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge, and judgment for which there may or may not be evidence in the medical literature		

RCC. This includes solid enhancing renal tumors and Bosniak 3/4 complex cystic masses. The evaluation, counseling, and intervention for these patients are discussed in an adjunctive article (Part I).

This guideline reflects significant advances in our understanding of the biology of both treated and untreated localized kidney cancer since the initial AUA Guidelines on this topic were released in 2009, and updated in 2013 and 2017.[1–3] As with the more recent guidelines on the topic of localized renal tumors, "index patients" have been removed reflecting the complex interaction between patient, tumor, and functional characteristics that influence management.[2] The current guidelines are supported by a comprehensive systematic review performed by the Agency for Healthcare Research and Quality, a project that was nominated and supported by the AUA.[4] The systematic review was then updated through October of 2020 and focused on contemporary literature regarding AS for diagnosed or suspected localized renal cancer as well as progression and recurrence risks following initial surveillance, extirpative or ablative therapies.

The full version of the updated AUA Guidelines for Renal Mass and Localized Renal Cancer (2021) is available at: https://www.auanet.org/guidelines/guidelines/renal-mass-and-localized-renal-cancer-evaluation-management-and-follow-up.

Epidemiology and Biologic Potential

Renal masses are a biologically heterogeneous group of tumors ranging from benign masses to cancers that can be indolent or aggressive.[5,6] There were an estimated 73,000 new cases of renal cancer in the United States in 2020, and 300,000 worldwide.[7] Incidence rates have increased dramatically over the past three decades—with the highest incidence in developed countries—believed due to increased use of axial imaging and longer life expectancies.[7]

The large majority (>90%) of kidney cancers are renal cortical tumors known as renal cell carcinoma (RCC). The primary predictors of a tumor's biology and prognosis include pathological stage, histology, and grade. These factors are favorable for most patients with clinically localized disease (Stage I-II) where cancer-specific survival rates approximate 80-90% at 5-years.[8]

Active Surveillance

The first part of this guideline focuses on the role of AS for the management of clinically localized renal masses (figure 1). A growing body of literature demonstrates that small, asymptomatic renal masses, even when proven malignant on needle biopsy, have a prolonged natural history that may be safely managed by AS with delayed intervention if necessary. Retrospective studies, systematic reviews and prospective data sets have consistently demonstrated a low risk of metastatic progression (<2%) for well selected patients over the initial 3 years following the institution of AS.[9]

Most patients with metastatic kidney cancer remain incurable. Therefore, the decision to embark on an initial course of AS or expectant management rather than treatment must be carefully considered in the context of competing medical and renal functional risks. Patient, tumor and treatment related factors must be carefully considered and communicated using a shared decision-making process consistent with the patient's inherent preferences and tolerance of uncertainty.[10] While

Renal Mass and Localized Renal Cancer
Active Surveillance

ACTIVE SURVEILLANCE (AS)

1. For patients with a solid renal mass < 2cm, or those that are complex but predominantly cystic, AS with potential for delayed intervention is an option for initial management.

2. Prioritize AS/Expectant Management when the anticipated risk of intervention or competing risks of death outweigh the potential oncologic benefits of intervention. If asymptomatic, periodic clinical surveillance/imaging can be based on shared decision-making.

3. When the risk/benefit analysis for treatment is equivocal and the patient prefers AS, clinicians should repeat imaging in 3-6 months to assess for interval growth and may consider RMB for additional risk stratification. Repeat cross-sectional imaging should be obtained 3-6 months later. Periodic clinical/imaging surveillance can then be based on growth rate and shared decision-making with intervention recommended if substantial interval growth or if other clinical/imaging findings suggest that the risk/benefit analysis is no longer equivocal or favorable for continued AS.

4. When the oncologic benefits of intervention outweigh the risks of treatment and competing risks of death, clinicians should recommend intervention. In this setting, AS may be pursued only if the patient is willing to accept the associated oncologic risk. Clinicians should encourage RMB for additional risk stratification. If the patient continues to prefer AS, close clinical and cross-sectional imaging surveillance with periodic reassessment and counseling should be recommended.

FACTORS FAVORING AS/EXPECTANT MANAGEMENT

Patient-related	Tumor-related
Elderly Life expectancy <5 years High comorbidities Excessive perioperative risk Frailty (poor functional status) Patient preference for AS Marginal renal function	Tumor size < 3cm Tumor growth < 5mm/year Non-infiltrative Low complexity Favorable histology Predominantly cystic

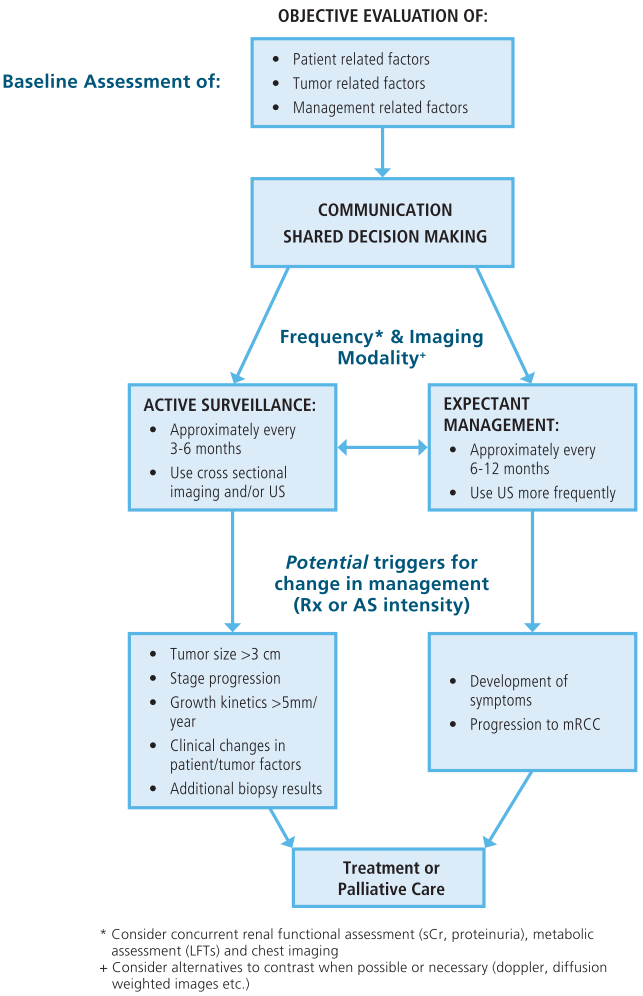

Figure 1. Renal Mass and Localized Renal Cancer: Evaluation, Management, and Follow-Up: Algorithm for Active Surveillance

radiographic surveillance strategies and triggers for intervention have not been fully defined, the guidelines build on a growing literature and experience which attempt to avoid overtreatment and the inherent risks therein while minimizing the likelihood of cancer-specific death attributed to RCC.

Follow-Up After Intervention

The second part of this guideline focuses on follow-up after intervention (figure 2). The prognosis of patients treated with surgery or thermal ablation for kidney cancer is primarily determined by tumor stage, with tumor size, grade, and histology also contributing substantially.[11–17] Current surveillance and survivorship strategies for patients with RCC have incorporated clinical history, physical examination, relevant laboratory testing, and chest and abdominal imaging.[18,19] This allows for assessment of potential complications or sequelae of intervention, functional recovery, and evaluation for common sites of recurrence, both local and systemic.

The premise of early detection of tumor recurrence after primary intervention is that it will result in patient cure, improved survival, or appropriate palliation. In addition, surveillance allows the urologist to provide a measure of reassurance to the patient who is worried about cancer recurrence. Follow-up also offers the opportunity to monitor treatment effects and address survivorship issues that may arise.

The current guideline updates previous risk-stratification systems, providing a more nuanced and clinically meaningful follow-up strategy, with emphasis on providing the practicing provider with a user-friendly protocol. Approximately 30% of recurrences are discovered after 5 years of treatment, underscoring the need to consider longer follow-up than advocated in most current surveillance protocols.[20] In addition to the routine abdominal and chest imaging modalities, additional site-specific imaging should be considered as warranted by clinical signs or symptoms suggestive of recurrence or metastatic spread. Current data do not support

Renal Mass and Localized Renal Cancer: Follow-up after Intervention

General Principles

GENERAL PRINCIPLES

1. Discuss the implications of stage, grade and histology including the risks of recurrence and possible sequelae of treatment. Patients with pathologically-proven benign renal masses should undergo occasional clinical evaluation and laboratory testing for sequelae of treatment but most do not require routine periodic imaging.
2. Patients with treated malignant renal masses should undergo periodic medical history, PE, laboratory studies, and imaging directed at detecting signs/symptoms of metastatic spread and/or local recurrence as well as evaluation for possible sequelae of treatment.
3. Patients with treated malignant renal masses should have periodic laboratory testing including SCr level, eGFR, and urinalysis. Other laboratory evaluations (e.g. CBC, LDH, LFTs, alkaline phosphatase and calcium level) may be obtained at the discretion of the clinician or if advanced disease is suspected.
4. Patients undergoing follow-up for treated renal masses with progressive renal insufficiency or proteinuria should be referred to nephrology.
5. Patients undergoing follow-up for treated malignant renal masses should only undergo bone scan if one or more of the following is present: clinical symptoms such as bone pain, elevated alkaline phosphatase, or radiographic findings suggestive of a bony neoplasm.
6. Patients undergoing follow-up for treated malignant renal masses with acute neurological signs or symptoms should undergo prompt CT or MRI scanning of the brain and/or spine.
7. For patients undergoing follow-up for treated malignant renal masses, additional site-specific imaging can be ordered as warranted by clinical symptoms suggestive of local recurrence or metastatic spread. PET scan should not be obtained routinely but may be considered selectively.
8. Patients with findings suggestive of metastatic renal malignancy should be evaluated to define the extent of disease and referred to medical oncology. Surgical resection or ablative therapies should be considered in select patients if isolated or oligo-metastatic disease is present.
9. Patients with findings suggesting a new renal primary or local recurrence of renal malignancy should undergo metastatic evaluation (including chest and abdominal imaging). If the new primary or recurrence is isolated to the ipsilateral kidney and/or retroperitoneum a urologist should be involved in the decision-making process and surgical resection or ablative therapies may be considered.

Follow-up after Surgery or Thermal Ablation

FOLLOW-UP AFTER SURGERY

1. Patients who have been managed with surgery (PN or RN) for a malignant renal mass should be classified into one of the following risk groups for surveillance:

Low Risk (LR):	**pT1 and Grade 1/2**
Intermediate Risk (IR):	**pT1 and Grade 3/4 or pT2 any Grade**
High Risk (HR):	**pT3 any Grade**
Very High Risk (VHR):	**pT4 or pN1, or sarcomatoid/rhabdoid dedifferentiation, or macroscopic positive margin**

If final microscopic surgical margins are positive for cancer, the risk category should be considered at least one level higher, and increased clinical vigilance should be exercised.

2. Patients managed with surgery (PN or RN) for a renal malignancy should undergo abdominal imaging according to Table 1, with CT or MRI pre- and post-intravenous contrast generally preferred. After 2 years, abdominal ultrasound alternating with cross-sectional imaging may be considered in the LR and IR groups at physician discretion. After 5 years, informed/shared decision-making should dictate further abdominal imaging.

3. Patients managed with surgery (PN or RN) for a renal malignancy should undergo chest imaging (CXR for LR and IR, and CT chest generally preferred for HR and VHR) according to Table 1. After 5 years, informed/shared decision-making discussion should dictate further chest imaging and CXR may be utilized instead of chest CT for HR and VHR.

FOLLOW-UP AFTER THERMAL ABLATION

1. Patients undergoing ablative procedures with biopsy that confirmed malignancy or was non-diagnostic should undergo pre- and post-contrast cross-sectional abdominal imaging within 6 months (if not contraindicated). Subsequent follow-up should be according to the recommendations for the intermediate risk (IR) postoperative protocol (Table 1).

TABLE 1: FOLLOW-UP PROTOCOLS BASED ON MONTHS AFTER SURGERY FOR RENAL CANCER *

RISK	3	6	9	12	18	24	30	36	48	60	72-84	96-120
LR				X		X			X	X	X	X
IR		X		X		X		X	X	X	X	X
HR		X		X	X	X	X	X	X	X	X	X
VHR	X	X	X	X	X	X	X	X	X	X	X	X

*Follow-up timeline is approximate and allows flexibility to accommodate reasonable patient, caregiver, and institutional needs. Each follow-up visit should include relevant history, physical examination, laboratory testing and abdominal and chest imaging. Overall, 30% of renal cancer recurrences after surgery are diagnosed beyond 60 months. Informed/shared decision-making should guide surveillance decisions beyond 60 months.

Figure 2. Renal Mass and Localized Renal Cancer: Evaluation, Management, and Follow-Up: Algorithm for Follow-Up after Intervention

the use of PET scan in the routine surveillance of patients with kidney cancer, and this test should only be considered selectively, such as when other tests are concerning but inconclusive.[21] Taking these and other considerations into account, the Panel provides updated follow-up strategies after intervention that should be useful for the practicing urologist and his/her team.

GUIDELINE STATEMENTS

Management

Active Surveillance (AS).

29. For patients with a solid renal mass < 2cm, or those that are complex but predominantly cystic, clinicians may elect AS with potential for delayed intervention for initial management. (Conditional Recommendation; Evidence Level: Grade C)

The oncologic risks of small renal masses < 2cm is very low in the majority of patients. Cancer-specific and metastasis-free survival rates approach 98-100% in most AS series when measured over 12-36 months.[9,22] Recent studies have also demonstrated that complex cystic masses, particularly Bosniak 3 category lesions and those that are predominantly cystic, also often have indolent tumor biology and favorable outcomes on AS.[23] AS with potential delayed intervention is therefore an acceptable option for the initial management of many of these patients after an informed discussion of the risks and benefits.

30. For patients with a solid or Bosniak 3/4 complex cystic renal mass, clinicians should prioritize AS/expectant management when the anticipated risk of intervention or competing risks of death outweigh the potential oncologic benefits of active treatment. In asymptomatic patients, the panel recommends periodic clinical surveillance and/or imaging based on shared decision making. (Clinical Principle)

Surveillance of a likely (or confirmed) renal malignancy poses some risk of progression and death from disease. However, for patients with limited life

expectancy, significantly elevated surgical risk, or those who potentially face end-stage renal disease, surveillance/expectant management is a rational non-interventional nephron-sparing strategy. The decision to prioritize observation when the anticipated risk of intervention or competing risks of death outweigh the potential oncologic benefits of intervention should jointly involve the physician, the patient and caregivers.

31. For patients with a solid or Bosniak 3/4 complex cystic renal mass in whom the risk/benefit analysis for treatment is equivocal and who prefer AS, clinicians should consider renal mass biopsy (RMB) (if the mass is solid or has solid components) for further oncologic risk stratification. Repeat cross-sectional imaging should be obtained approximately 3-6 months later to assess for interval growth. Periodic clinical/imaging surveillance can then be based on growth rate and shared decision-making with intervention recommended if substantial interval growth is observed or if other clinical/imaging findings suggest that the risk/benefit analysis is no longer equivocal or favorable for continued AS. (Expert Opinion)

In patients for whom the risk/benefit analysis for treatment is equivocal, RMB may improve oncologic risk assessment and guide clinical decision-making. An initial period of AS with delayed intervention is associated with acceptable oncologic outcomes.[22] Absolute triggers for intervention have not been prospectively defined. The decision to intervene is complex and based on multiple risks and tradeoffs. For those who prefer AS, diligent radiographic follow-up at 3-6 months is recommended.

32. For patients with a solid or Bosniak 3/4 complex cystic renal mass in whom the anticipated oncologic benefits of intervention outweigh the risks of treatment and competing risks of death, clinicians should recommend intervention. AS with potential for delayed intervention may be pursued only if the patient understands and is willing to accept the associated oncologic risks. In this setting, clinicians should encourage RMB (if the mass is predominantly solid) for additional risk stratification. If the patient continues to prefer AS, close clinical and cross-sectional imaging surveillance with periodic reassessment and counseling should be recommended. (Moderate Recommendation; Evidence Level: Grade C)

Metastatic RCC of any histology remains mostly incurable. In patients in whom the oncologic benefits of intervention outweigh the risks of treatment and competing risks of death, clinicians should recommend intervention with curative intent.

Follow-Up after Intervention

General Principles.

33. Clinicians coordinating follow-up for patients who have undergone intervention for a renal mass should discuss the implications of stage, grade, and histology including the risks of recurrence and possible sequelae of treatment. Patients with pathologically-proven benign renal masses should undergo occasional clinical evaluation and laboratory testing for sequelae of treatment but most do not require routine periodic imaging. (Expert Opinion)

The risk of recurrence for patients with a treated renal mass is dependent on stage, tumor size, grade, histology and method of treatment and should be reviewed with the patient during recovery after intervention. The possible sequelae of treatment and their implications should also be discussed. Most patients appreciate communication about these issues and such discussions can facilitate compliance with surveillance. Patients treated for benign tumors may still have sequelae of intervention although routine imaging surveillance is often not required.

34. Patients with treated malignant renal masses should undergo periodic medical history, physical examination, laboratory studies, and imaging directed at detecting signs and symptoms of metastatic spread and/or local recurrence as well as evaluation for possible sequelae of treatment. (Clinical Principle)

During surveillance, clinical evaluations should assess potential changes in the patient's health or development of new signs or symptoms that might suggest recurrence or adverse effects from treatment. Laboratory and radiographic testing are important adjuncts. Findings could prompt further diagnostic evaluation.

35. Patients with treated malignant renal masses should have periodic laboratory testing including serum creatinine, estimated glomerular filtration rate, and urinalysis. Other laboratory evaluations (eg, complete blood count, lactate dehydrogenase, liver function tests, alkaline phosphatase and calcium level) may be obtained at the discretion of the clinician or if advanced disease is suspected. (Expert Opinion)

Laboratory data can provide insight into possible disease status and also important information about potential short and long-term sequelae following treatment. Assessment of renal function should be prioritized, and additional laboratory tests may be considered for patients with a history of aggressive disease or when recurrence is suspected, although such testing is not routinely indicated. While

elevated pre-operative alkaline phosphatase[24] is a potential prognostic marker for RCC, retrospective reviews do not demonstrate utility of either bone scan or alkaline phosphatase in the initial evaluation or routine follow-up of asymptomatic patients with RCC.[24,25]

36. Patients undergoing follow-up for treated renal masses with progressive renal insufficiency or proteinuria should be referred to nephrology. (Expert Opinion)

Appropriate referral to nephrology may help prevent further deterioration of renal function that can affect bone and metabolic health as well as cardiovascular risk.

37. Patients undergoing follow-up for treated malignant renal masses should only undergo bone scan if one or more of the following is present: clinical symptoms such as bone pain, elevated alkaline phosphatase, or radiographic findings suggestive of a bony neoplasm. (Moderate Recommendation; Evidence Level: Grade C)

Without symptoms of bone pain or elevated alkaline phosphatase, the effective yield of current nuclear bone scan is very low.[26–29] Conversely, when suspicious musculoskeletal symptoms are present and/or the alkaline phosphatase is elevated, the incidence of metastatic disease is significant (up to approximately 10%), and a bone scan is a sensitive and useful test.[26,29,30]

38. Patients undergoing follow-up for treated malignant renal masses with acute neurological signs or symptoms should undergo prompt magnetic resonance imaging (MRI) or computed tomography (CT) scanning of the brain and/or spine. (Strong Recommendation; Evidence Level: Grade A)

Neurologic cross-sectional imaging (CT or MRI) is the diagnostic modality of choice to identify or exclude metastases to the brain and/or spine. MRI may be more sensitive than CT for the detection of small CNS neoplasms,[31] but CT for urgent evaluation of acute neurological signs or symptoms may be useful.[32,33]

39. For patients undergoing follow-up for treated malignant renal masses, additional site-specific imaging can be ordered as warranted by clinical symptoms suggestive of recurrence or metastatic spread. Positron emission tomography (PET) scan should not be obtained routinely but may be considered selectively. (Moderate Recommendation; Evidence Level: Grade C)

Clinicians should obtain imaging (CT, MRI, US, bone scan, plain films) tailored to any specific symptoms that patients may have. PET scan should not be routinely obtained in the follow-up after RCC treatment, as it can be inaccurate within and outside of the urinary system for patients with this malignancy.[21,34–36] Ongoing studies may uncover more helpful imaging agents.[37]

40. Patients with findings suggestive of metastatic renal malignancy should be evaluated to define the extent of disease and referred to medical oncology. Surgical resection or ablative therapies should be considered in select patients with isolated or oligo-metastatic disease. (Expert Opinion)

Multidisciplinary care including medical oncology expertise should be considered in patients with findings suspicious for metastatic disease. If isolated or oligo-metastatic disease is discovered, surgery and/or ablation should be considered as complete resection of single site or low volume disease can provide long-term disease-free periods for 20-30% of selected patients.[38] Performance status, time from initial treatment to metastasis, number and size of metastatic lesions, site of metastases, and factors reflecting the tumor biology of the primary lesion, including stage, grade, and histology can all influence outcome.

41. Patients with findings suggesting a new renal primary or local recurrence of renal malignancy should undergo metastatic evaluation including chest and abdominal imaging. If the new primary or recurrence is isolated to the ipsilateral kidney and/or retroperitoneum, a urologist should be involved in the decision-making process, and surgical resection or ablative therapies may be considered. (Expert Opinion)

Local recurrence is defined as any persistent or recurrent disease present in the treated kidney or associated renal fossa after initial treatment. If this occurs or a new renal primary is found, a metastatic evaluation should be performed. For select patients with isolated local recurrence, surgery or ablative therapy are the definitive management options.

Follow-Up After Surgery.

42. Clinicians should classify patients who have been managed with surgery (partial nephrectomy (PN) or radical nephrectomy RN) for a malignant renal mass into one of the following risk groups for follow-up:

Low Risk (LR):	pT1 and Grade 1/2
Intermediate Risk (IR):	pT1 and Grade 3/4, or pT2 any Grade
High Risk (HR):	pT3 any Grade
Very High Risk (VHR):	pT4 or pN1, or sarcomatoid/rhabdoid dedifferentiation, or macroscopic positive margin

If final microscopic surgical margins are positive for cancer, the risk category should be considered at least one level higher, and increased clinical vigilance should be exercised. (Expert Opinion)

A recent study compared several recurrence models and showed that these models only marginally outperformed TNM staging system.[39] With these data in mind, the Panel formulated a simple grouping to keep risk stratification convenient for routine patient care, while differentiating risk groups in a clinically meaningful fashion. The same follow-up schedule applies to all RCC histologies. Patients with microscopic positive surgical margins after PN should have closer follow-up.[40]

43. Patients managed with surgery (PN or RN) for a renal malignancy should undergo abdominal imaging according to table 2, with CT or MRI pre- and post-intravenous contrast preferred. (Moderate Recommendation; Evidence Strength: Grade C). After 2 years, abdominal ultrasound (US) alternating with cross-sectional imaging may be considered in the LR and IR groups at physician discretion. After 5 years, informed/shared decision-making should dictate further abdominal imaging. (Expert Opinion)

Recent studies have shown that patients who present with smaller[41] and asymptomatic recurrences (local and/or systemic)[42] after surgery for RCC tend to have a decreased cancer-specific mortality. Patients diagnosed during a scheduled surveillance program experienced longer survival and were more frequently able to receive tumor-directed therapy.[43] While previous guidelines advised that surveillance can be terminated 3-5 years after surgery, recent studies suggest that 30% of RCC recurrences are diagnosed beyond 5 years after surgery.[20] The option to use abdominal US instead of CT or MRI at physician discretion after 5 years of follow-up is intended to allow continuous monitoring after 5 years, while minimizing radiation exposure and cost in the LR and IR groups.

44. Patients managed with surgery (PN or RN) for a renal malignancy should undergo chest imaging (chest x-ray [CXR] for LR and IR; CT chest preferred for HR and VHR) according to table 2. (Moderate Recommendation; Evidence Strength: Grade C). After 5 years, informed/shared decision-making discussion should dictate further chest imaging and CXR may be utilized instead of chest CT for HR and VHR (Expert Opinion)

As pulmonary metastases are the most common site of renal cancer recurrence, timely detection of recurrent disease in the chest is optimized by a chest CT. The option to use CXR instead of chest CT after 5 years of follow up is intended to allow continuous monitoring after 5 years, while minimizing radiation exposure and cost in the HR and VHR groups.

Follow-up after TA.

45. Patients undergoing ablative procedures with biopsy that confirmed malignancy or was non-diagnostic should undergo pre- and post-contrast cross-sectional abdominal imaging within 6 months (if not contraindicated). Subsequent follow-up should be according to the recommendations for the IR postoperative protocol (table 2). (Expert Opinion)

Local recurrence is generally defined as any persistent/recurrent disease present in the treated kidney or associated renal fossa after initial treatment. Local recurrence or persistence after TA includes persistent enhancement of any treated mass, a visually enlarging neoplasm or new nodularity, or failure of regression in size of the treated lesion(s), or new satellite or port site lesions. This recommendation is based on a 5-10% local failure rate of ablative therapy supported by the literature and places a high value on early detection by CT or MRI to direct potential retreatment and successful salvage. Patients who cannot receive iodinated IV contrast should undergo MRI imaging pre- and post-gadolinium contrast. If patients cannot receive any conventional contrast, cross-sectional MRI with diffusion weighted imaging should be performed and can be complimented by contrast-enhanced ultrasound if a mass is suspected to evaluate for enhancement.

FUTURE DIRECTIONS

Active Surveillance

Priorities to improve the quality of AS as an option for the initial management of localized RCC include

Table 2. *Recommended follow-up schedule after surgery for renal cancer (in months)**

Risk	3	6	9	12	18	24	30	36	48	60	72-84	96-120
LR				x		x			x	x	x	x
IR		x		x		x		x	x	x	x	x
HR		x		x	x	x	x	x	x	x	x	x
VHR	x	x	x	x	x	x	x	x	x	x	x	x

* Follow-up timeline is approximate and allows flexibility to accommodate reasonable patient, caregiver, and institutional needs. Each follow-up visit should include relevant history, physical examination, laboratory testing, and abdominal and chest imaging. Overall, 30% of renal cancer recurrences after surgery are diagnosed beyond 60 months.[20] Informed/shared decision-making should guide surveillance decisions beyond 60 months.

clinical trials, quality collaborative initiatives, patient risk assessment tools, novel biomarkers, and improved imaging technologies. Each requires a commitment to continuous clinical improvement and scientific investigation.

In the last decade, clinical investigators have identified overtreatment as a significant risk in the management of human malignancies. While reducing cancer-specific mortality is a primary goal in clinical oncology, a growing body of literature also delineates how serious adverse events associated with cancer treatment may impact a patient's quality and quantity of life. The systematic study of the biology of untreated human cancers is fraught with social, moral and potentially legal implications given the complex, unique and unpredictable tumor-host interactions and other competing risks.

Initial efforts at developing frameworks and a standardized lexicon for AS research will improve data collection, registries and clinical trials in this important domain. The continued development of measures of patient and tumor characteristics and models to estimate and communicate risks and tradeoffs will be foundational to further efforts. On the patient side, these include research on competing risks and measurement tools to assess the morbidity and mortality from common co-existing diagnoses in patients with RCC. On the tumor side, this includes improved evaluation and diagnostic tools such as tumor radiomics, molecular imaging, and enhanced RMB which have great promise to improve our ability to discriminate benign versus malignant and indolent versus aggressive tumor biology.[44] Biomarkers identified through The Cancer Genome Atlas (TCGA)[45] and other efforts will need to be developed/validated as clinically useful assays for diagnosing, estimating prognosis, and monitoring purposes, potentially using circulating tumor cells.[46]

From the patient perspective, the development of aids to improve informed medical decision-making is requisite,[47] while from the physician perspective, randomized prospective trials comparing treatment to AS should be prioritized to assess oncologic/functional outcomes and treatment-related morbidities.

Follow-Up After Intervention

These guidelines for surveillance attempt to provide a risk-based approach to surveillance and monitoring. Any cancer surveillance regimen is a balancing act that includes many variables such as the likelihood of disease recurrence, benefit of therapeutic interventions and effectiveness of these modalities based on timing of recurrence detection, improvements in diagnostic and initial interventions, patient characteristics, as well as the burden and cost of monitoring. As electronic medical records and quality and safety initiatives intensify, tracking outcomes of all patients will become increasingly codified and more usable for research purposes. These data can then be used to inform a more evidence-based approach to the proper sequencing, timing, duration, and type of follow-up that improves patient outcomes with the most parsimonious monitoring.

Future research to make patient follow-up more efficient and effective could include one or many of these modalities: develop circulating biomarkers to supplement currently available imaging, develop novel functional or biomarker-based imaging, conduct clinical trials to compare currently available imaging modalities, as well as clinical trials to guide the frequency of imaging/follow-up, similar to studies done in testicular cancer (MRC TEO8*),[48] colon cancer (GILDA),[49] and non-small cell lung cancer (OFCT-0302).[50]

DISCLAIMER

This document was written by the Renal Mass Guideline Amendment Panel of the American Urological Association Education and Research, Inc., which was created in 2020. The Practice Guidelines Committee (PGC) of the AUA selected the committee chair. Panel members were selected by the chair. Membership of the Panel included specialists in urology and primary care with specific expertise on this disorder. The mission of the panel was to develop recommendations that are analysis based or consensus-based, depending on panel processes and available data, for optimal clinical practices in the treatment of early stage testicular cancer. Funding of the panel was provided by the AUA. Panel members received no remuneration for their work. Each member of the panel provides an ongoing conflict of interest disclosure to the AUA, and the Panel Chair, with the support of AUA Guidelines staff and the PGC, reviews all disclosures and addresses any potential conflicts per AUA's Principles, Policies and Procedures for Managing Conflicts of Interest. While these guidelines do not necessarily establish the standard of care, AUA seeks to recommend and to encourage compliance by practitioners with current best practices related to the condition being treated. As medical knowledge expands and technology advances, the guidelines will change. Today these evidence-based guidelines statements represent not absolute mandates but provisional proposals for treatment under the specific conditions described in each document. For all these reasons, the guidelines do not pre-empt physician judgment in individual cases. Treating physicians must take into account variations in

resources, and patient tolerances, needs, and preferences. Conformance with any clinical guideline does not guarantee a successful outcome. The guideline text may include information or recommendations about certain drug uses ("off label") that are not approved by the Food and Drug Administration (FDA), or about medications or substances not subject to the FDA approval process. AUA urges strict compliance with all government regulations and protocols for prescription and use of these substances. The physician is encouraged to carefully follow all available prescribing information about indications, contraindications, precautions and warnings. These guidelines and best practice statements are not intended to provide legal advice about use and misuse of these substances. Although guidelines are intended to encourage best practices and potentially encompass available technologies with sufficient data as of close of the literature review, they are necessarily time-limited. Guidelines cannot include evaluation of all data on emerging technologies or management, including those that are FDA-approved, which may immediately come to represent accepted clinical practices. For this reason, the AUA does not regard technologies or management which are too new to be addressed by this guideline as necessarily experimental or investigational.

DISCLOSURES

All panel members completed COI disclosures. Disclosures listed include both topic– and non-topic-related relationships. Consultant/Advisor: Sam S. Chang, MD, MBA: GLG, Janssen, BMS, Pfizer, Urogen, Virtuoso Surgical, mIR; Peter E. Clark, MD: Galil Medical, Merck; Jose A. Karam: Merck, Pfizer; Robert G. Uzzo, MD, MBA: UroGen Pharma, Amgen, Merck. Scientific Study or Trial: Sam S. Chang, MD, MBA: NIH; Jose A. Karam, MD: Roche/Genentech, Mirati; Robert G. Uzzo, MD, MBA: Pfizer, Genentech. Investment Interest: Jose A. Karam, MD: MedTek, Allogene, Romtech. Health Publishing: Sam S. Chang, MD, MBA: Uro Today; Jose A. Karam, MD: Frontiers in Genitourinary Oncology, Annals of Surgical Oncology, Cancer, Clinical Genitourinary Cancer. Meeting Participant or Lecturer: Robert G. Uzzo, MD, MBA: Janssen.

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