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Renal Mass and Localized Renal Cancer: Evaluation, Management, and Follow-Up: AUA Guideline: Part I

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Purpose: This AUA Guideline focuses on evaluation/counseling/management of adult patients with clinically-localized renal masses suspicious for cancer, including solid-enhancing tumors and Bosniak 3/4 complex-cystic lesions.

Materials/Methods: The Renal Mass and Localized Renal Cancer guideline underwent an update literature review which resulted in the 2021 amendment. When sufficient evidence existed, the body of evidence was assigned a 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: Great progress has been made regarding the evaluation/management of clinically-localized renal masses. These guidelines provide updated, evidence-based recommendations regarding evaluation/counseling including the evolving role of renal-mass-biopsy (RMB). Given great variability of clinical/oncologic/functional characteristics, index patients are not utilized and the panel advocates individualized counseling/management. Options for intervention (partial-nephrectomy (PN), radical-nephrectomy (RN), and thermal-ablation (TA)) are reviewed including recent data about comparative-effectiveness/potential morbidities. Oncologic issues are prioritized while recognizing the importance of functional-outcomes for survivorship. Granular criteria for RN are provided to help reduce overutilization of RN while also avoiding imprudent PN. Priority for PN is recommended for clinical T1a lesions, along with selective utilization of TA, which has good efficacy for tumors$\leq$3.0 cm. Recommendations for genetic-counseling have been revised and considerations for adjuvant-therapies are addressed. Active-surveillance and follow-up after intervention are discussed in an adjunctive article.

Conclusion: Several factors require consideration during counseling/management of patients with clinically-localized renal masses including general health/comorbidities, oncologic-considerations, functional-consequences, and relative efficacy/potential morbidities of various management-strategies.

Key Words: Kidney cancer, biopsy, partial nephrectomy, radical nephrectomy, thermal ablation, active surveillance

Abbreviations and Acronyms

AHRQ = Agency for Healthcare Research and Quality
AUA = American Urological Association
CKD = Chronic Kidney Disease
eGFR = Estimated Glomerular Filtration rate
GFR = Glomerular Filtration Rate
PN = Partial Nephrectomy
PGC = Practice Guidelines Committee
RN = Radical Nephrectomy
RFA = Radiofrequency Ablation
RCC = Renal Cell Carcinoma
RMB = Renal Mass Biopsy
TA = Thermal Ablation

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BACKGROUND

Objective/Methods

This AUA Guidelines focuses primarily on evaluation/counseling/intervention for patients with clinically-localized renal masses suspicious for renal cell carcinoma (RCC) in adults, including solid-enhancing tumors and Bosniak 3/4 complex cystic masses. Some patients

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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		

with clinically-localized renal masses may present with findings suggesting aggressive tumor biology or may be upstaged on exploration or final pathology. Management considerations pertinent to the urologist in such patients are also addressed. Active surveillance and follow-up after intervention are discussed in an adjunctive article.

The ensuing guidelines reflect significant advances over the past several years, since the initial AUA Guidelines on this topic were released in 2009 and 2017.[1,2] Importantly, "index patients" have been removed reflecting the complex interaction between patient, tumor, and functional characteristics that influence management, and individualized counseling/management is advised.[2] The current guidelines are supported by a comprehensive systematic review performed by AHRQ.[3] The systematic review was then updated (October 2020) and focused on the contemporary literature regarding diagnostic imaging, the role of renal-mass-biopsy (RMB), and the comparative efficacy/potential morbidities of the various management strategies for clinically-localized disease.

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

Renal masses are biologically heterogeneous ranging from benign tumors to indolent or aggressive cancers.[4,5] There were an estimated 73,000 new cases of RCC in the United States in 2020, and 300,000 worldwide.[6]

Presentation/Diagnosis

Greater than 50% of renal masses are now diagnosed incidentally.[7] The "classic triad" of symptoms (hematuria/flank pain/abdominal mass) is typically associated with locally-advanced or metastatic RCC.

Tumor Characteristics

Most kidney cancers (>90%) are renal-cortical tumors known as RCC, with major sub-classifications including clear cell, papillary, and chromophobe. Each subtype has distinct morphologic appearance, clinical characteristics and prognostic significance.[7] Prognosis is determined primarily by pathological stage, histology, and grade.[7]

Overview of Treatment Alternatives

The guideline statements focus on PN, RN, and TA for the management of clinically-localized renal masses (figure 1). PN and RN are the most widely utilized surgical strategies and data regarding comparative efficacy/potential morbidities are robust.[3] Radiofrequency-ablation and cryoablation are the most widely investigated modalities for TA.[3] AS is now also established as an initial management strategy for some patients and is addressed in an adjunctive article.

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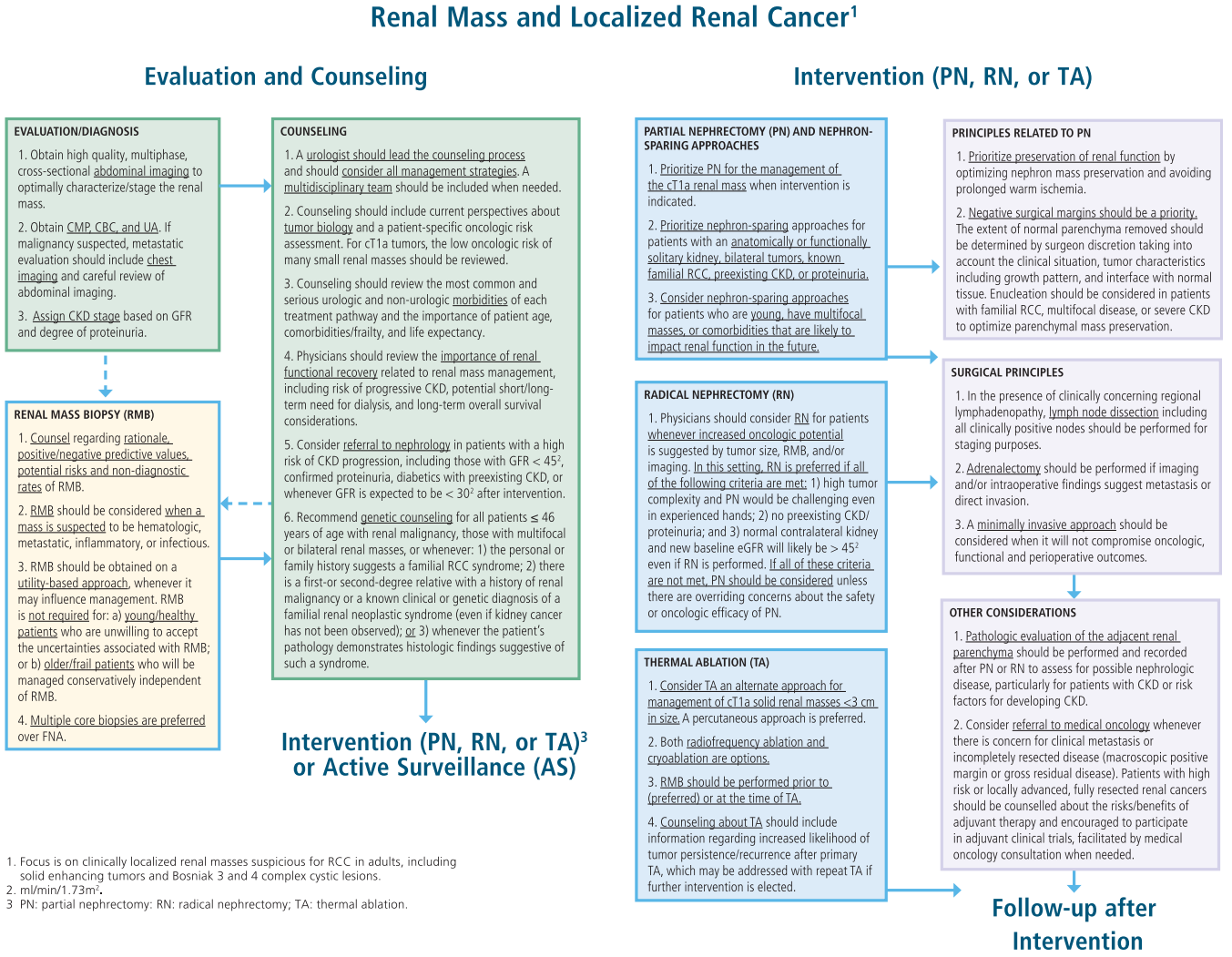

Figure 1. Renal Mass and Localized Renal Cancer Evaluation, Management and Follow-Up: Algorithm for Evaluation, Counseling, and Intervention.

GUIDELINE STATEMENTS

Initial Evaluation and Diagnosis

Evaluation.

1. In patients with a solid or complex cystic renal mass, clinicians should obtain high quality, multiphase, cross-sectional abdominal imaging to optimally characterize and clinically stage the renal mass. Characterization of the renal mass should include assessment of tumor complexity, degree of contrast enhancement (where applicable), and presence or absence of fat. (Clinical Principle)

Male sex and tumor size are the most reliable predictors of malignancy,[3] however degree and pattern of enhancement and tumor complexity can help estimate risk of malignancy, generate a differential-diagnosis, assess clinical stage/anatomic relationships, select interventions, and gauge risk of complications. Presence of macroscopic-fat is essentially diagnostic for benign angiomyolipoma. MRI can now be obtained safely even in patients with severe chronic kidney disease (CKD) or end-stage-renal-disease based on recent recommendations from American College of Radiology.[8]

2. In patients with suspected renal malignancy, clinicians should obtain a comprehensive metabolic panel, complete blood count, and urinalysis. Metastatic evaluation should include chest imaging to evaluate for possible thoracic metastases. (Clinical Principle)

Evaluation for proteinuria, CKD, hematuria, hypercalcemia, hepatic dysfunction, and blood count abnormalities should be pursued, as they may reflect poor health status or advanced cancer. The most common site of metastasis for RCC is the lung and risk-based metastatic evaluation should include chest imaging and careful review of the abdominal imaging at minimum.[7]

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3. For patients with a solid or Bosniak 3/4 complex cystic renal mass, clinicians should assign CKD stage based on glomerular filtration rate (GFR) and degree of proteinuria. (Expert Opinion)

Patients with localized RCC often have multiple risk factors for decreased GFR which should be quantified. Identification and proper classification of CKD as outlined in the Kidney-Disease: Improving-Global-Outcomes (KDIGO) Guidelines should be performed taking into account: 1) GFR; 2) degree of proteinuria; and 3) etiology of CKD.[9]

Counseling.

4. In patients with a solid or Bosniak 3/4 complex cystic renal mass, a urologist should lead the counseling process and should consider all management strategies. A multidisciplinary team should be included when necessary. (Expert Opinion)

Given the complexities underlying the natural history and management of localized renal masses, a urologist is best suited to lead the evaluation/counseling process.[3] Involvement by other specialists may be required based on specific factors.

5. Clinicians should provide counseling that includes current perspectives about tumor biology and a patient-specific risk assessment inclusive of sex, tumor size/complexity, histology (when obtained), and imaging characteristics. For cT1a tumors, the low oncologic risk of many small renal masses should be reviewed. (Clinical Principle)

Several parameters can be used to counsel patients about their risk of malignancy and death from a localized renal mass and can impact individualized decision-making.[3] Overall, 20-25% of cT1a tumors are benign and only 15-20% are high-grade or locally-invasive.[7,10]

6. During counseling of patients with a solid or Bosniak 3/4 complex cystic renal mass, clinicians must review the most common and serious urologic and non-urologic morbidities of each treatment pathway and the importance of patient age, comorbidities/frailty, and life expectancy. (Clinical Principle)

Each management strategy for localized renal masses is associated with a unique profile of perioperative morbidities, functional outcomes, and health-related quality of life implications.[3,7] Age, comorbidities, and life-expectancy help determine overall survival and may impact the risk profile for intervention.[3,7,11]

7. Clinicians should review the importance of renal functional recovery related to renal mass management, including the risks of progressive CKD, potential short- or long-term need for renal replacement therapy, and long-term overall survival considerations. (Clinical Principle)

All management strategies for localized renal masses have implications for renal function both short and long-term. Numerous variables can influence functional outcomes including the amount of parenchyma removed/ablated, ischemia type/duration, and patient age/comorbidities.[7,12,13] Patients with preexisting CKD due to medical etiologies have reduced overall survival and increased risk for progressive decline in GFR.[14,15]

8. Clinicians should consider referral to nephrology in patients with a high risk of CKD progression, including those with estimated glomerular filtration rate (eGFR) less than 45 mL/min/1.73m^2, confirmed proteinuria, diabetics with preexisting CKD, or whenever eGFR is expected to be less than 30 mL/min/1.73m^2 after intervention. (Expert Opinion)

Certain patients are at high-risk for progression of CKD postoperatively (Supplementary figure 1, https://www.jurology.com).[9] Decline in renal function related to nephron-mass loss in these patients may be exacerbated by resultant hyperfiltration and the deleterious impact of pre-existing comorbidities. Nephrology referral will ensure proper management and functional surveillance of these patients.

9. Clinicians should recommend genetic counseling for any of the following: all patients ≤46 years of age with renal malignancy, those with multifocal or bilateral renal masses, or whenever 1) the personal or family history suggests a familial renal neoplastic syndrome; 2) there is a first-or second-degree relative with a history of renal malignancy or a known clinical or genetic diagnosis of a familial renal neoplastic syndrome (even if kidney cancer has not been observed); *or* 3) the patient's pathology demonstrates histologic findings suggestive of such a syndrome. (Expert Opinion)

Recognition of patients with familial RCC allows for proactive management and screening of blood relatives which may lessen the morbidity and mortality of these syndromes (Supplementary table 1, https://www.jurology.com).[16] Hereditary RCC typically presents at younger age, and renal mass patients who are ≤46 years old should be considered for genetic counseling.[17] The indications for genetic counseling for RCC have expanded substantially over the past 5 years.[16]

Renal Mass Biopsy (RMB).

10. When considering the utility of RMB, patients should be counseled regarding rationale, positive and negative predictive values, potential risks and non-diagnostic rates of

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RMB. (Moderate Recommendation; Evidence Level: Grade C)

Based on meta-analysis that compared RMB with surgical pathology, the sensitivity (97%), specificity (94%), and positive-predictive-value (99%) of core RMB are excellent and a diagnosis of malignancy can be trusted. In addition, histologic determination of RCC subtype is highly reliable, although accuracy for tumor grade is variable and the non-diagnostic rate of RMB is 14%, which can be substantially reduced with repeat biopsy.[18] The negative-predictive-value of RMB is 81%, suggesting that a non-malignant biopsy result may not truly indicate that a benign entity is present. There have been no reported cases of RCC tumor seeding in the contemporary literature, and complications are infrequent (clinically significant pain (1.2%), gross hematuria (1.0%), pneumothorax (0.6%), and hemorrhage requiring transfusion (0.4%)).

11. Clinicians should consider RMB when a mass is suspected to be hematologic, metastatic, inflammatory, or infectious. (Clinical Principle)

If the radiographic or clinical picture suggests metastatic cancer, RMB can confirm a diagnosis of metastasis from a non-renal primary malignancy or lymphoma, both of which are typically treated systemically.[7] When there is concern for an inflammatory or infectious process, RMB can confirm the diagnosis, direct therapy, and provide drainage.[7]

12. In the setting of a solid renal mass, RMB should be obtained on a utility-based approach whenever it may influence management. RMB is not required for 1) young or healthy patients who are unwilling to accept the uncertainties associated with RMB; or 2) older or frail patients who will be managed conservatively independent of RMB findings. (Expert Opinion)

Patients with severe CKD often have benign or indolent tumors and counseling and management can be complex, and RMB should be considered in this challenging patient population.[19] RMB should also be considered for additional oncologic risk stratification when there are difficult decisions about PN versus RN or AS versus intervention.[7,20]

13. For patients with a solid renal mass who elect RMB, multiple core biopsies should be performed and are preferred over fine needle aspiration. (Moderate Recommendation; Evidence Level: Grade C)

RMB may be performed under CT or US guidance, with at least 2-3 cores being obtained with a 16-18 gauge needle to optimize diagnostic yield.[3,18]

Management

Partial nephrectomy (PN) and nephron-sparing approaches.

14. Clinicians should prioritize PN for the management of the cT1a renal mass when intervention is indicated. In this setting, PN minimizes the risk of CKD or CKD progression and is associated with favorable oncologic outcomes, including excellent local control. (Moderate Recommendation; Evidence Level: Grade B)

The European randomized trial (EORTC-30904) suggests that PN provides similar oncological outcomes compared to RN for small renal masses[21], and the AHRQ systematic review reaffirms this for appropriately selected patients.[2,3] PN is also associated with better functional outcomes when compared to RN (Supplementary figures 2 and 3, https://www.jurology.com).[2,3] PN provides more favorable local recurrence-free survival when compared to a single session of TA (Supplementary figure 4, https://www.jurology.com).[3,7] Many small renal masses have relatively low oncologic risk and RN should be avoided if possible.[3,7] PN can be associated with urologic complications but most can be managed successfully with conservative measures.[3,7]

15. Clinicians should prioritize nephron-sparing approaches for patients with solid or Bosniak 3/4 complex cystic renal masses and an anatomic or functionally solitary kidney, bilateral tumors, known familial RCC, preexisting CKD, or proteinuria. (Moderate Recommendation; Evidence Level: Grade C)

Absolute indications for nephron-sparing approaches include situations in which RN would render the patient anephric or high-risk for renal replacement therapy.[7] Patients with familial RCC are at increased risk for tumor recurrence and often require multiple renal interventions throughout their lifetime.[7,22] Patients with pre-existing CKD or proteinuria are at increased risk for progressive CKD and nephron-sparing approaches should also be prioritized in these patients.[9]

16. Nephron-sparing approaches should be considered for patients with solid or Bosniak 3/4 complex cystic renal masses who are young, have multifocal masses, or comorbidities that are likely to impact renal function in the future, including but not limited to moderate to severe hypertension, diabetes mellitus, recurrent urolithiasis, or morbid obesity. (Moderate Recommendation; Evidence Level: Grade C)

Young patients with longer life expectancy are theoretically at increased risk for contralateral disease as well as competing health risks that can impact renal function on a longitudinal basis. Patients with multifocal tumors may have familial RCC and are at risk for *de novo* recurrences.[22] Patients with significant risk for future CKD such as those with severe hypertension, diabetes mellitus,

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strong stone diathesis, or morbid-obesity should also be considered for nephron-sparing approaches to optimize their remaining renal function.[9,17]

17. In patients who elect PN, clinicians should prioritize preservation of renal function by optimizing nephron mass preservation and avoiding prolonged warm ischemia. (Expert Opinion)

One of the main objectives of PN is to preserve renal function, which is particularly important in patients with a solitary kidney, bilateral tumors or preexisting CKD/proteinuria.[7,9] The main determinant of functional recovery after PN is nephron-mass preservation, with ischemia playing a secondary role.[12] The threshold of warm-ischemia at which irreversible damage begins to occur is not well-defined, although most studies suggest approximately 25-30 minutes.[13] In general, recovery from cold ischemia is more reliable with intervals of 60-90 minutes being generally well-tolerated.[7,12,13]

18. For patients undergoing PN, clinicians should prioritize negative surgical margins. The extent of normal parenchyma removed should be determined by surgeon discretion taking into account the clinical situation and tumor characteristics, including growth pattern, and interface with normal tissue. Tumor enucleation should be considered in patients with familial RCC, multifocal disease, or severe CKD to optimize parenchymal mass preservation. (Expert Opinion)

During PN, complete excision with negative surgical margins is a priority to optimize oncologic outcomes.[7] Concurrent efforts to maximize renal parenchymal preservation are also important considerations. The amount of normal tissue excised during PN should be determined by individual surgeon judgment, taking into account patient and tumor characteristics while minimizing the risks of residual disease.[23]

Radical Nephrectomy (RN). **19. Clinicians should consider RN for patients with a solid or Bosniak 3/4 complex cystic renal mass whenever increased oncologic potential is suggested by tumor size, RMB (if obtained), and/or imaging. (Moderate Recommendation; Evidence Level: Grade B) In this setting, RN is preferred if all of the following criteria are met: 1) high tumor complexity and PN would be challenging even in experienced hands; 2) no preexisting CKD or proteinuria; and 3) normal contralateral kidney and new baseline eGFR will likely be greater than 45 mL/min/1.73m^2 even if RN is performed. If all of these criteria are not met, PN should be considered unless there are overriding concerns about the safety or oncologic efficacy of PN. (Expert Opinion)**

Patients with potentially aggressive tumor, no preexisting CKD/proteinuria, and a normal contralateral kidney that can provide new-baseline GFR >45 ml/min/1.73m^2 should be considered for RN, particularly if there is high tumor-complexity.[7,15] In this setting, the risk of perioperative morbidity with PN will be increased and oncologic outcomes may also be compromised. Furthermore, the downside of RN for such patients appears to be inconsequential based on studies with 10-year follow-up.[24,25] Beyond this, most cT1b/T2 tumors should be considered for PN. Decisions about RN/PN can be complex and impactful, and these evidence-based criteria should help to reduce overutilization of RN while also avoiding imprudent PN.[7,24,25]

Surgical Principles.

20. For patients who are undergoing surgical excision of a renal mass with clinically concerning regional lymphadenopathy, clinicians should perform a lymph node dissection including all clinically positive nodes for staging purposes. (Expert Opinion)

If suspicious lymphadenopathy is identified on imaging or during surgical exploration, a lymph node dissection (LND) should be performed with removal of all clinically evident nodes, if feasible, primarily for staging and prognostic purposes.[26,27] Based on current data there is a strong consensus that LND need not be performed routinely in patients with localized kidney cancer and clinically negative nodes.[28] However, for patients with risk factors for LN involvement such as a large primary tumor (>10 cm), clinical stage T3/T4, high tumor grade (3/4), sarcomatoid features, or histologic tumor necrosis, selective performance of LND should be considered at the time of renal cancer surgery.[26] This is primarily for staging purposes, as recent studies have been unable to confirm a survival benefit for LND among patients undergoing surgery for non-metastatic RCC.[29] If lymph node involvement is confirmed on final pathology, adjuvant therapy and medical oncology consultation should be considered (See also Statement 24).

21. For patients who are undergoing surgical excision of a renal mass, clinicians should perform adrenalectomy if imaging and/or intraoperative findings suggest metastasis or direct invasion of the adrenal gland. (Clinical Principle)

Adrenal involvement with RCC is a poor prognostic finding and fortunately relatively uncommon outside of the advanced disease setting.[27] Several studies have shown that occult adrenal involvement is uncommon in patients with clinically localized kidney cancer, and the adrenal gland can be spared

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in these patients without compromising oncologic outcomes. Adrenalectomy should be performed if preoperative imaging or intraoperative inspection suggests metastasis or adrenal enlargement. The one exception is when the patient has a well-characterized non-functioning adenoma, which may not mandate surgical excision. Adrenalectomy can have important prognostic utility and may occasionally have therapeutic potential if the adrenal is the only site of local or metastatic spread.[7]

22. In patients undergoing surgical excision of a renal mass, a minimally invasive approach should be considered when it would not compromise oncologic, functional, and perioperative outcomes. (Expert Opinion)

Multiple studies demonstrate both recuperative and cosmetic advantages to minimally invasive RN in comparison to open surgery.[30] Laparoscopic and robotic PN have demonstrated equivalent surgical margin status and oncological outcomes when compared to open surgery in well-selected patients.[31] The current data suggest that the benefits of minimally invasive surgery are realized in the short-term, perioperative period and are equivalent to open surgery with intermediate- and long-term follow-up.[32] While minimally-invasive approaches have also been reported in increasingly complex indications (large renal masses, renal vein thrombi and patients with solitary kidneys), patient safety and adherence to prior guideline statements regarding oncologic outcomes, indications for nephron-sparing surgery, and preservation of renal function should be prioritized relative to the choice of surgical access approach.[7]

Other Considerations.

23. Pathologic evaluation of the adjacent renal parenchyma should be performed and recorded after PN or RN to assess for possible intrinsic renal disease, particularly for patients with CKD or risk factors for developing CKD. (Clinical Principle)

Proper evaluation of non-neoplastic kidney disease is often not performed or reported[33] but is essential to achieve optimal patient management. Given that diabetes and hypertension are independent risk factors for CKD and RCC, diabetic nephropathy and hypertensive nephropathy are found in 8-20% and at least 14% of nephrectomies, respectively.[34] Recognizing this general deficiency, the College of American Pathologists has established a requirement that pathologic evaluation of the renal parenchyma for possible nephrologic disease should be included in all synoptic reports for kidney cancer.[35]

24. Clinicians should consider referral to medical oncology whenever there is concern for potential clinical metastasis or incompletely resected disease (macroscopic positive margin or gross residual disease). Patients with high-risk or locally advanced, fully resected renal cancers should be counselled about the risks/benefits of adjuvant therapy and encouraged to participate in adjuvant clinical trials, facilitated by medical oncology consultation when needed. (Clinical Principle)

Recurrence risk stratification tools for patients with fully-resected high-risk RCC are available.[36] In 2017, the FDA approved sunitinib malate for adjuvant treatment for patients with high-risk clear-cell RCC after surgery based on an improvement in recurrence-free survival in the STRAC trial; however, significant differences in overall survival were not observed.[37] In contrast, other randomized trials evaluating TKIs in this setting have been negative, although some included other histologies, enrolled lower risk patients, and/or allowed more flexibility for dose-reduction.[38] While the current standard remains close clinical/radiographic observation, patients with a high-risk of recurrence should be counseled regarding systemic adjuvant options and/or considered for enrollment into adjuvant clinical trials.

Thermal Ablation (TA).

25. Clinicians should consider TA as an alternate approach for the management of cT1a solid renal masses <3 cm in size. For patients who elect TA, a percutaneous technique is preferred over a surgical approach whenever feasible to minimize morbidity. (Moderate Recommendation; Evidence Level: Grade C)

The literature regarding TA for localized renal masses has further matured and follow-up in some TA studies has now reached 5 years or more. Results with TA are particularly encouraging for smaller tumors (<3 cm) making it a reasonable alternate approach in this setting. The AHRQ meta-analysis demonstrated comparable metastasis-free survival for PN and TA.[3] However, local recurrence-free survival is generally reported as favoring surgical extirpation (Supplementary figure 4, https://www.jurology.com, see Statement 14).[3] These differences largely disappear when additional salvage therapies are also considered (Supplementary figure 5, https://www.jurology.com).[3] TA also has a favorable morbidity profile in comparison to extirpative surgery including lower transfusion rates, length of hospital stay, and conversion to RN, while minor and major Clavien complication rates do not differ significantly between TA and PN.[3] Both percutaneous and laparoscopic approaches to TA have similar

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efficacy. However, the percutaneous approach is associated with shorter procedure time, quicker recovery, and lower narcotic requirements and should be the preferred approach for TA, whenever feasible.

26. Both radiofrequency ablation (RFA) and cryoablation may be offered as options for patients who elect TA. (Conditional Recommendation; Evidence Level: Grade C)

Comparisons of RFA and cryoablation are limited by the absence of randomized studies and variability in patient selection, tumor size and location, technique, and laparoscopic or percutaneous approach in retrospective series. Single institution studies have reported comparable oncologic outcomes (local recurrence-free survival and cancer-specific survival), impact on renal function, and complication rates for the two modalities.[39,40,41] Meta-analyses of the literature have confirmed no significant differences between cryoablation and RFA in treatment outcomes as defined by complications, metastatic progression, or cancer-specific survival.[42]

27. A RMB should be performed prior to (preferred) or at the time of ablation to provide pathologic diagnosis and guide subsequent surveillance. (Expert Opinion)

Although solid, enhancing renal masses are most often RCC, the differential diagnosis also includes benign tumors and metastatic lesions.[7] TA by its nature will lead to tissue necrosis and therefore will not allow clinicians to acquire diagnostic tissue after ablation has been performed. A diagnostic RMB prior to TA is therefore the only realistic opportunity to render a diagnosis in patients who elect this management strategy.[7] Performing RMB prior to TA as a separate procedure may facilitate more rational counseling and avoid treatment of benign tumors. However, in many cases RMB as a separate procedure can increase the risk and cost associated with the TA management strategy. Therefore, decisions about timing of RMB relative to TA should be made on an individualized basis.

28. Counseling about TA should include information regarding an increased likelihood of tumor persistence or local recurrence after primary TA relative to surgical excision, which may be addressed with repeat ablation if further intervention is elected. (Strong Recommendation; Evidence Level: Grade B)

In general, local recurrence-free survival favors surgical extirpation over TA; however, these differences largely disappear when additional salvage therapies are also considered (See Supplementary figures 4 and 5, https://www.jurology.com and Statement 25). A small minority of patients with local recurrence after TA are not candidates for salvage TA due to tumor progression and may require surgical salvage, including occasional need for RN.[3,7]

FUTURE DIRECTIONS

Evaluation/Diagnosis: Tumor radiomics, molecular imaging, and enhanced RMB with molecular profiling have great promise to discriminate benign versus malignant and indolent versus aggressive tumor biology.[43,44] Biomarkers identified through The Cancer Genome Atlas (TCGA)[45–47] will need to be developed and validated as clinically useful assays for diagnosing and monitoring purposes, potentially using circulating-tumor-cells.[48]

Counseling/Outcomes-based Research: Improved assessment of tumor biology and higher quality of data from prospective trials are needed to facilitate more informed patient counseling. The development of aids to improve informed medical decision-making is ongoing.[49]

Management: Randomized prospective trials comparing PN versus RN,[24,50] PN versus TA, standard PN versus TE, and AS versus intervention, should be prioritized to assess oncologic and functional outcomes and treatment-related morbidities. Non-extirpative methods, eg, stereotactic-body-radiation-therapy or high-intensity-focused-ultrasound, are still investigational.

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

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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.

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