

AUA Guidelines Renal Mass and Localized Kidney Cancer

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AUA Guideline for Renal Mass and Localized Kidney Cancer Panel *Representatives from many Allied Fields*

- **Steven C Campbell, Cleveland Clinic, Panel Chair**
- **Robert G Uzzo, Fox Chase, Vice Chair, representing SUO**
- **Bradley C Liebovich, Mayo Clinic, representing SUO**
- **Peter E Clark, Vanderbilt, member of AUA Guidelines Committee**
- **Mohamad E Allaf, Johns Hopkins, member of AHRQ team**
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- **Eric Bass, Johns Hopkins, leader of AHRQ**
- **Anthony Chang: U. Chicago, representing College American Pathology**
- **Susie Hu, Brown University, representing American Society Nephrology**
- **Brian J Davis, Mayo Clinic, RT oncology, representing AC Radiology**
- **Debra A Gervais, MGH, ACR and the Society Interventional Radiology**
- **Leo Giambarresi: Patient Advocate**

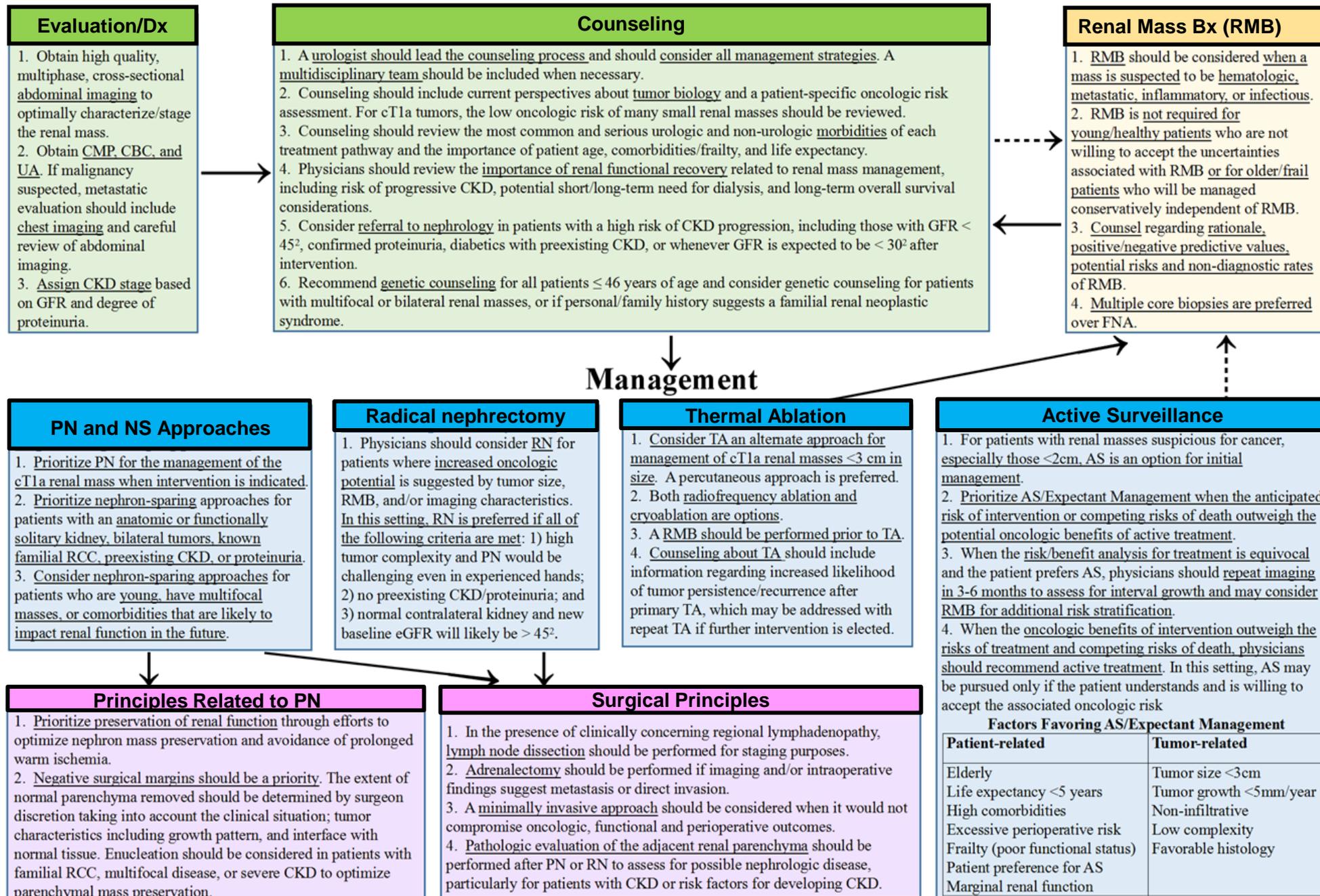
Primary Focus

- Clinically localized renal masses suspicious for cancer in adults, including solid enhancing renal tumors and Bosniak 3 and 4 complex cystic renal masses

Methods for AUA Guidelines

- **Standard for AUA Guidelines process: Rigorous, evidence-based approach, with extensive peer review**
- **Systematic review and meta-analysis (AHRQ)**
- **One face-face meeting, but also several conference calls**
- **Multiple Collaborations: SUO, CAP, SIR, Endourology Society, ASN, ACR**

Renal Mass and Localized Renal Cancer¹



1. Focus is on clinically localized renal masses suspicious for RCC in adults, including solid enhanced tumors and Bosniak 3 and 4 complex cystic lesions. 2. ml/min/1.73m².

What's New?

No index patients: recognizing great variance in patient/oncologic/functional characteristics, the panel recommends individualized counseling/management, representing a major change from the 2009 Guidelines

2009 Guidelines

Index patients defined by:

-Healthy vs. Unhealthy

-T1a vs. T1b

Presumes black and white -- In reality there are many shades of grey and individualized counseling and management is recommended

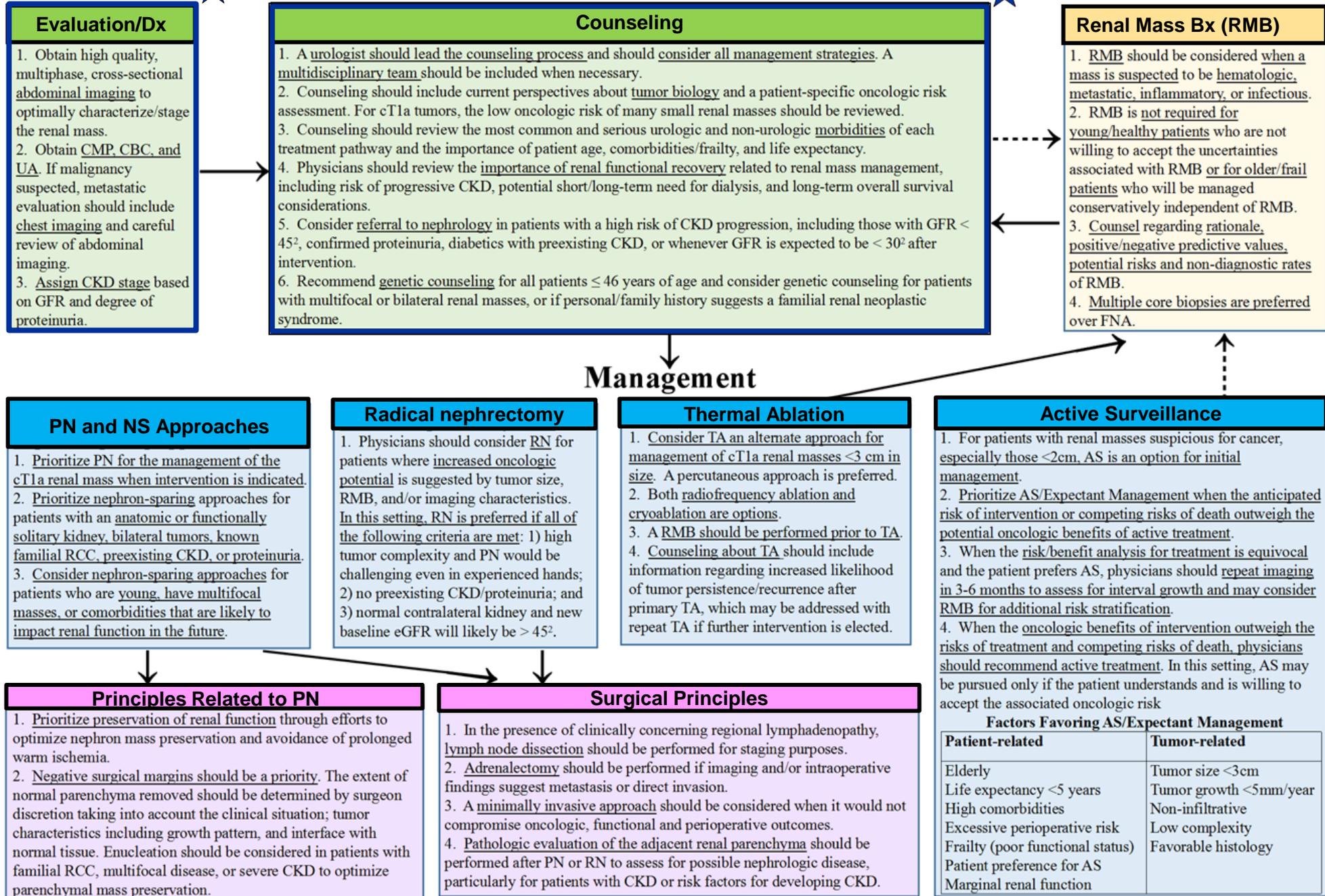
What's New?

- Increased emphasis on functional aspects, recognizing importance of functional outcomes for survivorship for most patients with localized RCC
 - Patients with localized RCC typically do not die of kidney cancer
 - In EORTC 30904 only 12/545 (2.8%) patients died of kidney cancer with median follow-up of 9.3 years

What's New?

- Restricted role for RN, well-defined selection criteria
- Primary role for PN: T1a, and otherwise
- Selective utilization of TA: tumor most effective for <3 cm
- Considerations for shared decision-making about AS explicitly defined

Renal Mass and Localized Renal Cancer¹



Evaluation/Dx

1. Obtain high quality, multiphase, cross-sectional abdominal imaging to optimally characterize/stage the renal mass.
2. Obtain CMP, CBC, and UA. If malignancy suspected, metastatic evaluation should include chest imaging and careful review of abdominal imaging.
3. Assign CKD stage based on GFR and degree of proteinuria.

Counseling

1. A urologist should lead the counseling process and should consider all management strategies. A multidisciplinary team should be included when necessary.
2. Counseling should include current perspectives about tumor biology and a patient-specific oncologic risk assessment. For cT1a tumors, the low oncologic risk of many small renal masses should be reviewed.
3. Counseling should 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.
4. Physicians should review the importance of renal functional recovery related to renal mass management, including risk of progressive CKD, potential short/long-term need for dialysis, and long-term overall survival considerations.
5. Consider referral to nephrology in patients with a high risk of CKD progression, including those with GFR < 45², confirmed proteinuria, diabetics with preexisting CKD, or whenever GFR is expected to be < 30² after intervention.
6. Recommend genetic counseling for all patients ≤ 46 years of age and consider genetic counseling for patients with multifocal or bilateral renal masses, or if personal/family history suggests a familial renal neoplastic syndrome.

Renal Mass Bx (RMB)

1. RMB should be considered when a mass is suspected to be hematologic, metastatic, inflammatory, or infectious.
2. RMB is not required for young/healthy patients who are not willing to accept the uncertainties associated with RMB or for older/frail patients who will be managed conservatively independent of RMB.
3. Counsel regarding rationale, positive/negative predictive values, potential risks and non-diagnostic rates of RMB.
4. Multiple core biopsies are preferred over FNA.

Management

PN and NS Approaches

1. Prioritize PN for the management of the cT1a renal mass when intervention is indicated.
2. Prioritize nephron-sparing approaches for patients with an anatomic or functionally solitary kidney, bilateral tumors, known familial RCC, preexisting CKD, or proteinuria.
3. Consider nephron-sparing approaches for patients who are young, have multifocal masses, or comorbidities that are likely to impact renal function in the future.

Radical nephrectomy

1. Physicians should consider RN for patients where increased oncologic potential is suggested by tumor size, RMB, and/or imaging characteristics. 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/proteinuria; and 3) normal contralateral kidney and new baseline eGFR will likely be > 45².

Thermal Ablation

1. Consider TA an alternate approach for management of cT1a renal masses < 3 cm in size. A percutaneous approach is preferred.
2. Both radiofrequency ablation and cryoablation are options.
3. A RMB should be performed prior to TA.
4. Counseling about TA should include information regarding increased likelihood of tumor persistence/recurrence after primary TA, which may be addressed with repeat TA if further intervention is elected.

Active Surveillance

1. For patients with renal masses suspicious for cancer, especially those < 2cm, AS 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 active treatment.
3. When the risk/benefit analysis for treatment is equivocal and the patient prefers AS, physicians should repeat imaging in 3-6 months to assess for interval growth and may consider RMB for additional risk stratification.
4. When the oncologic benefits of intervention outweigh the risks of treatment and competing risks of death, physicians should recommend active treatment. In this setting, AS may be pursued only if the patient understands and is willing to accept the associated oncologic risk

Factors Favoring AS/Expectant Management

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

Principles Related to PN

1. Prioritize preservation of renal function through efforts to optimize nephron mass preservation and avoidance of prolonged warm ischemia.
2. Negative surgical margins should be a priority. The extent of normal parenchyma removed should be determined by surgeon discretion taking into account the clinical situation; tumor characteristics including growth pattern, and interface with normal tissue. Enucleation should be considered in patients with familial RCC, multifocal disease, or severe CKD to optimize parenchymal mass preservation.

Surgical Principles

1. In the presence of clinically concerning regional lymphadenopathy, lymph node dissection should be performed for staging purposes.
2. Adrenalectomy should be performed if imaging and/or intraoperative findings suggest metastasis or direct invasion.
3. A minimally invasive approach should be considered when it would not compromise oncologic, functional and perioperative outcomes.
4. Pathologic evaluation of the adjacent renal parenchyma should be performed after PN or RN to assess for possible nephrologic disease, particularly for patients with CKD or risk factors for developing CKD.

1. Focus is on clinically localized renal masses suspicious for RCC in adults, including solid enhanced tumors and Bosniak 3 and 4 complex cystic lesions. 2. ml/min/1.73m².

Evaluation/Diagnosis: Statements 1-3

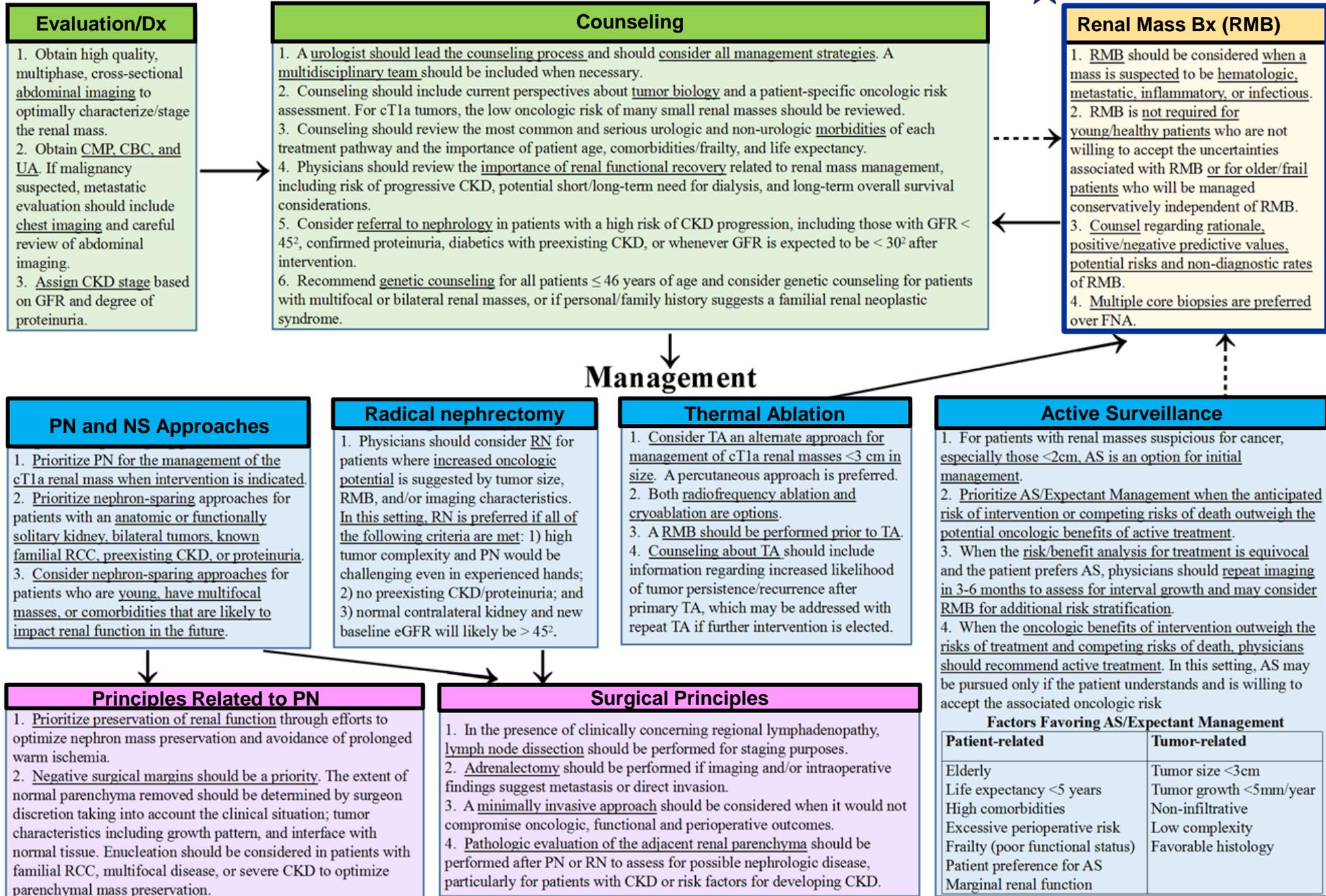
Counseling: Statements 4-9

Evaluation: specific recommendations about imaging, laboratory evaluation, metastatic workup, and staging of CKD are provided

Counseling: a urologist should lead the counseling process and a multidisciplinary team should be included when necessary. Counseling should address oncologic/functional issues, and potential morbidities. Specific recommendations for genetic counseling or referral to nephrology are also provided

Please refer to the final Guidelines document for important details about each of these issues

Renal Mass and Localized Renal Cancer¹



1. Focus is on clinically localized renal masses suspicious for RCC in adults, including solid enhanced tumors and Bosniak 3 and 4 complex cystic lesions. 2. ml/min/1.73m².

Renal Mass Biopsy (RMB)

Statements 10-11

Renal mass biopsy should be considered when a mass is suspected to be hematologic, metastatic, inflammatory, or infectious. (Clinical Principle)

Beyond this RMB should be obtained on a utility-based approach. For instance, RMB is **not** required for young or healthy patients who are unwilling to accept the uncertainties associated with RMB or for older or frail patients who will be managed conservatively independent of RMB findings. (Expert Opinion)

Please refer to the final Guidelines document for important details about each of these issues

RMB

Statements 12-13

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

- Safe: hematoma (4.9%), clinically significant pain (1.2%), gross hematuria (1.0%), PTX (0.6%) and hemorrhage requiring transfusion (0.4%). No reported cases of RCC tumor seeding in the contemporary literature
- Positive bx can be trusted: Sensitivity 98%, specificity 96%, and PPV 99.8%.
- Non-diagnostic rate ≈14%, can be substantially reduced with repeat biopsy
- Histologic eval. RCC subtype very accurate, but accuracy for grade variable
- Non-malignant bx result may not truly indicate that a benign entity is present

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

Partial Nephrectomy (PN) and Nephron-Sparing Approaches



1. Prioritize PN for the management of the cT1a renal mass when intervention is indicated.
2. Prioritize nephron-sparing approaches for patients with an anatomic or functionally solitary kidney, bilateral tumors, known familial RCC, preexisting CKD, or proteinuria.
3. Consider nephron-sparing approaches for patients who are young, have multifocal masses, or comorbidities that are likely to impact renal function in the future.



Principles Related to PN

1. Prioritize preservation of renal function through efforts to optimize nephron mass preservation and avoidance of prolonged warm ischemia.
2. Negative surgical margins should be a priority. The extent of normal parenchyma removed should be determined by surgeon discretion taking into account the clinical situation; tumor characteristics including growth pattern, and interface with normal tissue. Enucleation should be considered in patients with familial RCC, multifocal disease, or severe CKD to optimize parenchymal mass preservation.

PN and Nephron-Sparing Approaches

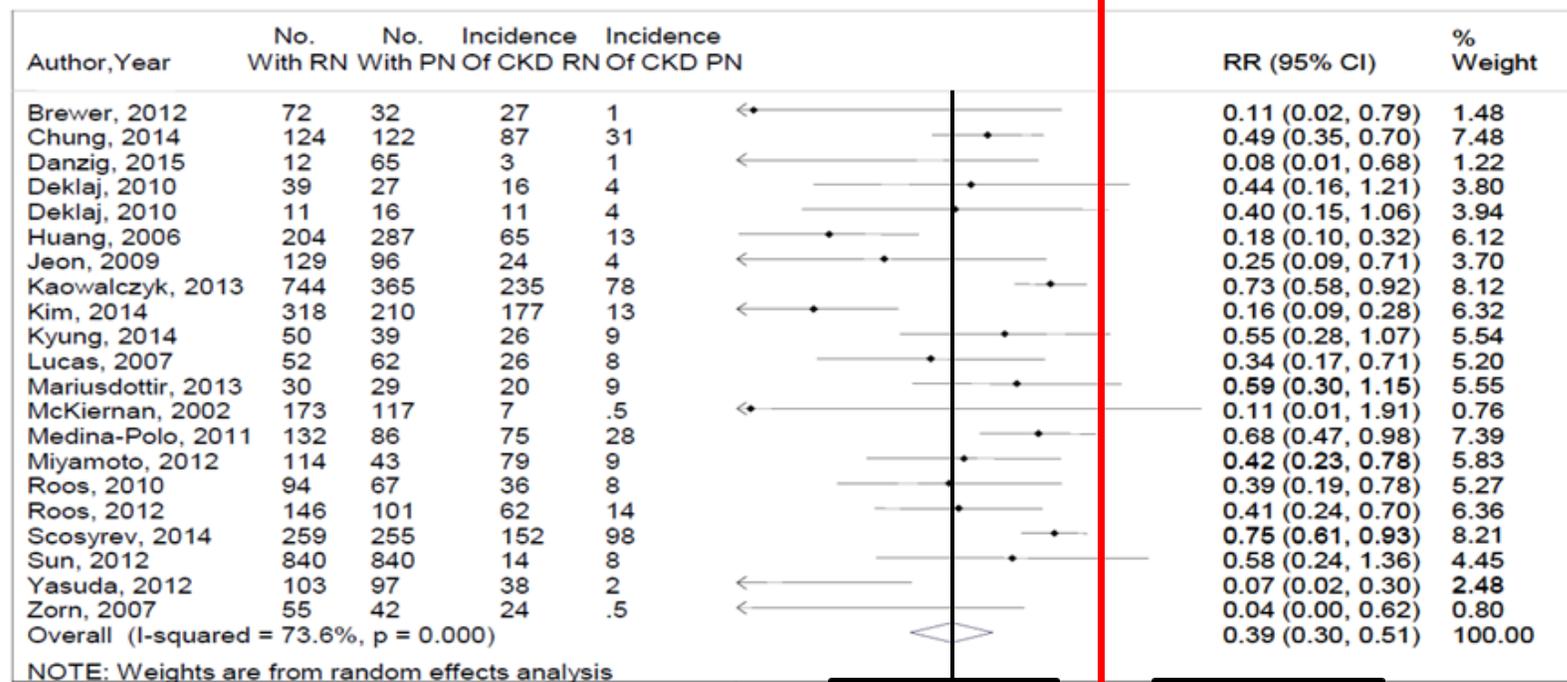
Principles Related to PN

Statement 14

Physicians 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)

- EORTC 30904 and AHRQ Metanalysis: PN provides similar oncologic outcomes as RN for appropriately selected patients. PN also provides more favorable LRF survival when compared to single session of TA
- Many SRM's have low oncologic risk and RN is therapeutic overkill, and should be avoided if possible
- Morbidity: PN can be associated with urologic complications but most can be successfully managed with conservative measures

Meta-analysis of the Incidence of Stage 3 CKD with RN vs. PN



Risk Ratio and 95% Confidence Intervals of Incidence of CKD stage 3

CKD = chronic kidney disease; No. = number; PN = partial nephrectomy; RN = radical nephrectomy; RR = risk ratio; TA = thermal ablation; WMD = weighted mean difference
 Note: The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Statements 15-16

Physicians 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)

Physicians should consider nephron-sparing approaches 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, such as moderate to severe hypertension, diabetes mellitus, recurrent urolithiasis, or morbid obesity. (Conditional Recommendation; Evidence Level: Grade C)

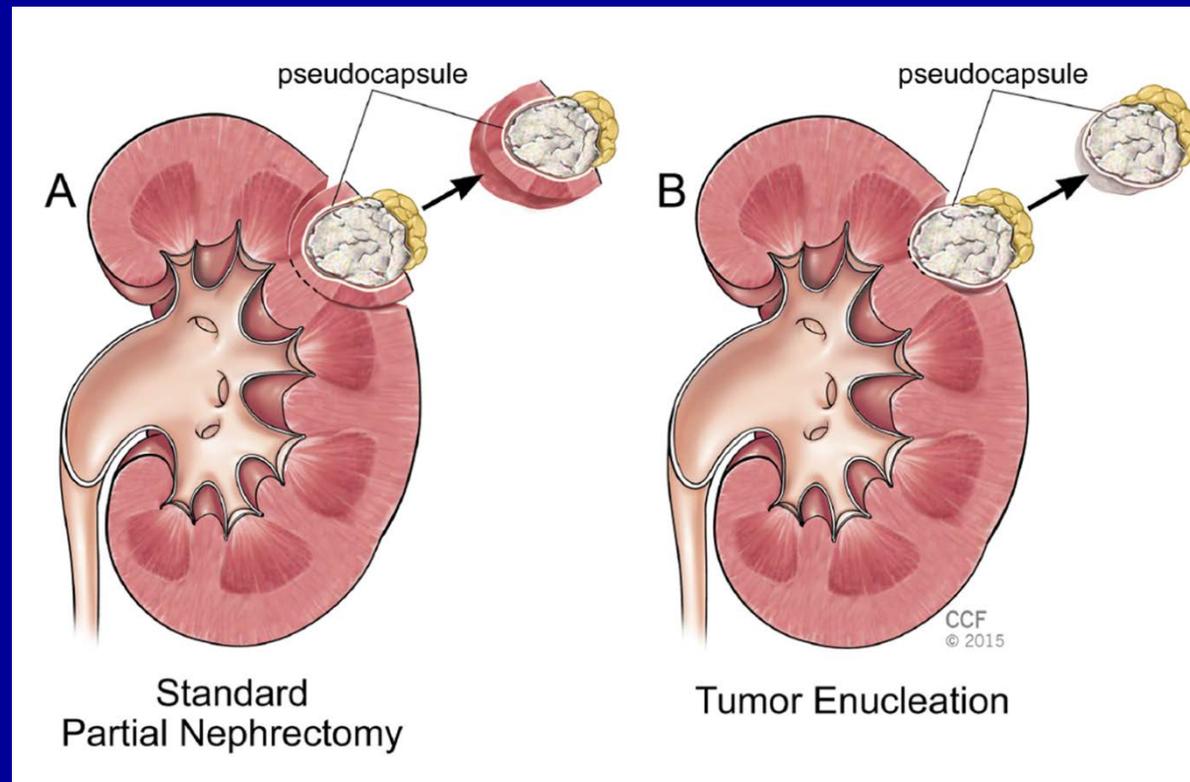
Principles for PN: Statements 17-18

In patients who elect PN, physicians should prioritize preservation of renal function through efforts to optimize nephron mass preservation and avoidance of prolonged warm ischemia. (Expert Opinion)

For patients undergoing PN, negative surgical margins should be a priority. The extent of normal parenchyma removed should be determined by surgeon discretion taking into account the clinical situation, 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)

TE versus SPN for Sporadic RCC?

Current data suggest that with appropriate patient selection (homogeneous, well ncapsulated, etc), TE can provide strong outcomes, but exact criteria for selection are not well-defined, and we will need prospective study to support TE for more routine use in sporadic RCC



Indications for TE: Panel Recommendations

- Familial RCC
- Multifocal Disease
- Severe CKD, near dialysis, where preserving parenchymal mass is essential
- Beyond this TE can be considered for sporadic RCC based on surgeon discretion taking into account the clinical situation and tumor characteristics including growth pattern and interface with normal tissue

RN and Surgical Principles

Partial Nephrectomy (PN) and Nephron-Sparing Approaches

1. Prioritize PN for the management of the cT1a renal mass when intervention is indicated.
2. Prioritize nephron-sparing approaches for patients with an anatomic or functionally solitary kidney, bilateral tumors, known familial RCC, preexisting CKD, or proteinuria.
3. Consider nephron-sparing approaches for patients who are young, have multifocal masses, or comorbidities that are likely to impact renal function in the future.

Radical nephrectomy

1. Physicians should consider RN for patients where increased oncologic potential is suggested by tumor size, RMB, and/or imaging characteristics. 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/proteinuria; and 3) normal contralateral kidney and new baseline eGFR will likely be $> 45\%$.

Principles Related to PN

1. Prioritize preservation of renal function through efforts to optimize nephron mass preservation and avoidance of prolonged warm ischemia.
2. Negative surgical margins should be a priority. The extent of normal parenchyma removed should be determined by surgeon discretion taking into account the clinical situation; tumor characteristics including growth pattern, and interface with normal tissue. Enucleation should be considered in patients with familial RCC, multifocal disease, or severe CKD to optimize parenchymal mass preservation.

Surgical Principles

1. In the presence of clinically concerning regional lymphadenopathy, lymph node dissection should be performed for staging purposes.
2. Adrenalectomy should be performed if imaging and/or intraoperative findings suggest metastasis or direct invasion.
3. A minimally invasive approach should be considered when it would not compromise oncologic, functional and perioperative outcomes.
4. Pathologic evaluation of the adjacent renal parenchyma should be performed after PN or RN to assess for possible nephrologic disease, particularly for patients with CKD or risk factors for developing CKD.

Statement 19

Physicians should consider RN for patients with a solid or Bosniak 3/4 complex cystic renal mass where increased oncologic potential is suggested by tumor size, RMB, and/or imaging characteristics and in whom active treatment is planned. (Conditional 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/1.73m². (Expert Opinion)

- Increased oncologic potential correlates with:
 - Increased tumor size: directly correlates as continuous variable
 - High grade, unfavorable histology (if RMB performed)
 - Infiltrative appearance
 - Locally invasive features (possible invasion of fat, venous, or LN involvement)

Role of RN

Well-Defined Criteria for Patient Selection

In addition to increased oncologic risk, if the following 3 criteria are all present, then RN is preferred:

- High tumor complexity, PN would be challenging even in experienced hands
→ increased risk morbidity, less normal parenchyma can be saved in some of these cases
- No preexisting CKD or proteinuria (as already discussed, these are indications for PN if possible)
- Normal contralateral kidney that will likely provide eGFR of >45 ml/min/1.73m²
- Otherwise PN should be considered if feasible

Surgical Principles: Statements 20-23

Specific recommendations regarding the following issues are provided:

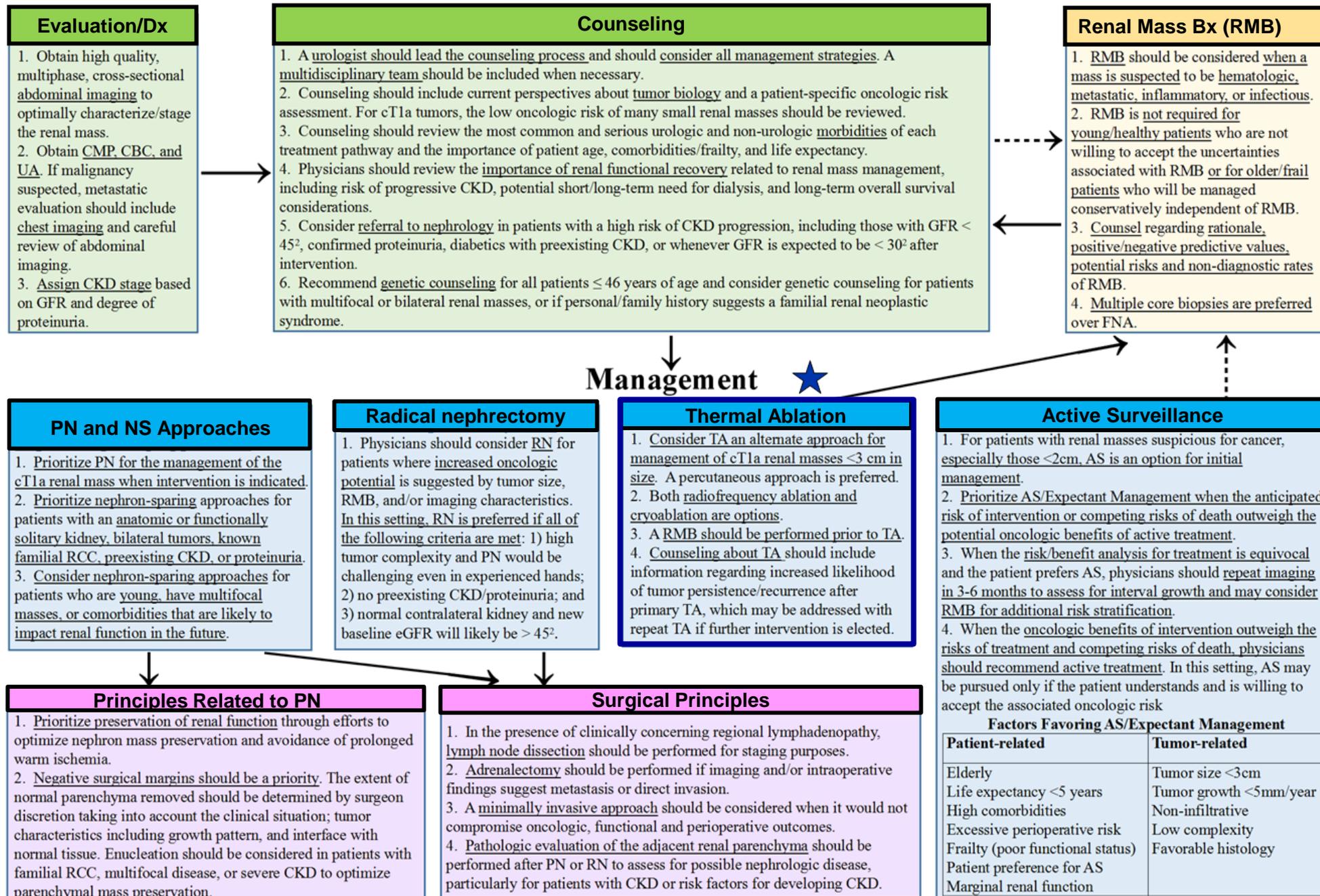
For patients who are undergoing surgical excision of a renal mass with clinically concerning regional **lymphadenectomy**, physicians should perform a lymph node dissection for staging purposes. (Expert Opinion)

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

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)

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

Renal Mass and Localized Renal Cancer¹



1. Focus is on clinically localized renal masses suspicious for RCC in adults, including solid enhanced tumors and Bosniak 3 and 4 complex cystic lesions. 2. ml/min/1.73m².

Thermal Ablation

Statements 24-27

Physicians should consider thermal ablation (TA) as an alternate approach for the management of cT1a renal masses <3 cm in size.

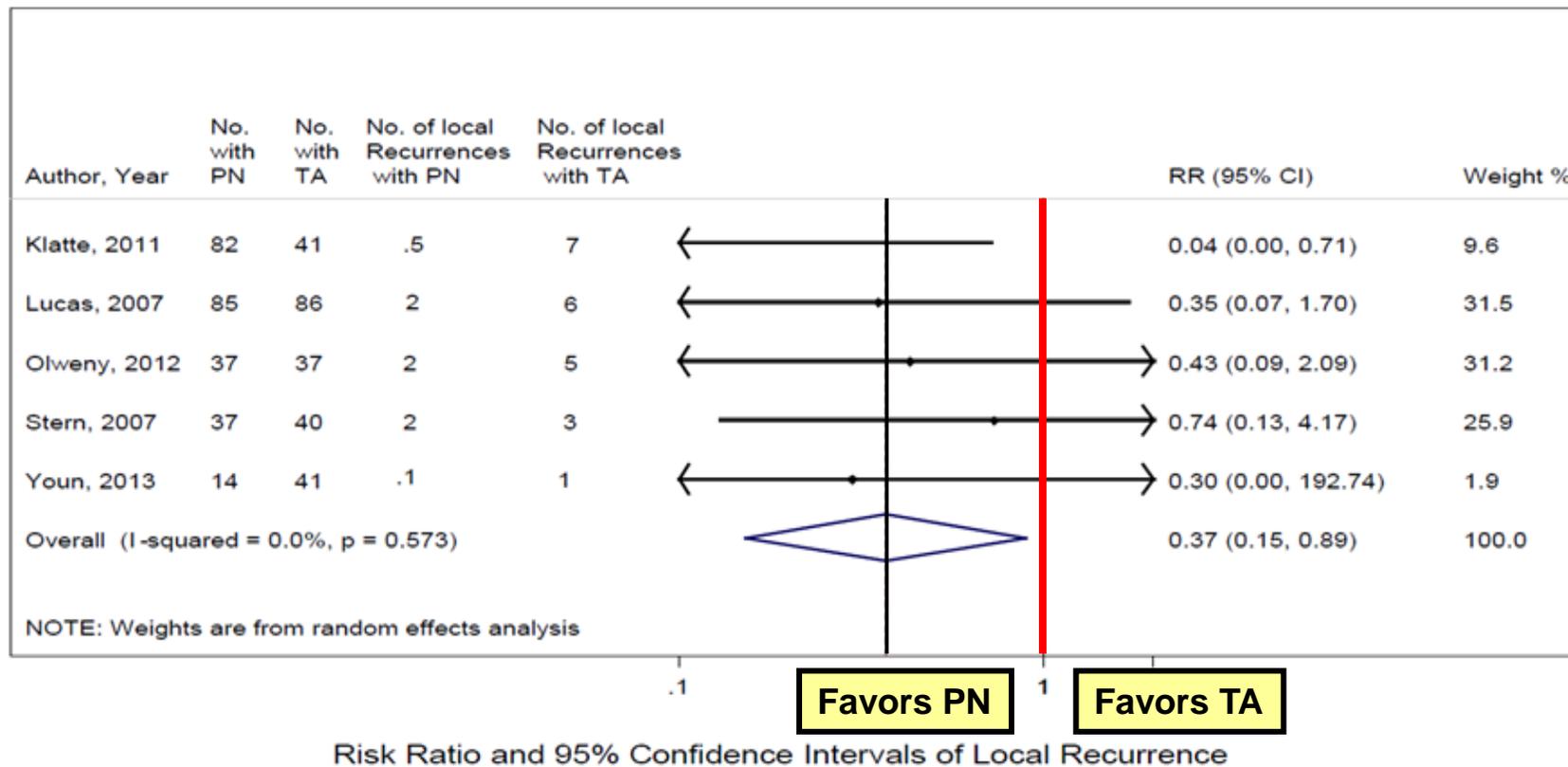
Counseling about TA should include information regarding an increased likelihood of tumor persistence or local recurrence after primary thermal ablation relative to surgical extirpation, which may be addressed with repeat ablation if further intervention is elected

For patients who elect TA, a percutaneous technique is preferred. Both RFA and cryoablation are options. RMB should be performed prior to ablation

Please refer to the final Guidelines document for important details about each of these issues

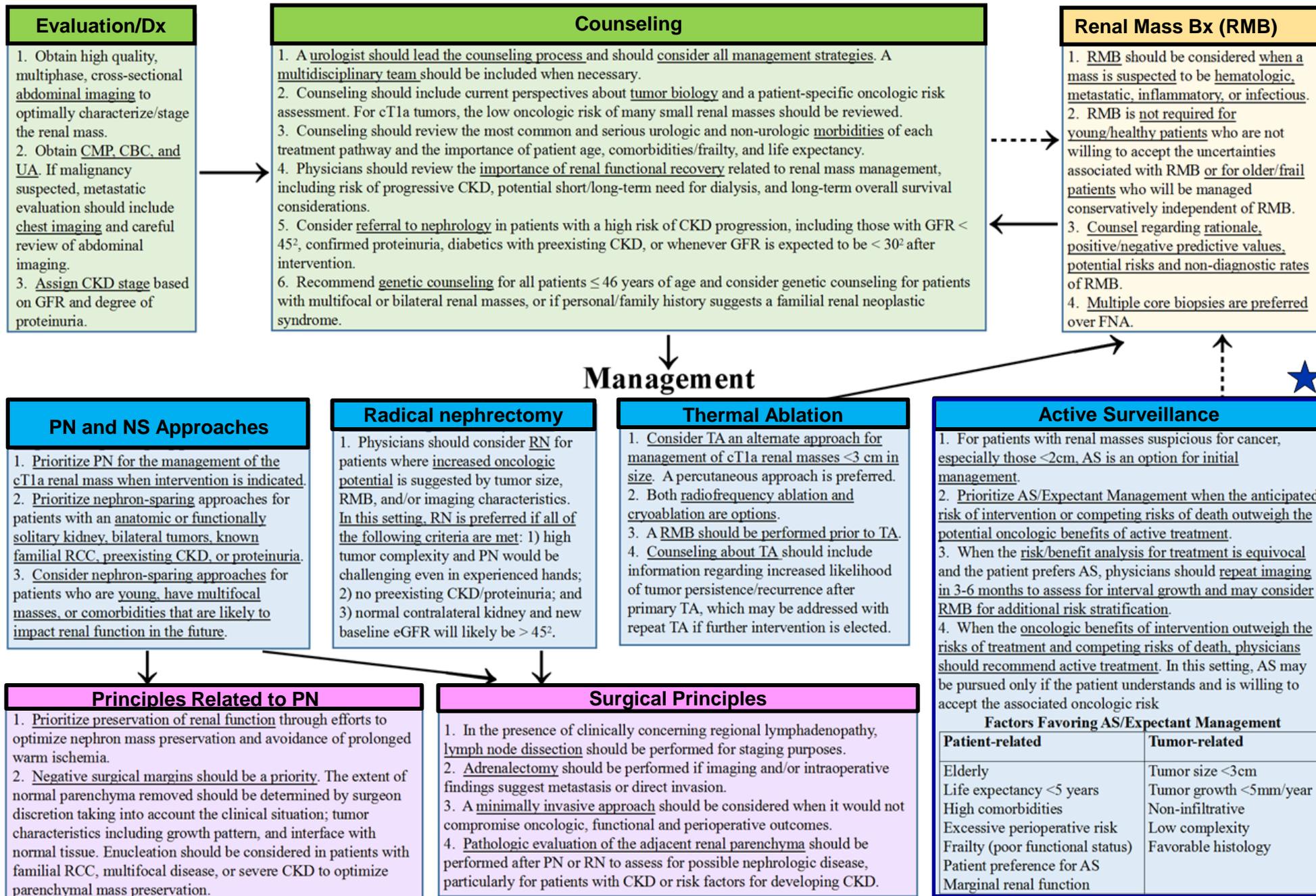
Meta-analysis of local recurrence (LR) rates for PN vs. primary TA

(Studies with follow-up of 48 months \pm 12 months)



CI = confidence interval; N = number; PN = partial nephrectomy; RN = radical nephrectomy; RR = risk ratio for local recurrence; TA = thermal ablation
 Note: The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Renal Mass and Localized Renal Cancer¹



AS and Expectant Management

Statements 28-31

For patients with small solid or Bosniak 3/4 complex cystic renal masses, especially those <2cm, AS is an option for initial management (*Even in healthy patients*).

Shared-decision making about AS/Expectant Management versus Intervention requires careful consideration of the anticipated risks of intervention and competing risks of death versus the potential oncologic benefits of active treatment.

Please refer to the final Guidelines document for important details about each of these issues

Patient/tumor related factors favoring AS/Expectant Management versus Intervention

	Patient-related factors	Tumor factors
Favor AS or Expectant Management	<ul style="list-style-type: none"> Elderly Life expectancy <5 years High comorbidities Excessive perioperative risk Poor functional status Marginal renal function Patient preference to avoid risks of Rx 	<ul style="list-style-type: none"> Tumor size <3cm Tumor growth <5mm/year Non-infiltrative on imaging Low complexity Favorable histology (if RMB performed)
Favor Intervention	<ul style="list-style-type: none"> Young Life expectancy >5 years Low comorbidity Acceptable periop risk Good functional status Anticipate adequate function following intervention Patient preference for Rx 	<ul style="list-style-type: none"> Tumor size >3cm Tumor growth >5mm/year Infiltrative on imaging High complexity Unfavorable histology (if RMB performed)

AUA Guideline for Renal Mass and Localized Kidney Cancer: Panel: Thank You!

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