Management of Renal Masses and Localized Renal Cell Carcinoma: Current State of the Evidence

Focus of This Summary

This is a summary of a systematic review that evaluated the recent evidence regarding the benefits and adverse effects of strategies for evaluating and treating patients with a renal mass suspicious for localized renal cell carcinoma. This review includes 147 studies reported in 150 publications from January 1, 1997, through May 1, 2015. The full report, listing all studies, is available at *www.effectivehealthcare.ahrq.gov/renal-cancer*. This summary is provided to assist in informed clinical decisionmaking. However, reviews of evidence should not be construed to represent clinical recommendations or guidelines.

Background

Kidney cancer affects approximately 65,000 new patients each year, with more than 13,000 deaths annually. Renal cell carcinoma accounts for more than 94 percent of kidney malignancies. The 5-year survival rates for localized renal cell carcinoma range from greater than 85 percent to 95 percent, depending on the stage of the tumor.

All imaging-enhanced solid renal masses and cystic lesions with solid components are suspicious for renal cell carcinoma. About 20 percent of surgically resected renal masses are benign. Most tumors are detected incidentally during an evaluation for unrelated or nonspecific symptoms. Percutaneous renal mass sampling of solid masses may be offered as a diagnostic adjunct to imaging studies such as computed tomography, magnetic resonance imaging, or ultrasonography. Percutaneous renal mass sampling can be performed by fine needle aspiration or core biopsy.

Several options exist for managing clinically localized renal masses suspicious for renal cell carcinoma, including active surveillance, thermal ablation, and surgery (partial or radical nephrectomy). Surgical removal (either partial or radical nephrectomy) is the gold standard for treating renal cell carcinoma. The National Comprehensive Cancer Network (NCCN) Guideline recommends partial nephrectomy as standard treatment for patients with clinical stage T1a tumors (≤4 cm in diameter) and T1b tumors (4–7 cm) and recommends radical nephrectomy for patients for whom partial nephrectomy is not feasible. Thermal ablation and active surveillance are considered options for patients with clinical stage T1a tumors, although these strategies are generally reserved for less-healthy patients. Active surveillance has emerged as a primary management option for patients with a limited life expectancy or with extensive comorbidities. Radical nephrectomy is recommended as the standard of care for most patients with clinical stage T2 tumors.

This systematic review sought to determine the effectiveness and comparative effectiveness of strategies for evaluating and treating patients with a renal mass suspicious for clinical stage T1 or T2 renal cell carcinoma.

Conclusions

Diagnostic evaluation

- No current composite model* reliably predicts malignancy at initial diagnosis in patients with renal masses limited to the kidney parenchyma without evidence for regional or distant metastases.
  - Tumor size and male sex are the factors that are statistically significantly associated with malignancy.
- Percutaneous renal mass sampling using core biopsy is a low-risk procedure. However, its usefulness is limited by a 14-percent nondiagnostic rate and data indicating that 37 percent of patients with a negative biopsy result had malignant disease found during surgery.

Management strategies

- Overall survival and cancer-specific survival rates were generally similar across management strategies. The local recurrence rate was higher with thermal ablation than with radical or partial nephrectomy.
- Perioperative outcomes (blood loss and transfusion rates) were lower with thermal ablation than with either type of nephrectomy.
- Thermal ablation and partial nephrectomy offer improved renal functional outcomes over radical nephrectomy.
- Although active surveillance may have reasonable survival outcomes in selected populations, comparative data are lacking.
- While evidence does not support one management strategy over another, patient factors (e.g., comorbidities, life expectancy), tumor characteristics (e.g., size, location), and patient values and preferences play important roles in decisionmaking.

* Composite models include the use of a combination of demographics, clinical characteristics, blood and urine test results, and tumor imaging characteristics.

AHRQ Agency for Healthcare Research and Quality
Effective Health Care Program

Overview of Clinical Research Evidence for Diagnostic Evaluation

Preoperative composite profiles (*see Appendix Table 1*):

- While preoperative composite profiles were not consistently predictive of malignancy in patients with renal masses limited to the kidney parenchyma without evidence for regional or distant metastases (●○○), some other associations were observed:
  - Increased tumor size and male sex were consistently associated with an increased risk of malignancy (●●○).
  - An increased RENAL nephrometry score** was also predictive of malignancy (●○○).

Percutaneous renal mass sampling (*see Appendix Table 2*):

- Studies of percutaneous renal mass sampling primarily involved core biopsy, which had a sensitivity of 97.5 percent, specificity of 96.2 percent, and a positive predictive value of 99.8 percent. However, core biopsy had a negative predictive value of 68.5 percent and a nondiagnostic rate of 14 percent (●●○).
  - The most common direct complications associated with percutaneous renal mass sampling were hematoma (4.9%) and significant pain (1.2%) (●○○).
  - Of those patients with a nondiagnostic biopsy result who underwent surgery, 90.4 percent had malignant tumors.
  - Repeat biopsy led to a diagnosis in 80 percent of patients who had initially nondiagnostic biopsy results.

** The RENAL Nephrometry Scoring System is described in a footnote accompanying Appendix Table 1.

Strength of Evidence Scale†

High:	●●●	High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect.
Moderate:	●●○	Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.
Low:	●○○	Low confidence that the evidence reflects the true effect. Further research is likely to change our confidence in the estimate of effect and is likely to change the estimate.
Insufficient:	○○○	Evidence either is unavailable or does not permit a conclusion.

† The overall evidence grade was assessed based on the ratings for the following domains: study limitations, directness, consistency, precision, and reporting bias. Other domains that were considered, as appropriate, included dose-response association, plausible confounding, and strength of association (i.e., magnitude of effect). For additional details on the methodology used to assess strength of evidence, please refer to: Owens DK, Lohr KN, Atkins D, et al. AHRQ series paper 5: grading the strength of a body of evidence when comparing medical interventions—Agency for Healthcare Research and Quality and the Effective Health-Care Program. J Clin Epidemiol. 2010 May;63(5):513-23. PMID: 19595577.

Overview of Clinical Research Evidence for Management Strategies

Table 1: Key Findings and Strength of Evidence for the Management Strategies Used for Localized Renal Cancer (*For additional details, see Appendix Tables 3 and 4.*)

Outcome	Partial Nephrectomy vs. Thermal Ablation	Partial Nephrectomy vs. Radical Nephrectomy	Radical Nephrectomy vs. Thermal Ablation	Radical Nephrectomy vs. Active Surveillance
Cancer-Specific Survival	Similar (●○○)	Similar (●●○)	Similar (●●○)	Similar[a] (●○○)
Overall Survival at 5 Years	Favors PN (●○○)[b]	Similar (●○○)	(○○○)	Similar (●○○)
Local Recurrence-Free Survival	Favors PN (●●○)	Similar (●●○)	Favors RN (●○○)	(○○○)
Metastasis-Free Survival	Similar (●●○)	Similar (●○○)	Similar (●○○)	Similar (●○○)
Renal Function	Similar (●○○)	Better with PN (●●○)	Better with TA (●●○)	Better with AS (●○○)
Perioperative Outcomes: Estimated Blood Loss and Transfusion Rates	Lower with TA (●●○)	Lower with RN (●●○)	Similar (●○○)	(○○○)
Perioperative Outcomes: Length of Hospital Stay	Lower with TA (●●○)	Similar (●●○)	Lower with TA (●○○)	(○○○)
Urological and Nonurological Complications[c]	Varied across studies (●○○)	Lower with RN (●○○)	Varied across studies (●○○)	(○○○)
Acute Kidney Injury Rates	Similar (●○○)	Similar (●○○)	Similar (●○○)	(○○○)
Minor and Major Clavien[d] Complication Rates	Similar (●○○)	Similar (●○○)	Similar[e] (●○○)	(○○○)

AS = active surveillance; PN = partial nephrectomy; RN = radical nephrectomy; TA = thermal ablation

[a] This finding was based on a single study in older patients (age ≥75 years) wherein the radical nephrectomy group had tumors with greater oncologic potential.

[b] The improved survival with partial nephrectomy was likely because of the older age and higher comorbidity rates in the thermal ablation group.

[c] Urological complications included hemorrhage, urine leakage, hematuria, loss of kidney function, ureteral injury, or urinary tract infection. Nonurological complications included hematologic (thromboembolic), gastrointestinal, cardiovascular, respiratory, neurological, and wound complications or infectious disease.

[d] The Clavien-Dindo classification system is used to grade complications from urological surgical interventions: Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004;244:931-7. PMID: 15273542.

[e] This finding was based on a single study in 60 patients.

Gaps in Knowledge and Other Issues

- The applicability of results from analyses of renal mass biopsy are limited by:
  - The localization and characteristics of the biopsied mass
  - The significant heterogeneity in tumor characteristics observed in renal tumors
  - The lack of a standardized biopsy protocol
  - Weak study designs (e.g., retrospective studies)
  - The lack of reporting on the levels of surgeon/pathologist/radiologist expertise
  - Poor reporting of clinical staging
  - Inconsistent reporting of treatment outcomes
- Currently, there is no composite model that reliably predicts malignancy at initial diagnosis in patients with renal masses limited to the kidney parenchyma without evidence for regional or distant metastases.
- Most of the patient populations in the reported composite models had a mean age of 60 years or older, and details about their specific preoperative or tumor characteristics were limited. As such, younger patients and those with other comorbidities may have differing risks of malignancy from those reported in the studies.
- The evidence regarding management strategies for renal masses suspicious for localized renal cell carcinoma is based almost entirely on retrospective studies. Selection bias plays a prominent role in treatment selection, thereby limiting the applicability of the findings from retrospective observational studies to specific patient groups.
- Although patient demographics, clinical characteristics, and disease stage are important in evaluating interventions used to manage renal cancer, all these data were dramatically underreported.
- The strength of evidence was insufficient to permit determination of the effectiveness of any of the treatment strategies for quality of life.
- The lack of sufficient data comparing active surveillance with other treatment approaches limits the applicability of the review's findings pertaining to this management strategy.
- The emergence of new technologies could also affect the applicability of the results of studies related to thermal ablation and minimally invasive nephrectomies.
- Additional research into genetic tools for subtyping tumors is needed to improve prediction of outcomes in patients.

Key Points for Discussions With Patients and Caregivers

- Patients might be aware that biopsies are performed for the diagnosis of various types of cancer. When considering a biopsy to diagnose renal carcinoma, clinicians may wish to discuss with patients whether a biopsy is warranted and what the potential benefits and risks of doing a biopsy are based on their personal and tumor characteristics. A consultation with a urologist may also be suggested.
- Based on the patient's personal and tumor characteristics, the clinician may wish to discuss which treatment options might be suitable and what their respective benefits and harms could be.

Ordering Information

For electronic copies of this clinician research summary and the full systematic review, visit *www.effectivehealthcare.ahrq.gov/renal-cancer*.

Source

The information in this summary is based on *Management of Renal Masses and Localized Renal Cancer*, Comparative Effectiveness Review No. 167, prepared by the Johns Hopkins University Evidence-based Practice Center under Contract No. 290-2012-00007-I for the Agency of Healthcare Research and Quality, February 2016. Available at *www.effectivehealthcare.ahrq.gov/renal-cancer*. This summary was prepared by the John M. Eisenberg Center for Clinical Decisions and Communications Science at Baylor College of Medicine, Houston, TX.

(Appendix begins on Page 4)

Appendix

Appendix Table 1: Summary of Findings and Strength of Evidence for Preoperative Predictors of Malignant or Benign Pathology of Renal Tumors

Predictor	No. of Studies (N)	Key Findings	Odds Ratio (95% CI)	Strength of Evidence
Tumor Size	12 (9,401)	A positive relationship between tumor size and malignancy risk was found.	1.326 (1.220 to 1.430)[a]	●●○
Sex	16 (10,475)	Men were more likely to have malignant tumors.	2.707 (2.391 to 3.023)	●●○
Incidental Presentation	5 (4,229)	No significant relationship was found.	0.78 (0.48 to 1.08)	●●○
Preoperative Composite Models	20 (12,149)	None reliably predicted malignancy.	NA	●○○
Tumor Characteristics	9 (6,942)	A positive relationship between the RENAL nephrometry score[b] and malignancy risk was found.	NA	●○○
Age	15 (10,150)	No significant relationship was found.	0.998 (0.993 to 1.004)[c]	●○○

CI = confidence interval; N = number of subjects; NA = not applicable

[a] The odds ratio represents the effect size per tumor size in centimeters.

[b] The RENAL nephrometry scoring system is an objective scoring system that describes the "complexity" of solid renal masses based on these characteristics: R = radius (size) of the tumor; E = exophytic or endophytic nature of the tumor; N = nearness of the tumor to the renal collecting system; A = location of the tumor in the anterior or posterior aspect of the kidney; L = location of the tumor relative to the renal polar anatomy.

[c] The odds ratio represents the effect size per age in years.

Appendix Table 2: Summary of Findings and Strength of Evidence for Accuracy and Harms of Percutaneous Renal Mass Sampling With Biopsy

Procedure	Outcome	No. of Studies (N)	Key Findings	Strength of Evidence
Biopsy	Diagnostic accuracy for malignancy	18 (2,203)[a]	Sensitivity: 97.5% Specificity: 96.2% Positive predictive value: 99.8% Negative predictive value: 68.5% Nondiagnostic rate: 14%	●●○
	Harms	16 (2,422)[b]	A small but notable proportion of patients experienced harms. Hematoma (4.9%) and clinically significant pain (1.2%) were the most common direct complications. Tumor seeding was not reported in any study included in the review. Studies in which harms, if any, were reported were inconsistent.	●○○

N = number of subjects

[a] All were open-biopsy studies.

[b] Fifteen of the studies concerned open biopsy, and one concerned fine needle aspiration.

(Appendix continued on Page 5)

Appendix Table 3: Summary of Findings and Strength of Evidence for the Comparative Effectiveness of Localized Renal Mass Treatment Strategies for Oncologic Outcomes and Overall Survival

Outcome	No. of Studies (N)	Key Findings	Risk Ratio or Hazard Ratio (95% CI)	SOE
Partial Nephrectomy (PN) vs. Thermal Ablation (TA)				
Cancer-specific survival	9 (14,625)	A meta-analysis suggested better survival with PN, but it was driven mainly by one large study with a high risk of bias.	RR of mortality 0.33 (0.25 to 0.44)	●○○
Metastasis-free survival	8 (2,462)	Similar results	RR of metastasis 1.53 (0.27 to 8.63)	●●○
Local recurrence-free survival	14 (3,916)	Better with PN. *Allowing for multiple retreatments led to a more comparable efficacy rate for TA.*	RR of recurrence 0.37 (0.15 to 0.89) RR of recurrence 1.21 (0.58 to 2.50) for studies of secondary efficacy of TA (secondary efficacy refers to retreatment with TA)	●●○
Overall survival	13 (8,451)	Better with PN, likely because of older age and more comorbidities in the TA group.	RR of mortality 0.39 (0.25 to 0.61)	●○○
Radical Nephrectomy (RN) vs. Partial Nephrectomy (PN)				
Cancer-specific survival	37 (77,671) RCT: 1 Inst: 25 SEER: 11	Similar results across SEER and institutional studies.[a] The RCT reported few cancer deaths, which did not permit firm conclusions.	SEER studies: HR 1.18 (0.94 to 1.42) Non-SEER studies: HR 1.08 (0.87 to 1.33)	●●○
Metastasis-free survival	13 (2,513)	Similar results	RR of metastasis 0.35 (0.08 to 1.46)	●○○
Local recurrence-free survival	21 (10,090)	Similar results	RR of recurrence 0.78 (0.52 to 1.16)	●●○
Overall survival	36 (72,308) RCT: 1 Inst: 25 SEER: 10	Similar results, but studies were inconsistent. SEER analyses showed better survival with PN, but institutional cohort studies and the RCT showed similar survival in both groups.	SEER studies: HR 1.23 (1.13 to 1.33) Non-SEER studies: HR 1.09 (0.88 to 1.34)	●○○
Radical Nephrectomy (RN) vs. Thermal Ablation (TA)				
Cancer-specific survival	2 (10,803)	Similar results	NA	●●○
Metastasis-free survival	2 (217)	Similar results	NA	●○○
Local recurrence-free survival	2 (217)	Better results with RN, but all studies had a small sample size.	NA	●○○
Radical Nephrectomy (RN) vs. Active Surveillance (AS)				
Cancer-specific survival	1 (251)	Similar results, despite the greater oncologic potential of tumors treated with RN.	NA	●○○
Metastasis-free survival	1 (251)	Similar results	NA	●○○
Overall survival	1 (251)	Similar results but with a wide CI.	HR 0.75 (0.45 to 1.26)	●○○

CI = confidence interval; HR = hazard ratio; Inst = institutional cohort studies; N = number of subjects; NA = not applicable; RCT = randomized controlled trial; RR = risk ratio; SEER = Surveillance, Epidemiology, and End Results; SOE = strength of evidence

[a] SEER studies were conducted using the Surveillance, Epidemiology, and End Results (SEER) dataset, while institutional studies were conducted among cohorts of patients in academic or clinical institutions.

(Appendix continued on Page 6)

Appendix Table 4: Summary of Findings and Strength of Evidence for the Comparative Effects of Renal Mass Treatment Strategies on Renal Outcomes, Perioperative Outcomes, and Harms[a]

Outcome	No. of Studies (N)	Key Findings	Risk Ratio or Hazard Ratio (95% CI)	SOE
Partial Nephrectomy (PN) vs. Thermal Ablation (TA)				
Continuous renal functional outcomes	19 (2,867)	No significant difference in change in eGFR.	WMD 1.0 (−0.2 to 2.1) ml/min/1.73 m^2	●○○
Categorical renal functional outcomes	11 (1,893)	No statistically significant differences in rates of CKD stages ≥3, ≥3b, and ≥4 or in rates of ESRD.	CKD stage ≥3: RR 0.88 (0.60 to 1.30) CKD stage ≥3b: RR 2.78 (0.47 to 16.54) CKD stage ≥4: RR 0.76 (0.54 to 1.07) ESRD: RR 0.92 (0.19 to 4.39)	●○○
Perioperative outcomes	15 (3,356)	Estimated blood loss, transfusion rate, rate of conversion to open surgery, and length of hospital stay all favored TA.	Transfusion: RR 1.62 (1.07 to 2.46)	●●○
Harms	21 (3,746)	Urological and nonurological complications in the PN and TA groups were variable across studies. Rates of AKI and of minor and major Clavien complications were similar.	AKI: RR 1.03 (0.56 to 1.89) Minor Clavien: RR 1.2 (0.9 to 1.7) Major Clavien: RR 1.12 (0.63 to 1.97)	●○○
Radical Nephrectomy (RN) vs. Partial Nephrectomy (PN)				
Continuous renal functional outcomes	34 (9,221)	A larger decrease in eGFR with RN.	WMD −3.6 (−4.1 to −3.2) ml/min/1.73 m^2	●●○
Categorical renal functional outcomes	24 (11,236)	The incidences of all stages of CKD (stage 3 to ESRD) were lower with PN.	CKD stage ≥3: RR 0.39 (0.30 to 0.51) CKD stage ≥3b: RR 0.37 (0.26 to 0.53) CKD stage ≥4: RR 0.76 (0.54 to 1.07) ESRD: RR 0.47 (0.25 to 0.86)	●●○
Perioperative outcomes	23 (6,587) RCT: 1 Ret: 22	Consistently higher estimated blood loss and transfusion rate with PN. Similar rates of conversion to open surgery and lengths of hospital stay.	Transfusion: RR 0.75 (0.60 to 0.94)	●●○
Harms	32 (16,965) RCT: 1 Ret: 31	The RCT showed higher rates of urological complications with PN. Retrospective studies showed higher rates of urological complications with PN but no differences in rates of AKI, minor or major Clavien complications, or nonurological complications.	AKI: RR 1.3 (0.9 to 2.0) Major Clavien: RR 0.71 (0.49 to 1.05) Minor Clavien: RR 0.87 (0.73 to 1.04)	●○○
Radical Nephrectomy (RN) vs. Thermal Ablation (TA)				
Continuous renal functional outcomes	7 (390)	A larger decrease in eGFR with RN.	WMD 9.94 (7.61 to 12.26) ml/min/1.73 m^2	●●○
Categorical renal functional outcomes	4 (1,125)	The rate of CKD (stage ≥3) was higher with RN.	RR 3.48 (1.08 to 11.15)	●●○
Perioperative outcomes	3 (11,404)	No study evaluated estimated blood loss. The rates of blood transfusion were similar. Length of hospital stay favored TA.	Transfusion: RR 1.08 (0.63 to 1.87)	●○○
Harms	7 (2,000)	Inconsistently reported. AKI rates were not significantly different, but data were limited. In the single study reporting minor and major Clavien complication rates, major rates were similar but minor rates were higher with TA (16.0% vs. 2.6%).	AKI: RR 1.57 (0.88 to 2.80)	●○○
Radical Nephrectomy (RN) vs. Active Surveillance				
Continuous renal functional outcomes	2 (334)	The decline in eGFR was less with active surveillance.	NA	●○○
Categorical renal functional outcomes	2 (471)	The rate of new-onset CKD (stage ≥3) was lower with active surveillance (3–6% vs. 40–76%).	NA	●○○

AKI = acute kidney injury; CI = confidence interval; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; ESRD = end-stage renal disease; N = number of subjects; RCT = randomized controlled trial; Ret = retrospective study; RR = risk ratio; SOE = strength of evidence; WMD = weighted mean difference

[a] Harms refer to adverse events directly related to the management strategy.

AHRQ Pub. No. 16(17)-EHC001-3-EF
July 2017
www.ahrq.gov