Management of Renal Masses and Localized Renal Cancer: Systematic Review and Meta-Analysis

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Purpose: Several options exist for management of clinically localized renal masses suspicious for cancer, including active surveillance, thermal ablation and radical or partial nephrectomy. We summarize evidence on effectiveness and comparative effectiveness of these treatment approaches for patients with a renal mass suspicious for localized renal cell carcinoma.

Materials and Methods: We searched MEDLINE®, Embase® and the Cochrane Central Register of Controlled Trials from January 1, 1997 through May 1, 2015. Paired investigators independently screened articles to identify controlled studies of management options or cohort studies of active surveillance, abstracted data sequentially and assessed risk of bias independently. Strength of evidence was graded by comparisons.

Results: The search identified 107 studies (majority T1, no active surveillance or thermal ablation stratified outcomes of T2 tumors). Cancer specific survival was excellent among all management strategies (median 5-year survival 95%). Local recurrence-free survival was inferior for thermal ablation with 1 treatment but reached equivalence to other modalities after multiple treatments. Overall survival rates were similar among management strategies and varied with age and comorbidity. End-stage renal disease rates were low for all strategies (0.4% to 2.8%). Radical nephrectomy was associated with the largest decrease in estimated glomerular filtration rate and highest incidence of chronic kidney disease. Thermal ablation offered the most favorable perioperative outcomes. Partial nephrectomy showed the highest rates of urological complications but overall rates of minor/major complications were similar among interventions. Strength of evidence was moderate, low and insufficient for 11, 22 and 30 domains, respectively.

Conclusions: Comparative studies demonstrated similar cancer specific survival across management strategies, with some differences in renal functional

Abbreviations and Acronyms

AHRQ = Agency for Healthcare Research and Quality

CSS = cancer specific survival

eGFR = estimated glomerular filtration rate

LRFS = local recurrence-free survival

OS = overall survival

PN = partial nephrectomy

RCC = renal cell carcinoma

RCT = randomized controlled trial

RN = radical nephrectomy

SEER = Surveillance, Epidemiology and End Results

SR = systematic review

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References 51 through 88 can be obtained at http://jurology.com/.

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outcomes, perioperative outcomes and postoperative harms that should be considered when choosing a management strategy.

Key Words: carcinoma, renal cell; comparative effectiveness research; disease management; kidney neoplasms; surgical procedures, operative

RENAL masses are a biologically heterogeneous group of tumors ranging from benign neoplasms to cancers that can be indolent or aggressive.[1,2] Although the true incidence of renal masses suspicious for malignancy is unknown, approximately 80% of surgically resected tumors are malignant.[1,3] All solid renal masses and cystic lesions with solid components are suspicious for renal cell carcinoma, which affects approximately 65,000 new patients yearly and has a 5-year mortality rate of 35%.[4]

Several options exist for management of clinically localized renal masses suspicious for RCC, including active surveillance, thermal ablation and surgery. Surgery, including PN and RN, is an option for masses of all sizes (clinical stage T1 or T2), although PN is preferred for lesions smaller than 7 cm in diameter (clinical stage T1).[5] Given the increased incidence of early, low stage tumors without improvement in cancer related deaths, active surveillance has emerged as an option for patients with small renal masses (4 cm or less, clinical stage T1a), a low likelihood of aggressive malignancy, a procedure limiting comorbidity and/or a limited life expectancy. If thermal ablation is used, which may include cryoablation and radio frequency ablation, the ideal circumstance is a small, clinically localized mass (clinical stage T1) and the procedure can be performed laparoscopically or percutaneously. Each management strategy has relative merits and risks in comparison to the others. As such, professional organizations, including the American Urological Association, European Association of Urology and the National Comprehensive Cancer Network®, refrain from defining strict selection criteria (ie patient or tumor) for particular treatment strategies, and selection criteria vary by organizational guidelines.[5–7] Additional controversies exist regarding the ideal management for renal masses of different stages. For example PN has emerged as the recommended treatment for clinical stage T1 renal masses, yet the single RCT comparing RN and PN revealed no difference in overall survival among patients with kidney cancer.[8] We performed this systematic review to better compare the effectiveness of the treatment options, taking into consideration oncologic outcomes, renal functional outcomes and complications, as well as competing health risks of patients with a renal mass suspicious for RCC.

METHODS

Data Sources and Searches

We report results from a broader systematic review.[9] Full details on methods are available from the evidence report. We searched MEDLINE®, Embase® and the Cochrane Central Register of Controlled Trials from January 1, 1997 (the year the TNM Classification of Malignant Tumours staging system for renal cell carcinoma was modified and the distinctions of T1a/T1b and T2a/T2b were created) through May 1, 2015. Therefore, clinical stage definitions are those of the American Joint Committee on Cancer as follows. T1a is defined as tumor 4 cm or smaller, T1b greater than 4 to 7 cm, T2a greater than 7 to 10 cm and T2b greater than 10 cm, N0 as node negative and M0 as no evidence of distant metastases. We also requested information from device manufacturers and searched ClinicalTrials.gov for relevant studies.

Study Selection, Data Extraction and Quality Assessment

Paired investigators independently screened articles to assess eligibility using predefined criteria to identify controlled studies of the management options or single cohort studies of active surveillance (Appendix 1). Paired investigators abstracted data sequentially and independently assessed risk of bias for individual studies. We used the Cochrane Collaboration tool for assessing risk of bias of RCTs.[10] For nonrandomized studies of treatment interventions we used ACROBAT-NRSI (A Cochrane Risk of Bias Assessment Tool: for Non-Randomized Studies of Interventions).[11] Differences between reviewers were resolved through consensus.

Data Synthesis and Analysis

All studies were summarized qualitatively. LRFS was defined as the absence of any persistent or recurrent disease in the treated region of the kidney or associated renal fossa after a single, curative intent initial treatment. This definition included persistent enhancement of any treated mass, a visually enlarging neoplasm, new nodularity, failure of regression in size of the treated lesions and new satellite or port site lesions.

We conducted meta-analyses for outcomes using a random effects model with the DerSimonian and Laird method when there were at least 2 sufficiently homogeneous studies. We identified substantial statistical heterogeneity as an I^2 statistic with a value greater than 50%. All meta-analyses were conducted using Stata® 12.1.

We graded the strength of evidence using the scheme recommended by the Methods Guide for Effectiveness and Comparative Effectiveness Reviews.[12] Strength of evidence is an assessment that goes beyond evidence