

Overall Survival after Partial Versus Radical Nephrectomy for a Small Renal Mass: Systematic Review of Observational Studies

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Abstract

Introduction: In EORTC trial 30904 of partial versus radical nephrectomy overall survival was significantly better in the radical nephrectomy arm. However, many observational studies reported better survival after partial than radical nephrectomy. We present an updated systematic review of observational studies of overall survival after partial versus radical nephrectomy with assessment of quality of evidence.

Methods: The literature search was performed until December 31, 2013, and all studies reporting overall survival after partial vs radical nephrectomy were included in the initial review. Further inclusion criteria for complete review were malignant tumors 7 cm or smaller, or benign tumors of any size, and survival analysis performed with adjustment for confounding variables. Studies not meeting these criteria were excluded from full review because of selection bias in favor of patients treated with partial nephrectomy who were younger and with less advanced tumors.

Results: A total of 34 studies were included in the initial review and 13 were included in the full review. The 13 studies were based on the SEER database (6) or on institutional cohorts (7). In 8 of the 13 studies the estimated hazard ratios were significantly below 1, indicating better overall survival after partial nephrectomy, while in the remaining 5 studies estimated HR was not significantly different from 1. Median HR was 0.80 (interquartile range 0.57 to 0.96, absolute range 0.40 to 1.10).

Conclusions: In most observational studies overall survival was better after partial than after radical nephrectomy. However, because residual confounding could be present despite adjustment for measured covariates, another randomized trial of partial vs radical nephrectomy may be needed to confirm or refute the findings of EORTC 30904.

Key Words: nephrectomy; carcinoma, renal cell

Abbreviations and Acronyms

CCI = Charlson Comorbidity Index

CKD = chronic kidney disease

eGFR = estimated glomerular filtration rate

EORTC = European Organisation for Research and Treatment of Cancer

IV = instrumental variables

OS = overall survival

PN = partial nephrectomy

PS = performance status

RCC = renal cell carcinoma

RCT = randomized controlled trial

RN = radical nephrectomy

SEER = Surveillance, Epidemiology, and End Results

Optimal surgical management of a renal mass suspicious of cT1 RCC in patients with a normal contralateral kidney is a subject of controversy. Historically, most cases of suspected organ confined RCC were managed with radical nephrectomy but in recent years partial nephrectomy has become the new standard of care, primarily driven by evidence from

observational studies. In these studies RN and PN for cT1 tumors resulted in excellent oncologic control with a low risk of recurrence but PN was associated with a lower risk of significant renal dysfunction and better overall survival.¹ In a meta-analysis of 20 observational studies OS was better after PN than after RN, with a pooled HR of 0.80 and a 95% CI of 0.74 to 0.87 ($p < 0.001$), although there was also evidence of statistical heterogeneity, indicating that individual studies were not estimating a treatment effect of the same magnitude.² In 8 of the 20 studies OS was better after RN although there were no statistically significant differences. In the remaining 12 studies OS was better after PN, with a statistically significant difference in 8. Severe chronic kidney disease was significantly

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less likely after PN than after RN in most observational studies. In a meta-analysis of 10 observational studies the pooled estimate of the hazard ratio (PN vs RN) for this end point was 0.39 (95% CI 0.33–0.47), although definitions of severe CKD varied from an estimated glomerular filtration rate of less than 60 mL/minute/1.73 m² to kidney failure.¹

Because these results come from observational studies, they may potentially be influenced by selection bias. Many of these studies had no upper limit on tumor size and, therefore, included patients with locally advanced tumors mostly treated with RN. In addition, many studies did not control for known predictors of OS (eg age or tumor size) that were unequally distributed between PN and RN cases, producing bias in favor of PN in survival analyses. Also, in many of these studies there was a tendency toward lower kidney cancer mortality after PN, which can only be explained by selection bias.

In a small phase II randomized trial D'Armiento et al reported identical OS after PN vs RN (median 8 years in each group).³ However, only 40 patients were enrolled in the study and, thus, power and precision of estimation were low. In contrast, in the only phase III randomized trial (EORTC 30904) of PN vs RN overall survival was significantly better after RN.⁴ In this trial 541 patients with a small (5 cm or less) renal mass and a normal contralateral kidney were randomized to RN (273) or PN (268). At a median followup of 9.3 years for OS, 18% of the patients in the RN and 25% of those in the PN group had died (HR 1.50, 95% CI 1.03–2.16, $p = 0.03$). Death due to kidney cancer occurred in 1.5% of RN and 3.0% of PN subjects ($p = 0.23$).⁴ In the RN vs PN groups eGFR reached less than 60 in 85.7% vs 64.7% (difference 21.0%, 95% CI 13.8%–28.3%), less than 30 in 10.0% vs 6.3% (difference 3.7%, 95% CI –1.0%–8.5%) and less than 15 in 1.5% vs 1.6% (difference –0.1%, 95% CI –2.2%–2.1%).⁵

The increased risk of eGFR less than 60 with RN did not translate into a survival advantage favoring PN. Given that Level 1 evidence from EORTC 30904 contradicted findings previously reported from many observational studies, we thought that observational evidence needed to be carefully examined in an updated systematic review. A previous systematic review and meta-analysis included studies published through February 2011.¹ However, in the last 3 years many additional observational studies have been published. We present an updated systematic review of observational studies of PN vs RN for small renal masses with the end point of OS. Our objectives were to identify all relevant publications, assess the quality of the studies, identify potential mechanisms of uncontrolled confounding in individual studies and summarize available evidence. We also compared the quality of evidence available from observational studies with that provided by EORTC 30904.

Methods

Studies eligible for this systematic review were identified through PubMed®/MEDLINE®, Embase™ and Web of Science® databases using search key words radical nephrectomy, partial nephrectomy, nephron sparing surgery, overall survival

and all cause mortality. We also examined lists of references in review articles and original articles on this subject. The literature search was performed to December 31, 2013 independently by 3 investigators. All studies reporting a comparison of OS after PN vs after RN were included in the initial review. Further inclusion criteria for full review were analyses limited to malignant tumors 7 cm or smaller, or benign tumors of any size and survival analysis performed with adjustment for baseline predictors of OS (such as age or tumor size) that were unequally distributed between PN and RN cases. Studies not meeting these criteria were excluded from full review because they had identifiable selection bias in favor of patients treated with PN who usually were younger and with less advanced tumors.

The information extracted from each publication included for full review was data source (eg tumor registry vs medical center), number of subjects in each comparison group, year of treatment, histological type, tumor size, age at surgery, sex, CCI, followup for OS, method(s) of adjustment for baseline covariates and adjusted HRs for OS after PN vs after RN with 95% CIs.

Results

We identified 34 studies of PN vs RN with the end point of OS. Of these studies 21 did not meet the eligibility criteria for full review (fig. 1). Eleven studies had no upper limit on tumor size, thus including many cases of locally advanced disease mostly treated with RN.^{6–16} Of these 11 studies no tumor characteristics were reported in 1¹¹ and pT3 cases were excluded in 1, although 17% had stage pT2,¹⁴ and there was no followup beyond 30 days postoperatively in 1.⁷ In the other 9 studies the median study specific percentage of nonorgan confined cases was 32% (range 14% to 54%).

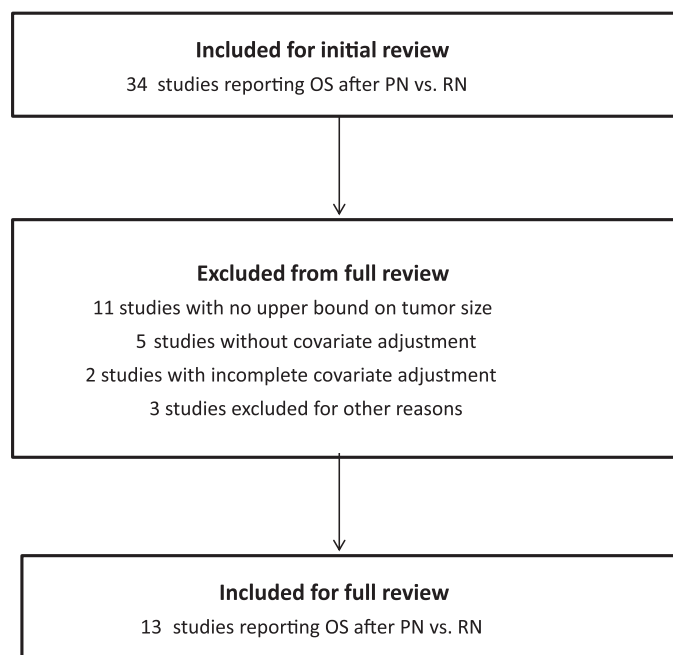


Figure 1. Studies included for initial and full review

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