Cochrane
Library

Cochrane Database of Systematic Reviews

Partial nephrectomy versus radical nephrectomy for clinical localised renal masses (Review)

Kunath F, Schmidt S, Krabbe LM, Miernik A, Dahm P, Cleves A, Walther M, Kroeger N

Kunath F, Schmidt S, Krabbe LM, Miernik A, Dahm P, Cleves A, Walther M, Kroeger N.
Partial nephrectomy versus radical nephrectomy for clinical localised renal masses.
Cochrane Database of Systematic Reviews 2017, Issue 5. Art. No.: CD012045.
DOI: [10.1002/14651858.CD012045.pub2](https://doi.org/10.1002/14651858.CD012045.pub2).

www.cochranelibrary.com

TABLE OF CONTENTS

HEADER	1
ABSTRACT	1
PLAIN LANGUAGE SUMMARY	2
SUMMARY OF FINDINGS	3
BACKGROUND	5
OBJECTIVES	6
METHODS	6
RESULTS	10
Figure 1.	11
Figure 2.	13
DISCUSSION	15
AUTHORS' CONCLUSIONS	16
ACKNOWLEDGEMENTS	16
REFERENCES	17
CHARACTERISTICS OF STUDIES	26
DATA AND ANALYSES	35
Analysis 1.1. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 1 Time-to-death of any cause.	36
Analysis 1.2. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 2 Serious adverse events (Surgery-related mortality).	36
Analysis 1.3. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 3 Cancer-specific survival.	36
Analysis 1.4. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 4 Time-to-recurrence.	37
Analysis 1.5. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 5 Spleen damage.	37
Analysis 1.6. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 6 Pleural damage.	37
Analysis 1.7. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 7 Perioperative bleeding.	38
Analysis 1.8. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 8 Urinary fistula.	38
Analysis 1.9. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 9 Reoperation due to side-effects (due to bleeding, urinary fistula, bowel obstruction, pleuropneumonia).	38
Analysis 1.10. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 10 Cardiovascular-related mortality.	38
Analysis 1.11. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 11 Liver-related mortality.	39
Analysis 1.12. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 12 Renal-related mortality.	39
Analysis 1.13. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 13 Infection-related mortality.	39
Analysis 1.14. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 14 Chronic pulmonary disease-related mortality.	40
APPENDICES	40
CONTRIBUTIONS OF AUTHORS	45
DECLARATIONS OF INTEREST	45
SOURCES OF SUPPORT	46
DIFFERENCES BETWEEN PROTOCOL AND REVIEW	46
NOTES	46
INDEX TERMS	46

[Intervention Review]

Partial nephrectomy versus radical nephrectomy for clinical localised renal masses

Frank Kunath^{1,2}, Stefanie Schmidt², Laura-Maria Krabbe^{2,3}, Arkadiusz Miernik^{2,4}, Philipp Dahm⁵, Anne Cleves⁶, Mario Walther⁷, Nils Kroeger^{2,8}

¹Department of Urology, University Hospital Erlangen, Erlangen, Germany. ²UroEvidence@Deutsche Gesellschaft für Urologie, Berlin, Germany. ³Department of Urology, University of Muenster Medical Center, Muenster, Germany. ⁴Department of Urology, Medical University Centre Freiburg, Freiburg, Germany. ⁵Urology Section, Minneapolis VA Health Care System, Minneapolis, Minnesota, USA. ⁶Velindre NHS Trust, Cardiff University Library Services, Cardiff, UK. ⁷Ernst-Abbe-Hochschule Jena, Jena, Germany. ⁸Department of Urology, University Hospital Greifswald, Greifswald, Germany

Contact address: Nils Kroeger, Department of Urology, University Hospital Greifswald, 17489 Greifswald, Greifswald, Germany. kroegern@uni-greifswald.de, md.nkroeger@gmail.com.

Editorial group: Cochrane Urology Group.

Publication status and date: New, published in Issue 5, 2017.

Citation: Kunath F, Schmidt S, Krabbe LM, Miernik A, Dahm P, Cleves A, Walther M, Kroeger N. Partial nephrectomy versus radical nephrectomy for clinical localised renal masses. *Cochrane Database of Systematic Reviews* 2017, Issue 5. Art. No.: CD012045. DOI: [10.1002/14651858.CD012045.pub2](https://doi.org/10.1002/14651858.CD012045.pub2).

Copyright © 2017 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

ABSTRACT

Background

Partial nephrectomy and radical nephrectomy are the relevant surgical therapy options for localised renal cell carcinoma. However, debate regarding the effects of these surgical approaches continues and it is important to identify and summarise high-quality studies to make surgical treatment recommendations.

Objectives

To assess the effects of partial nephrectomy compared with radical nephrectomy for clinically localised renal cell carcinoma.

Search methods

We searched CENTRAL, MEDLINE, PubMed, Embase, Web of Science, BIOSIS, LILACS, Scopus, two trial registries and abstracts from three major conferences to 24 February 2017, together with reference lists; and contacted selected experts in the field.

Selection criteria

We included a randomised controlled trial comparing partial and radical nephrectomy for participants with small renal masses.

Data collection and analysis

One review author screened all of the titles and abstracts; only citations that were clearly irrelevant were excluded at this stage. Next, two review authors independently assessed full-text reports, identified relevant studies, evaluated the eligibility of the studies for inclusion, assessed trial quality and extracted data. The update of the literature search was performed by two independent review authors. We used Review Manager 5 for data synthesis and data analyses.

Main results

We identified one randomised controlled trial including 541 participants that compared partial nephrectomy to radical nephrectomy. The median follow-up was 9.3 years.

Based on low quality evidence, we found that time-to-death of any cause was decreased using partial nephrectomy (HR 1.50, 95% CI 1.03 to 2.18). This corresponds to 79 more deaths (5 more to 173 more) per 1000. Also based on low quality evidence, we found no difference in serious adverse events (RR 2.04, 95% CI 0.19 to 22.34). Findings are consistent with 4 more surgery-related deaths (3 fewer to 78 more) per 1000.

Based on low quality evidence, we found no difference in time-to-recurrence (HR 1.37, 95% CI 0.58 to 3.24). This corresponds to 12 more recurrences (14 fewer to 70 more) per 1000. Due to the nature of reporting, we were unable to analyse overall rates for immediate and long-term adverse events. We found no evidence on haemodialysis or quality of life.

Reasons for downgrading related to study limitations (lack of blinding, cross-over), imprecision and indirectness (a substantial proportion of patients were ultimately found not to have a malignant tumour). Based on the finding of a single trial, we were unable to conduct any subgroup or sensitivity analyses.

Authors' conclusions

Partial nephrectomy may be associated with a decreased time-to-death of any cause. With regards to surgery-related mortality, cancer-specific survival and time-to-recurrence, partial nephrectomy appears to result in little to no difference.

PLAIN LANGUAGE SUMMARY

Partial nephrectomy for the treatment of clinically localised renal carcinomas

Review question

We reviewed the evidence to compare the effects of removing only the tumour (partial nephrectomy) versus removing the entire kidney (radical nephrectomy) in individuals with a small kidney cancer that has not spread to other parts of the body.

Background

Small kidney tumours are often discovered on imaging studies (like CT scans) ordered for other reasons. Some of these tumours are cancer that can spread to other parts of the body, cause problems like bleeding or pain and even lead to death. The best way to treat these tumours is surgery that removes the tumour. This can be done by just removing the tumour (and some of the surrounding tissue) or by removing the tumour and the whole kidney. We do not know what is better.

Study characteristics

We searched the medical literature until 24 February 2017. We included one study with 541 study participants that randomly assigned participants with localised tumours of the kidney that were thought to be cancerous. On average, participants were followed for 9.3 years.

Key results

Participants who had only the tumour taken out appear to be more likely to die from any cause than participants that had the tumour and the whole kidney taken out. There appeared to be little to no difference in the time until the tumour comes back or in the risk of serious complications resulting in death. We did not find any evidence as to how the groups compared when it comes to the need for haemodialysis or how their quality of life compared.

Quality of the evidence

The quality of evidence was low. This means that we have limited confidence in the results and that the true effect of partial nephrectomy may be substantially different.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Partial nephrectomy compared to radical nephrectomy for clinical localized renal masses

Partial nephrectomy compared to radical nephrectomy for clinical localized renal masses

Bibliography: Kunath F, Schmidt S, Krabbe L, Miernik A, Cleves A, Walther M, Kroeger N. Partial nephrectomy versus radical nephrectomy for clinical localized renal masses. Cochrane Database of Systematic Reviews 2017, Issue 3.

Outcomes	Nº of participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with radical nephrectomy	Risk difference with Partial nephrectomy
Time-to-death of any cause (anticipated absolute effects refer to all-cause mortality; median follow-up duration: 9.3 years)	541 (1 RCT)	⊕⊕○○ LOW 1, 2	HR 1.50 (1.03 to 2.18)	Study population 183 per 1.000	79 more per 1.000 (5 more to 173 more)
Serious adverse events (Surgery-related mortality)	541 (1 RCT)	⊕⊕○○ LOW 1, 3	RR 2.04 (0.19 to 22.34)	Study population 4 per 1.000	4 more per 1.000 (3 fewer to 78 more)
Time-to-recurrence (anticipated absolute effects refer to recurrence; median follow-up duration: 9.3 years)	541 (1 RCT)	⊕⊕○○ LOW 1, 2, 4	HR 1.37 (0.58 to 3.24)	Study population 33 per 1.000	12 more per 1.000 (14 fewer to 70 more)
Permanent haemodialysis - not measured	-	-	-	-	-
Quality of Life - not measured	-	-	-	-	-

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio

GRADE Working Group grades of evidence

High quality: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

- ¹ CI consistent with both minimal or large effect size/ small risk or large risk increase (imprecision)
- ² Downgraded for lack of blinding (performance bias)
- ³ Downgraded for lack of blinding (performance and detection bias)
- ⁴ Large proportion of subjects did not have malignant tumours (15%; indirectness)

BACKGROUND

Description of the condition

Renal cell carcinoma is projected to be associated with 63,990 newly diagnosed kidney cancer cases and 14,400 cancer-related deaths in 2017 in the United States (Siegel 2017). Due to the increased availability and utilisation of computed tomography (CT) and magnetic resonance imaging (MRI), more renal masses are being detected, and a stage-migration has occurred during recent years (Cohen 2005; Gill 2010). Incidentally discovered renal masses currently comprise 48% to 66% of tumours, compared with only 3% to 13% in the 1970s (Volpe 2004). While open radical nephrectomy has been the gold standard for any renal tumour surgery in the past, partial nephrectomy is now increasingly employed for renal tumour surgery for clinically localised renal masses.

Description of the intervention

Partial nephrectomy has a long history in kidney surgery. The first documented partial nephrectomy was performed by Vincent Czerny for angiosarcoma in 1887 (Herr 2005). Only a few partial nephrectomies were performed for renal tumours in the following decades. Partial nephrectomy was seen as simply unnecessary when a normal contralateral kidney was present (Herr 2005). Pathological studies by Bell demonstrated that tumours less than 5 cm metastasised in only 7% of cases (Bell 1938). Additionally, Vermooten suggested that tumours could be removed with a safety margin of only 1 cm without an increased risk of recurrence (Herr 2005; Vermooten 1950). However, since small renal tumours can metastasize, most urologists argued that radical nephrectomy should be performed in all cases. Consequently, partial nephrectomy had been mostly reserved for those patients with an imperative indication like a solitary kidney, poor renal function or bilateral tumours. Since the 1970s, urologists began to question this surgical dogma (Herr 2005).

The technique of radical nephrectomy was systematically described by Robson in 1963 (Robson 1963). It was also Robson and colleagues who first described the outcomes of a series of 88 patients treated with radical nephrectomy between 1949 and 1964 (Robson 1969). The most common surgical approaches for radical nephrectomy were thoracoabdominal (transpleural) or, in cases of lower pole tumours, transperitoneal incisions. According to Robson and colleagues, anatomical structures requiring removal are the perinephric fat, overlying peritoneum, and adrenal gland. It was also recommended to routinely perform lymph node dissection of the para-aortic lymph nodes from the bifurcation of the aorta to the crus of the diaphragm. During recent years, the original technique has been modified. Additional clinical aspects influencing the original approach have been extensively evaluated. For example, it has been shown that the likelihood of adrenal metastases is very low in the absence of pre-operative radiological signs of adrenal involvement (Kuczyk 2002). Furthermore, even in clinically suspected lymph node metastases, true pathological node positivity is only present in around 20% of these cases, and is far lower in individuals without clinical signs of lymph node involvement (Blom 2009). Routine adrenalectomy, as well as lymphadenectomy, is not recommended as a routine part of partial or radical nephrectomy in the absence of a radiological suspicion of adrenal or nodal involvement (Ljungberg 2015).

The indications for partial nephrectomy have been expanded over the years. Indications have changed from individuals with imperative indications (e.g. solitary kidney, bilateral tumours or high renal insufficiency risk) to all individuals with renal masses less than 4 cm in diameter. Today, guidelines recommend partial nephrectomy whenever technically feasible, independent of tumour size (Campbell 2009; Ljungberg 2015). The rates of partial nephrectomy have increased in past decades, comprising about 30% of all renal surgeries for clinically localised renal masses in 2005 (Bianchi 2013). However, open surgical approaches are still far more common than laparoscopic or robotic-assisted techniques, although broad adoption of robotic-assisted surgery has added to the increased utilisation of minimally invasive techniques (Bianchi 2013; Ghani 2014).

Adverse effects of the intervention

Surgical treatments are never without risks and adverse events. For radical nephrectomy, these immediate surgical complications are mainly vascular (severe haemorrhage in 1.2%); however, since the adoption of laparoscopic surgery, blood loss has significantly decreased (Hemal 2007). Splenic injury is seen in less than 1% of patients. Partial nephrectomy is prone to a slightly different spectrum of adverse events. The total rate of adverse events can be as high as 20% to 25% in individuals undergoing partial nephrectomy (Gill 2007; Simhan 2011). The most common adverse events include haemorrhage in 1.2% to 4.5%, urinary fistula in up to 17% and acute renal failure in up to 25% of patients (Ljungberg 2015). Transfusion rates are not routinely reported but can be as high as 50%, while the transfusion rates decline with more experience in partial nephrectomy (Duque 1998).

The adverse events are important due to special considerations in the treated population. Although partial nephrectomy with its inherent complications might be beneficial for a young person who is at risk of additional medical co-morbidities as well as potential tumour growth in the contralateral kidney, the population of the frail and elderly pose a challenge to the treating surgeon in terms of decision making between the different available techniques. This is of utmost importance because tumours amenable to partial nephrectomy might also be candidate tumours for active surveillance due to the low possibility for significant growth and invasive potential.

How the intervention might work

Renal surgery is a curative treatment option for most individuals with localised renal cell carcinoma. Radical nephrectomy is a safe standard procedure and has demonstrated reliable oncological control. Thus, new surgical approaches have to offer similar cancer-specific survival rates. On the other hand, surgeons need to consider that the majority of individuals with localised renal cell carcinoma will survive their cancer and therefore every effort has to be made to minimise treatment-related morbidity. Thus, improved surgical approaches have to induce lower co-morbidity rates than radical nephrectomy. The most important radical nephrectomy-related co-morbidity is renal insufficiency. Partial nephrectomy preserves the part of the kidney uninvolved by the tumour at the time of surgical treatment. Therefore, partial nephrectomy might be associated with lower proportions of surgically induced chronic kidney disease (Kim 2012; MacLennan 2012). Less frequent chronic kidney disease rates may result in better all-cause outcomes for individuals with localised renal cell carcinoma.

Why it is important to do this review

Partial nephrectomy is a commonly used surgical approach for the growing number of clinically localised renal masses (Tobert 2014). This clinical practice is based on the results of retrospective studies that have strongly suggested the superiority of partial nephrectomy over radical nephrectomy in terms of time-to-death of any cause, development of renal insufficiency and even cancer-specific survival (Tobert 2014). Retrospective studies have shown that tertiary centres primarily use partial nephrectomy routinely (Patel 2012). In light of a perceived under-utilisation of partial nephrectomy, urological societies have called for the use of partial nephrectomy rather than radical nephrectomy for clinically localised renal masses (Campbell 2009; Ljungberg 2015). The European Association of Urology guidelines state that partial nephrectomy "is recommended in patients with clinical T1a tumours and should be favoured above radical nephrectomy in clinical T1b tumours whenever technically feasible" (Grade A and B recommendations) (Ljungberg 2015). Systematic reviews included not only randomised controlled trials but also several retrospective observational studies (Kim 2012; MacLennan 2012; Gu 2016; Mir 2016; Mir 2016a). The quality of retrospective studies is often strongly impaired by selection bias. However, renal cell carcinoma treatment recommendations of the world's largest urological associations are based on the findings of these retrospective studies (Campbell 2009; Ljungberg 2015). Therefore, it is important to identify and summarise high-quality studies to make surgical treatment recommendations. Additionally, it is of the utmost importance to summarise the available high-quality evidence, as well as the gaps in our knowledge, to give clinicians the opportunity to account for the missing information in daily clinical decision making.

OBJECTIVES

To assess the effects of partial nephrectomy compared with radical nephrectomy for clinically localised renal cell carcinoma.

METHODS

Criteria for considering studies for this review

Types of studies

We considered parallel-group randomised controlled trials for inclusion and excluded cluster-randomised trials as well as cross-over trials as they are not applicable to this disease setting and the type of interventions of interest. We considered studies for inclusion irrespective of their publication status or language of publication.

Types of participants

We considered studies for inclusion that included participants with unilateral localised renal cell carcinoma. We defined localised renal cell carcinoma for the purpose of this review as clinical stage I or stage II, as defined by the 2009 tumour node metastasis (TNM) classification system (Sobin 2010). We made no exclusions based on age or ethnicity. For studies that also included participants with advanced stages of renal cell carcinoma, we initially planned assessing the data only of the subgroup of participants with localised renal cell carcinoma.

Diagnostic criteria for localised renal cell carcinoma

We considered studies for inclusion that included participants with histologically proven renal cell carcinoma. According to the TNM classification, stage I and stage II tumours are defined as:

- Stage I
 - * T1 (tumor ≤ 7 cm in the greatest dimension, limited to the kidney). T1 is further divided into T1a (≤ 4 cm) and T1b (> 4 cm but ≤ 7 cm).
 - * N0 (No regional lymph node metastasis).
 - * M0 (No distant metastasis).
- Stage II
 - * T2 (tumor > 7 cm in the greatest dimension, limited to the kidney). T2 is additionally divided into T2a (> 7 cm but ≤ 10 cm) and T2b (> 10 cm).
 - * N0 (No regional lymph node metastasis).
 - * M0 (No distant metastasis).

Types of interventions

We investigated the following experimental intervention versus comparator intervention.

Experimental intervention

Partial nephrectomy, defined as surgical extirpation of the renal mass with or without a rim of normal renal parenchyma leaving healthy tissue in place of the ipsilateral renal unit. We planned inclusion of open, laparoscopic and robotic surgical interventions.

Comparator intervention

Radical nephrectomy, defined as surgical extirpation of the whole renal unit including the tumour. We planned the inclusion of open, laparoscopic and robotic surgical interventions.

Comparison

Partial nephrectomy versus radical nephrectomy.

Minimum duration of intervention

We considered studies for inclusion with a minimum follow-up of 6 months.

Minimum duration of follow-up

We considered studies for inclusion with a minimum duration of follow-up of one day after partial or radical nephrectomy.

Extended follow-up periods (also called open-label extension studies), defined as a follow-up of participants once the original trial was terminated as specified in the power calculation for this trial, are frequently of observational nature. We planned inclusion of open-label extension studies only for evaluation of adverse events.

Specific exclusion criteria

Studies comparing partial nephrectomy with solely ablation therapies for localised renal cell carcinoma, such as radio frequency ablation or cryotherapy, were not considered for inclusion in this review.

Types of outcome measures

We did not exclude studies from the review solely because no outcomes of interest were reported. In cases where none of our primary or secondary outcomes were reported, we planned on excluding the trial but providing some information in an additional table. If we were unable to retrieve the necessary information to analyse time-to-event outcomes, we planned to assess the number of events per total for dichotomised outcomes at certain time points.

Primary outcomes

- Time-to-death of any cause
- Serious adverse events

Secondary outcomes

- Cancer-specific survival
- Time-to-recurrence
- Immediate post-operative adverse events
- Long-term adverse events
- Quality of life

Method and timing of outcome measurement

- Time-to-death of any cause, measured at any time after participants were randomised to intervention/comparator groups. The rationale behind selection of time-to-death of any cause as a primary outcome measure is to compare both interventions regarding this endpoint, as it is the most important endpoint for participants.
- Serious adverse events. We initially planned that adverse events were considered to be serious when they required hospitalization, were life-threatening, or fatal, or were reported as such by the authors of the original publication. However, none of them were reported in the included randomised controlled trial and we defined therefore surgery-related mortality as a serious adverse event.
- Cancer-specific survival, measured as the date of randomisation to the date of death due to renal cell carcinoma. The rationale behind the endpoint of cancer-specific survival is to explore the level of oncological control between both interventions.
- Time-to-recurrence, measured as the date of randomisation to the date of first clinically detected disease recurrence. The rationale behind the endpoint of time-to-recurrence is to explore the level of local oncological control between both interventions, as, with limited follow-up, time-to-recurrence can be used as a surrogate endpoint for cancer-specific survival.
- Immediate post-operative adverse events, measured as the date of operation up to 30 days post surgery. We initially planned inclusion of the following adverse events: need for temporary haemodialysis, urinary tract infection, urinary leakage after partial nephrectomy, hemorrhage as well as need for re-operation or transfusion. The rationale for these outcome measures is the comparison of immediate adverse events which can then be balanced with the rate of oncological control as well as survival between both interventions. However, we included in the evaluation of this review the following reported immediate post-operative adverse events: spleen damage, pleural damage, perioperative bleeding, urinary fistula, and reoperation due to side-effects (due to bleeding, urinary fistula, bowel obstruction, pleuropneumonia).

- Long-term adverse events, measured as 31 days post surgery and after. We initially planned inclusion of the following adverse events: cardiovascular events, hypertension, need for permanent haemodialysis, development of chronic kidney disease (CKD). The rationale for these outcome measures is the comparison of long-term adverse events which can then be balanced with the rate of oncological control as well as survival between both interventions. However, we included in the evaluation of this review the following reported long-term adverse events: cardiovascular-related mortality, liver-related mortality, renal-related mortality, infection-related mortality, chronic pulmonary disease-related mortality.
- Quality of life; evaluated by a validated instrument. However, we did not identify a randomised controlled trial assessing quality of life outcomes.

Main outcomes for 'Summary of findings' table

We present a 'Summary of findings' table reporting the following outcomes listed according to priority:

1. Time-to-death of any cause
2. Serious adverse events
3. Time-to-recurrence
4. Permanent need for haemodialysis
5. Quality of life

Search methods for identification of studies

We conducted a combination of electronic and manual searches with no restrictions on the language of publication or publication status. See [Appendix 1](#) for full search strategies of each database.

Electronic searches

We searched the following electronic databases:

- Cochrane Central Register of Controlled Trials (CENTRAL; 2017, Issue 1) in the Cochrane Library (searched 24 February 2017)
- MEDLINE Ovid SP (In-Process & Other Non-Indexed Citations) (1946 to 24 February 2017)
- PubMed (provided by the US National Library of Medicine; epubs from 2013, last searched 24 February 2017)
- Embase OvidSP (1947 to 24 February 2017)
- Web of Science with Conference Citation Proceedings (Thomson Reuters Web of Knowledge; from 1945 to 24 February 2017)
- BIOSIS (from 1985 to 24 February 2017)
- LILACS (from 1986 to 24 February 2017)
- Scopus (from 1960 to 24 February 2017)

We searched the following trials registers.

- World Health Organization International Clinical Trials Registry Platform Search Portal (WHO ICTRP Search Portal; www.who.int/ictcp/en/; no restricted time period, last searched 24 February 2017)
- ClinicalTrials.gov (no restricted time period, last searched 24 February 2017)

We searched the electronically-available abstracts of the following major national and international urology cancer meetings:

- American Society of Clinical Oncology Annual Meeting (ASCO; jco.ascopubs.org; from 2004, last searched February 28, 2017)
- Annual Meeting of the European Association of Urology (EAU; www.uroweb.org; from 2004, last searched February 28, 2017)
- American Urological Association Annual Meeting (AUA; www.jurology.com/; from 2008, last searched February 28, 2017)

We applied a MEDLINE (via Ovid SP) email alert service to identify newly published trials using the same search strategy as described for MEDLINE (for details on search strategies, see [Appendix 1](#)). Should we identify new trials for inclusion, we will evaluate these, incorporate the findings into our review and will update this Cochrane Review.

Searching other resources

We screened the reference lists of publications identified as potentially relevant to this review for additional studies. In addition, we contacted leading experts in the field of renal cell carcinoma treatment to request information on unpublished studies (for details see [Appendix 2](#)).

Data collection and analysis

Selection of studies

We identified duplicate studies by checking potentially-relevant studies for author names, locations and settings, details of interventions, numbers of participants, baseline data, study date, and duration of the study using [Endnote](#). We used Covidence for selection of studies, e.g. for the process of selection of included and excluded studies (www.Covidence.org). One review author (FK) screened for relevance all titles and abstracts of records identified by the search. At this stage we excluded only records that were clearly irrelevant (e.g. animal/in vitro research and testing, studies including solely participants with benign tumours). Next, two review authors (FK, SS) independently scanned the abstract, title, or both, of every remaining record to determine which trials we should assess further. Two review authors (FK, SS) independently investigated all potentially-relevant records as full text, mapped records to studies, and classified studies as included studies, excluded studies, studies awaiting classification, or ongoing studies in accordance with the criteria for each provided in the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011b](#)). We resolved any disagreements regarding study eligibility through discussion and consensus or by recourse to a third review author (NK). We documented reasons for exclusion of studies that may have reasonably been expected to be included in the review in a 'Characteristics of excluded studies' table. We include an adapted PRISMA flow diagram showing the process of study selection ([Liberati 2009](#)).

Data extraction and management

Two review authors (FK, SS) independently extracted key participant and intervention characteristics using a data extraction form based on the recommendations of the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011b](#)). Disagreement was resolved by consensus or, if required, by consultation with a third review author (NK).

We initially planned to provide information, including trial identifier, about potentially relevant ongoing studies in the table

'Characteristics of ongoing studies'. However, we did not identify ongoing randomised controlled trials.

We identified the protocol for the included study ([Van Poppel 2007](#)); and compared the reported primary, secondary and other outcomes with data in publications (see 'Characteristics of included studies' table).

We extracted the following information (see 'Characteristics of included studies' table).

- Study design
- Study dates
- Study settings and country
- Participant inclusion and exclusion criteria
- Participant details, baseline demographics (age, gender, co-morbidities, performance status), tumour characteristics (TNM classification, tumour size, positive surgical margins, renal cell carcinoma subtype, presence of malignancy)
- Number of participants by study and by study arm
- Details of relevant experimental and comparator interventions
- Definitions of relevant outcomes, and method and timing of outcome measurement as well as any relevant subgroups
- Study funding sources
- Declarations of interest by primary investigators

Dealing with duplicate and companion publications

For duplicate publications, companion documents or multiple reports of a primary trial, we maximised the information yield by collating all available data and used the most complete data set aggregated across all known publications (see 'Included studies'). We listed multiple reports of the primary trial as secondary references under the study ID of the included trial.

Data from clinical trial registers

We extracted the data of the included study that were published in clinical trial registers (see 'Characteristics of included studies'). However, we identified no other completed or ongoing registered randomised controlled trials.

Assessment of risk of bias in included studies

Two review authors (FK, SS) independently assessed the risk of bias of each included study using Cochrane's 'Risk of bias' assessment tool ([Higgins 2011c](#)). Disagreement was resolved by consensus or through discussion with a third review author (NK). We assessed the following domains.

- Random sequence generation (selection bias due to inadequate generation of a randomised sequence)
- Allocation concealment (selection bias due to inadequate concealment of allocation prior to assignment)
- Blinding of participants and personnel (performance bias due to knowledge of the allocated interventions by participants and personnel during the trial)
- Blinding of outcome assessment (detection bias due to knowledge of the allocated interventions by outcome assessment)
- Incomplete outcome data (attrition bias due to amount, nature or handling of incomplete outcome data)

- Selective reporting (reporting bias due to selective outcome reporting)
- Other sources of bias (bias due to problems not covered elsewhere)

We judged 'Risk of bias' domains as 'low risk', 'high risk' or 'unclear risk' and evaluated individual bias items as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011c).

The judgements (low, unclear or high risk) were justified in order to maintain transparency, and we indicated the source of information for the 'Risk of bias' judgement by providing a quotation from the study text in the 'Risk of bias' table. We additionally provided a 'Risk of bias' summary figure to illustrate these findings.

The following risk of bias domains were assessed at trial level: random sequence generation, allocation concealment, selective reporting, other sources of bias.

The following risk of bias domains were assessed at outcome level: blinding of participants and study personnel, blinding of outcome assessment, incomplete outcome data.

We defined the following endpoints as subjective outcomes.

- Cancer-specific survival
- Serious adverse events
- Immediate post-operative adverse events
- Long-term adverse events
- Quality of life

We define the following endpoints as objective outcomes.

- Time-to-death of any cause
- Time-to-recurrence

Measures of treatment effect

We included only one randomised controlled trial and therefore meta-analyses was not possible. The extracted data were presented using Review Manager 5 (Review Manager 2014). We expressed time-to-event outcomes (e.g. time-to-death of any cause, cancer-specific survival, time-to-recurrence) as hazard ratios (HR) with 95% confidence intervals (CIs). Results of binary outcomes (e.g. adverse events) were expressed as risk ratios (RRs) with 95% CIs. We identified no study reporting continuous outcomes (e.g. quality of life).

Unit of analysis issues

We included only one parallel-grouped randomised controlled trial with one intervention and one control group (Van Poppel 2007). Therefore, the unit of analysis was the individual randomised participant. There was a single measurement for each outcome from each participant collected and analysed.

Dealing with missing data

Wherever possible, data were analysed using the intention-to-treat (ITT) approach. We carefully evaluated important numerical data such as screened, randomly assigned participants as well as intention-to-treat, and per-protocol populations. We investigated attrition rates (e.g. drop-outs, losses to follow-up, withdrawals)

and critically appraised issues of missing data. We did not impute missing data.

Assessment of heterogeneity

We included only one randomised controlled trial (Van Poppel 2007). Meta-analyses with evaluation of heterogeneity were not possible.

Assessment of reporting biases

We included only one randomised controlled trial and did not perform a funnel plot analysis (Van Poppel 2007). We obtained study protocols to assess the possible bias of selective outcome reporting.

Data synthesis

We included only one randomised controlled trial and did not perform a meta-analysis (Van Poppel 2007). We used Review Manager 5 for creating forest plots (Review Manager 2014). We performed statistical analyses according to the statistical guidelines described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011a). For dichotomous outcomes, we used the Mantel-Haenszel method; and for time-to-event outcomes, we used the generic inverse variance method. The included study did not report data for continuous outcomes.

Subgroup analysis and investigation of heterogeneity

We initially planned to perform subgroup analyses for the evaluation 'Stage Ia versus Stage Ib renal cell carcinoma' classified by the 2009 TNM classification system (Sobin 2010). However, we included only one randomised controlled trial and could therefore not perform subgroup analyses.

Sensitivity analysis

We initially planned to perform sensitivity analyses in order to explore the influence of the following factors (when applicable) on effect sizes: restricting the analysis by taking into account different follow-up periods as well as restricting the analysis by taking into account risk of bias, by excluding studies at 'high risk' or 'unclear risk'. However, we included only one randomised controlled trial and could not perform these sensitivity analyses.

'Summary of findings' table

We present the overall quality of the evidence for each outcome specified under 'Types of outcome measures: Summary of finding' according to the GRADE approach, which takes into account issues related not only to internal validity (risk of bias, inconsistency, imprecision, publication bias) but also to external validity, such as directness of results (GRADEpro GDT; Guyatt 2008). Two review authors (FK, SS) independently rated the quality of evidence for each outcome using the 'GRADE Guideline Development Tool' (GRADEpro GDT). In case of disagreement, we consulted the rest of the group and made a judgement based on consensus.

We present a summary of the evidence in a 'Summary of findings' table. It provides key information about the best estimate of the magnitude of the effect, in relative terms and as absolute differences, for each relevant comparison of alternative management strategies, numbers of participants and trials addressing each important outcome and rating of overall confidence in effect estimates for each outcome (Guyatt 2011;

Schünemann 2011). We created the 'Summary of findings' table based on the methods described in the *Cochrane Handbook for Systematic Reviews of Interventions* by means of Review Manager's (RevMan) table editor (Review Manager 2014). We justified all decisions to downgrade the quality of trials using footnotes, and we made comments to aid the reader's understanding of the Cochrane Review where necessary.

RESULTS

Description of studies

For a detailed description of trials, see the '[Characteristics of included studies](#)' and '[Characteristics of excluded studies](#)' sections.

Results of the search

For detailed information on the results of the search, see [Figure 1](#). A total of three articles on only one study were included in this systematic review (Van Poppel 2007). We did not identify any ongoing studies.

Figure 1. Study flow diagram (last searched 28/02/2017)

Figure 1. (Continued)

Included studies

For details on the included studies, see '[Characteristics of included studies](#)' table.

Source of data

All references to the included study were available as full-text publications in English language ([Van Poppel 2007](#)).

Comparisons

The included study compared partial nephrectomy with radical nephrectomy ([Van Poppel 2007](#)).

Overview of trial populations

In the included study 541 participants were randomised to either partial nephrectomy (n = 268) or radical nephrectomy (n = 273) ([Van Poppel 2007](#)). The trial included subjects with solitary renal masses suspected to be renal cell carcinoma.

Trial design

The included study was a parallel grouped randomised controlled clinical trial with non-inferiority design ([Van Poppel 2007](#)).

Settings

The included multicenter study was conducted at 45 institutions in 17 countries worldwide ([Van Poppel 2007](#)).

Participants

Participants with a solitary T1 or T2 N0 M0 renal tumour, suspicious for renal adenocarcinoma with a World Health Organization (WHO) performance status of 2 or less were included. The median age of participants was 62.0 (23.0 to 84.0) years and ranged from younger than 61 years (44.4%), through 61 to 70 years (34.7%) to older than 70 years (20.9%). Collectively, 65.8% of the participants were identified as male and 32.9% as female. The distribution of ethnic groups and of low- and middle-income countries was not reported ([Van Poppel 2007](#)). The tumour should not exceed 5 cm in diameter. Participants "with a solitary kidney, von Hippel-Lindau disease, multifocal disease, T3-T4 tumours, clinical presence of distant or lymphatic metastases, a WHO performance status >2, and participants with another carcinoma, except for adequately treated non-melanoma skin cancer" were excluded from the study ([Van Poppel 2007](#)).

Of the included participants, 85% had malignant tumours. Small renal masses comprised clear-cell renal cell carcinoma (67.8%),

chromophilic renal cell carcinoma (11.5%), chromophobe renal cell carcinoma (3.7%), tumours with sarcomatoid differentiation (0.7%), tumour of the collecting duct (0.4%), leiomyosarcoma (0.2%), lung metastasis (0.2%) as well as angiomyolipoma (3.3%), oncocytoma (6.5%), cysts (1.3%), cystic nephroma (0.2%), leiomyoma (0.2%) and metanephric adenoma (0.4%). Additionally, histological examination was missing in 3% of cases ([Van Poppel 2007](#)).

Participants with satellite or secondary lesions found by lymphadenectomy were not excluded (radical nephrectomy n = 14/290; partial nephrectomy n = 4/242; [Van Poppel 2007](#)).

Diagnosis

The included participants received physical examination, laboratory evaluation (erythrocyte sedimentation rate, haemoglobin, serum creatinine, alkaline phosphatase), intravenous urography if either microscopic or gross haematuria was present, ultrasonography of the kidney and the liver, chest x-ray, and a computed tomography scan of both kidneys. The pathologic tumour stage was determined according to the TNM classification system proposed by the Union Internationale Contre le Cancer (UICC; 1978)" ([Van Poppel 2007](#)).

Interventions

Radical nephrectomy "consisted of removal of the entire kidney with the adrenal and perinephric fat within the intact Gerota fascia. Limited lymphadenectomy could be done separately or en bloc and included the lymphatic tissue in the renal hilus (usually included in the radical nephrectomy specimen anyway) and the nodes around the vena cava at the level of the renal veins on the right side and on the aorta at the level of the artery on the left side" ([Van Poppel 2007](#)).

"The tumour removal was done by excavation (no enucleation), wedge resection, or partial nephrectomy after rigorous inspection of the entire renal capsula together with limited lymphadenectomy. Hilar clamping was not routinely done [...] When there was any doubt about the margin status, a frozen section analysis of the resection margins was performed. In the case of a positive resection margin, satellite or secondary lesions, radical nephrectomy was done" ([Van Poppel 2007](#)).

Overall, different surgical approaches were included whereby the most frequently applied surgical method for radical nephrectomy was laparotomy (53.6%); and for partial nephrectomy, flank incision (69.9%) ([Van Poppel 2007](#)).

Outcomes

The primary end point was time-to-death of any cause. Secondary end points were cancer-specific survival, time-to-recurrence and adverse events.

Excluded studies

We excluded 137 articles after evaluation of the full publication. The main reason for exclusion was a non-randomised study design. For

further details on reasons for study exclusions see 'Characteristics of excluded studies' table.

Risk of bias in included studies

For details on the risk of bias of the included trial see 'Characteristics of included studies' table. For an overview of review authors' judgements about each risk of bias item see Figure 2 and Summary of findings for the main comparison.

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

Allocation

Random sequence generation

We assume that randomisation was performed adequately at the EORTC Data Centre. However, information was not reported and therefore we judged the risk of bias to be unclear.

Allocation concealment

There was a central allocation and we judged the risk of bias to be low.

Blinding

Blinding of participants and personnel

The included study was an open randomised trial and did not involve blinding of the participants and/or personnel. For detail on our assessment of this risk of bias domain that we assessed at outcome level for objective and subjective outcomes, see 'Characteristics of included studies' section.

Blinding of outcome assessment

The included study did not involve blinding of the outcome assessment (or blinding was not reported). We judged that outcome assessment for objective outcomes are not likely to be influenced by lack of blinding (low risk of bias). However, we judged that subjective outcomes may have been influenced by lack of blinding, leading to high risk of bias ([Characteristics of included studies](#)).

Incomplete outcome data

Time-to-death of any cause, time-to-recurrence, cancer-specific survival, serious adverse events and long-term adverse events were analysed by intention-to-treat and all randomized participants were included in the analyses for these outcomes. We judged the risk of bias to be low.

Evaluation of immediate post-operative adverse events was an 'as-treated' analysis done with substantial departure of the intervention received from that assigned at randomisation leading to high risk of bias. We were unable to obtain the necessary data to re-analyze as per intention-to-treat.

Selective reporting

There is low risk of reporting bias because the study protocol is available and we were able to confirm that the published reports include all expected outcomes.

Other potential sources of bias

The 541 participants were randomized to either partial nephrectomy (n = 268) or radical nephrectomy (n = 273) but a large proportion of participants crossed over from the intervention to the control group and vice versa. Of the 268 participants randomized to partial nephrectomy, 39 received radical nephrectomy. Of the 273 participants randomized to radical nephrectomy, 16 received partial nephrectomy.

Effects of interventions

See: [Summary of findings for the main comparison Partial nephrectomy compared to radical nephrectomy for clinical localized renal masses](#)

1. Partial nephrectomy versus radical nephrectomy

Primary outcomes

1.1 Time-to-death of any cause

Partial nephrectomy was associated with a reduced time-to-death of any cause (HR 1.50, 95% CI 1.03 to 2.18; 541 participants; [Analysis 1.1](#)), which corresponded to 79 more deaths per 1000 (95% CI 5 more to 173 more per 1000) after a median follow-up duration of 9.3 years. The quality of evidence was rated as low due to study limitations and imprecision ([Summary of findings for the main comparison](#)).

1.2 Serious adverse events (Surgery-related mortality)

Deviating from the published protocol ([Krabbe 2016](#)), we redefined surgery-related mortality as a serious adverse event because no adverse event was reported that was named serious by the authors, yet surgery related mortality appeared important and closely related. Only three subjects in this trial died due to surgery, two in the partial nephrectomy arm and one in the radical nephrectomy

arm. The RR of surgery related mortality was 2.04 (95 % CI 0.19 to 22.34; 541 participants; [Analysis 1.2](#)). This corresponded to four more events per 1000 participants (95% CI 3 fewer to 78 more). The quality of the evidence for this outcome was low ([Summary of findings for the main comparison](#)). We downgraded for study limitations and imprecision ([Summary of findings for the main comparison](#)).

Secondary outcomes

1.3 Cancer-specific survival

Cancer-specific survival was similar between groups with a HR of 2.06 (95 % CI 0.62 to 6.84; 541 participants; [Analysis 1.3](#)).

1.4 Time-to-recurrence (local recurrence/lymph node metastases, distant metastases)

Time-to-recurrence was similar between groups with a HR of 1.37 (95% CI 0.58 to 3.24; 541 participants; [Analysis 1.4](#)). The quality of the evidence for this outcome was low ([Summary of findings for the main comparison](#)).

1.5 Immediate post-operative adverse events

1.5.1 Spleen damage

There was no difference between partial or radical nephrectomy for spleen damage (RR 1.99, 95% CI 0.18 to 21.84; 529 participants; [Analysis 1.5](#)).

1.5.2 Pleural damage

There was no difference between partial or radical nephrectomy for pleural damage (RR 1.12, 95% CI 0.67 to 1.86; 529 participants; [Analysis 1.6](#)).

1.5.3 Perioperative bleeding

The risk for perioperative bleeding was increased for partial nephrectomy if compared with radical nephrectomy (RR 1.94, 95% CI 1.38 to 2.73; 529 participants; [Analysis 1.7](#)).

1.5.4 Urinary fistula

The risk for urinary fistula was increased with partial nephrectomy if compared to radical nephrectomy (RR 20.92, 95% CI 1.23 to 355.20; 529 participants; [Analysis 1.8](#)).

1.5.5 Reoperation due to side-effects (due to bleeding, urinary fistula, bowel obstruction, pleuropneumonia)

There was no difference between partial or radical nephrectomy for reoperation due to side effects (RR 1.83, 95% CI 0.69 to 4.87; 529 participants; [Analysis 1.9](#)).

1.5.6 Urinary tract infection

We did not find evidence for this outcome.

1.5.7 Temporary haemodialysis

We did not find evidence for this outcome.

1.6 Quality of life

We did not find evidence for this outcome.

1.7 Long-term adverse events

1.7.1 Cardiovascular-related mortality

There was no difference between partial or radical nephrectomy for cardiovascular-related mortality (RR 1.27, 95% CI 0.72 to 2.24; 541 participants; [Analysis 1.10](#)).

1.7.2 Liver-related mortality

There was no difference between partial or radical nephrectomy for liver-related mortality (RR 9.17, 95% CI 0.50 to 169.45; 541 participants; [Analysis 1.11](#)).

1.7.3 Renal-related mortality

There was no difference between partial or radical nephrectomy for renal-related mortality (RR 2.04, 95% CI 0.62 to 6.69; 541 participants; [Analysis 1.12](#)).

1.7.4 Infection-related mortality

There was no difference between partial or radical nephrectomy for infection-related mortality (RR 0.68, 95% CI 0.11 to 4.03; 541 participants; [Analysis 1.13](#)).

1.7.5 Chronic pulmonary disease-related mortality

There was no difference between partial or radical nephrectomy for chronic pulmonary disease-related mortality (RR 1.53, 95% CI 0.26 to 9.07; 541 participants; [Analysis 1.14](#)).

1.7.6 Cardiovascular events

We did not find evidence for this outcome.

1.7.7 Hypertension

We did not find evidence for this outcome.

1.7.8 Permanent haemodialysis

We did not find evidence for this outcome.

1.7.9 Development of chronic kidney disease (CKD)

We did not find evidence for this outcome.

Subgroup analyses

We did not perform subgroup analyses because we only found a single trial. Additionally, the identified study did not present information in such a way as to permit additional analyses.

Sensitivity analyses

We performed none of the predefined sensitivity analyses due to the limited number of trials ($n = 1$).

Assessment of reporting bias

We did not draw funnel plots due to the limited number of trials ($n = 1$).

Ongoing trials

We found no ongoing randomised controlled trials.

DISCUSSION

Summary of main results

Based on a single randomised controlled trial, we found that partial nephrectomy was associated with a reduced time-to-death of any

cause, whereas serious adverse event rates, cancer-specific survival and time-to-recurrence were similar between the two groups. However, the quality of evidence for each of these outcomes was low, indicating that our confidence in this effect estimate is limited; the true effect may be substantially different from the results of our analysis. We did not find evidence for the outcomes of permanent haemodialysis or quality of life.

Overall completeness and applicability of evidence

We found a single randomised controlled trial that addressed our focused clinical question. In contrast to our predefined patient population of interest (patients with localised renal cell carcinoma), this trial enrolled patients with clinically suspected renal cell carcinoma leading to a patient population with 15% benign tumours and participants with secondary lesions found by lymphadenopathy. However, this may correspond to a patient population of clinical routine.

The central limitation of this review is its focus on randomised controlled trials only, which is consistent with past Cochrane methods. Given that we only found low quality evidence for all reported outcomes, it is possible that well-designed observational studies, in particular those using advanced statistical methods to address potential confounding, such as propensity weighting or instrumental variable analysis to address potential confounding, might have yielded higher quality evidence to help inform this question. In the absence of additional future randomised controlled trials, which appear unlikely, future updates of this review may formally incorporate evidence from prospective comparative observational studies ([Schunemann 2013](#)).

Quality of the evidence

We rated the quality of evidence as low for all outcomes ([Summary of findings for the main comparison](#)). Consistent issues that impacted all outcomes were lack of blinding, raising concerns about performance and detection bias; and cross-over, posing a risk of selection bias; and imprecision. In summary, the included study has methodological limitations leading to downgrading of the quality of evidence ([Van Poppel 2007](#)) ([Summary of findings for the main comparison](#)).

Potential biases in the review process

We searched multiple databases, including clinical trial registers, and contacted selected experts regarding the therapy of small renal masses. We believe that it is not likely that we have overlooked further relevant published or unpublished randomised controlled trials. However, it might be conceivable that we could have potentially missed additional trials in a language other than English that were not registered and were perhaps done relatively long ago.

Agreements and disagreements with other studies or reviews

The focus of this systematic review on randomised controlled trials is consistent with Cochrane methods for obtaining the best available evidence. The inclusion of only randomised controlled trials may be susceptible to bias due to the inclusion of highly selected participants and a small sample size leading to potential underestimation of rare but serious adverse events ([Chou 2010](#)). There are also other systematic reviews available evaluating the effect of partial and radical nephrectomy including retro-

and prospective comparative observational studies (Kim 2012; MacLennan 2012; Gu 2016; Mir 2016; Mir 2016a; Tobert 2014). None of the existing systematic reviews evaluated the quality of evidence according to GRADE although they frequently highlighted the methodological limitations of existing studies. Non-randomised studies often contain more participants with a long follow-up showing an increased external validity (Gartlehner 2008) and are particularly suitable for the evaluation of serious and/or rare adverse events. However, results of systematic reviews of non-randomised studies should be interpreted carefully because of the risk of selection bias and confounding. A matched cohort study using the Surveillance, Epidemiology, and End Results (SEER)-Medicare dataset demonstrated that partial nephrectomy improved overall survival compared with non-cancer controls. The authors concluded that apparent survival advantage conferred by partial nephrectomy is likely the result of selection bias involving unmeasured confounders (Shuch 2013). This was also a conclusion of Taubert et al. (Tobert 2014). There is evidence that in non-randomised studies partial nephrectomy was more frequently used in younger patients, in patients who had fewer co-morbidities, smaller tumour size, less aggressive pathology, lower Charlson scores, lower American Society of Anesthesiologists (ASA) score, less symptoms at presentation, better renal function and better quality of life scores compared with radical nephrectomy (Arnold 2013; Baillargeon Gagné 2010; Kaushik 2013; Kopp 2013; Lane 2010; Mano 2015; Matin 2002; Milonas 2013; Poulakis 2003; Simmons 2009; Takagi 2015; Vourganti 2011; Weight 2009; Woldrich 2012; Yasuda 2013; Zorn 2007).

The included study presented no information for our predefined outcome of permanent haemodialysis although it did include some information regarding postoperative renal function based on serum creatinine values. We did not include these results because this was not a predefined outcome of our review given its surrogate nature. In this trial after a median follow-up of 6.7 years, the risk of experiencing reduced renal function (estimated glomerular filtration rate (eGFR) < 60) was reduced with partial nephrectomy when compared with radical nephrectomy (RR 0.65, 95% CI 0.54 to 0.79; 514 participants; Van Poppel 2007). While the preservation of renal function appears desirable in all patients, it is uncertain how important this is in patients with a normally functioning contralateral kidney and a normal renal function at baseline. For example, it has been suggested that radical nephrectomy may be the preferred approach in older patients given that any renal function benefit is only realized over an extended period of time (An 2017).

Quality of life is an important outcome that was not assessed in this trial. A retrospective study has suggested that quality of life differences may already exist at baseline among patient in patients undergoing partial and radical nephrectomy in clinical practice (Arnold 2013), therefore emphasizing the risk of selection bias in observational studies which needs to be controlled for.

Relevant for evaluation of partial nephrectomy is the rate of local and distant disease recurrence. The included study presented

no difference between partial or radical nephrectomy regarding time-to-recurrence. This result is consistent with the findings of other available evidence (Gu 2016). Several non-randomised studies presented data supporting that there may be no difference between the different surgical approaches in localised (T1a-b) (Antonelli 2008; Antonelli 2012; Barbalias 1999; Blute 2006; Indudhara 1997; Kim 2010; Koo 2016; Li 2009a; Mano 2015; Mariusdottir 2013; McKiernan 2002; Minervini 2012; Mitchell 2006; Roos 2011a; Simmons 2009) and even in participants with more advanced stages (T3a N0 M0) of renal cell carcinoma (Polo 2012; Simmons 2009). Predictive factors for a decreased time-to-recurrence after 5 years from surgery may be lymphovascular invasion, Fuhrmann grade 3/4, tumour stage >T1, positive surgical margin, symptoms at presentation, macroscopic necrosis, and sarcomatoid differentiation (Abel 2010; Brookman May 2013; Brookman May 2013a; Koo 2016; Polo 2012).

AUTHORS' CONCLUSIONS

Implications for practice

We included only one randomised controlled trial containing methodological limitations. Partial nephrectomy may lead to a decreased time-to-death of any cause (or more deaths). With regards to surgery-related mortality, cancer-specific survival and time-to-recurrence, both approaches appear to have similar outcomes. Given the low quality of evidence we found for these comparisons, our confidence in the results is limited and the true effect may be substantially different.

Implications for research

Given the absence of high quality evidence, there is an important need for further methodologically rigorous studies to assess the potential benefits and harms of partial nephrectomy accounting for baseline renal function, tumour size and patient age. These issues would be ideally addressed in a large multicenter randomised controlled trial. Second to that, prospectively planned and well-designed comparative observational studies with long term follow-up using advanced statistical methods to control for confounding (as best as possible) could further improve our understanding of the role of partial nephrectomy.

ACKNOWLEDGEMENTS

The current review is an UroEvidence project. UroEvidence@Deutsche Gesellschaft für Urologie is the knowledge transfer centre of the German Society of Urology, in which methods of evidence-based medicine are linked to issues of urology. The aim is to provide doctors and patients with the latest, trustworthy and high-quality information.

The review authors thank Alea Miller of Cochrane Urology for her support. We also would like to acknowledge the support of Axel Merseburger, John Gore and Vikram Narayan.

REFERENCES

References to studies included in this review

Van Poppel 2007 {published data only}

Scosyrev E, Messing EM, Sylvester R, Campbell S, van Popel H. Renal function after nephron-sparing surgery versus radical nephrectomy: Results from EORTC Randomized Trial 30904. *European Urology* 2014;**65**:372-377.

Van Poppel H, Da Pozzo L, Albrecht W, Matveev V, Bono A, Borkowski A, et al. A prospective, randomized EORTC intergroup phase 3 study comparing the oncologic outcome of elective nephron-sparing surgery and radical nephrectomy for low-stage renal cell carcinoma. *European Urology* 2011;**59**:543-552.

* Van Poppel H, Da Pozzo L, Albrecht W, et al. A prospective randomised EORTC intergroup phase 3 study comparing the complications of elective nephron-sparing surgery and radical nephrectomy for low-stage renal cell carcinoma. *European Urology* 2007; Vol. 51:1606-1615.

References to studies excluded from this review

Abdollah 2014 {published data only}

Abdollah F, Suardi N, Capitanio U, Matloob R, Fossati N, Castiglione F, et al. The key role of time in predicting progression-free survival in patients with renal cell carcinoma treated with partial or radical nephrectomy: Conditional survival analysis. *Urologic Oncology: Seminars and Original Investigations* 2014;**32**(1):43.e9-43.e16.

Abel 2010 {published data only}

Abel EJ, Culp SH, Meissner M, Matin SF, Tamboli P, Wood CG. Identifying the risk of disease progression after surgery for localized renal cell carcinoma. *BJU International* 2010;**106**(9):1277-1283.

Acar 2009 {published data only}

Acar C, Sözen S, Üre I, Batur AF, Gürocak S, Küpeli B. Nephron-sparing treatments in small renal tumors: Surgical and ablative procedures. *Küçük böbrek tümörlerinde nefron koruyucu tedaviler: Cerrahi ve ablatif yöntemler* 2009;**35**(2):87-95.

Antonelli 2008 {published data only}

Antonelli A, Cozzoli A, Nicolai M, Zani D, Zanotelli T, Perucchini L, et al. Nephron-sparing surgery versus radical nephrectomy in the treatment of intracapsular renal cell carcinoma up to 7 cm. *European Urology* 2008;**53**(4):803-809. [DOI: [10.1016/j.eururo.2007.11.007](https://doi.org/10.1016/j.eururo.2007.11.007)]

Antonelli 2012 {published data only}

Antonelli A, Ficarra V, Bertini R, Carini M, Carmignani G, Corti S, et al. Elective partial nephrectomy is equivalent to radical nephrectomy in patients with clinical T1 renal cell carcinoma: results of a retrospective, comparative, multi-institutional study. *BJU International* 2012;**109**(7):1013-1018. [DOI: [10.1111/j.1464-410X.2011.10431.x](https://doi.org/10.1111/j.1464-410X.2011.10431.x)]

Antoniewicz 2012 {published data only}

Antoniewicz AA, Poletajew S, Borowka A, Pasierski T, Rostek M, Pikto-Pietkiewicz W. Renal function and adaptive changes in patients after radical or partial nephrectomy. *International Urology & Nephrology* 2012;**44**(3):745-51.

Arnold 2013 {published data only}

Arnold ML, Thiel DD, Diehl N, Wu KJ, Ames S, Parker AS. Comparison of baseline quality of life measures between renal cell carcinoma patients undergoing partial versus radical nephrectomy. *BMC Urology* 2013;**13**:52.

Azawi 2014 {published data only}

Azawi NH, Tesfalem H, Dahl C, Lund L. Do the different types of renal surgery impact the quality of life in the postoperative period?. *International Urology and Nephrology* 2014;**47**(2):263-269. [DOI: [10.1007/s11255-014-0893-9](https://doi.org/10.1007/s11255-014-0893-9)]

Azawi 2015 {published data only}

Azawi Nessn H, Tesfalem H, Dahl C, Lund L. Do the different types of renal surgery impact the quality of life in the postoperative period?. *International Urology & Nephrology* 2015;**47**(2):263-9.

Badalato 2012 {published data only}

Badalato GM, Kates M, Wisnivesky JP, Choudhury AR, McKiernan JM. Survival after partial and radical nephrectomy for the treatment of stage T1bN0M0 renal cell carcinoma (RCC) in the USA: a propensity scoring approach. *BJU International* 2012;**109**(10):1457-62.

Bagrodia 2010 {published data only}

Bagrodia A, Malcolm JB, DiBlasio CJ, Mehrazin R, Patterson AL, Wake RW, et al. Variation in the incidence of and risk factors for the development of nephrolithiasis after radical or partial nephrectomy. *BJU International* 2010;**106**(8):1200-1204. [DOI: [10.1111/j.1464-410X.2010.09246.x](https://doi.org/10.1111/j.1464-410X.2010.09246.x)]

Bagrodia 2011 {published data only}

Bagrodia A, Mehrazin R, Bazzi WM, Silberstein J, Malcolm JB, Stroup SP, et al. Comparison of rates and risk factors for development of osteoporosis and fractures after radical or partial nephrectomy. *Urology* 2011;**78**(3):614-619.

Baillargeon Gagné 2010 {published data only}

Baillargeon-Gagné S, Jeldres C, Lughezzani G, Sun M, Isbarn H, Capitanio U, et al. A comparative population-based analysis of the rate of partial vs radical nephrectomy for clinically localized renal cell carcinoma. *BJU International* 2010;**105**(3):359-364.

Barbalias 1999 {published data only}

Barbalias GA, Liatsikos EN, Tsintavis A, Nikiforidis G. Adenocarcinoma of the kidney: nephron-sparing surgical approach vs. radical nephrectomy. *Journal of Surgical Oncology* 1999;**72**(3):156-61.

Bazzi 2012 {published data only}

Bazzi WM, Stroup SP, Kopp RP, Cohen SA, Sakamoto K, Derweesh IH. Comparison of laparoendoscopic single-site and

multiport laparoscopic radical and partial nephrectomy: a prospective, nonrandomized study. *Urology* 2012;**80**(5):1039-45.

Bensalah 2008 {published data only}

Bensalah K, Raman JD, Bagrodia A, Marvin A, Lotan Y. Does obesity impact the costs of partial and radical nephrectomy? *Journal of Urology* 2008;**179**(5):1714-7; discussion 1717-8.

Bianchi 2013 {published data only}

Bianchi M, Becker A, Abdollah F, Trinh QD, Hansen J, Tian Z, et al. Rates of open versus laparoscopic and partial versus radical nephrectomy for T1a renal cell carcinoma: A population-based evaluation. *International Journal of Urology* 2013;**20**(11):1064-1071.

Bigot 2010 {published data only}

Bigot P, Bernhard JC, Crepel M, Bensalah K, Azzouzi AR, de la Taille A, et al. [How radical nephrectomy compares to partial nephrectomy for the treatment of pT1a papillary renal cell carcinomas?]. *Progres en Urologie* 2010;**20**(5):350-5.

Blute 2006 {published data only}

Blute ML. Comparison of outcomes in elective partial vs radical nephrectomy for clear cell renal cell carcinoma of 4-7 cm. Dash A, Vickers AJ, Schachter LR, Bach AM, Snyder ME, Russo P, Department of Urology, Memorial Sloan-Kettering Cancer Center, New York, NY. *Urologic Oncology: Seminars and Original Investigations* 2006;**24**(6):557.

Bohle 2008 {published data only}

Bohle A. A prospective randomized EORTC intergroup phase 3 study comparing the complications of elective nephron-sparing surgery and radical nephrectomy for low-stage renal cell carcinoma. *International Braz J Urol* 2008;**34**(3):389.

Boorjian 2013 {published data only}

Boorjian S. Commentary on "Long-term survival following partial vs. radical nephrectomy among older patients with early-stage kidney cancer." Tan HJ, Norton, EC, Ye Z, Hafez KS, Gore JL, Miller DC, Dow Division of Health Services Research, Department of Urology, University of Michigan, Ann Arbor, MI: *JAMA* 2012;**307**(15):1629-35. *Urologic Oncology* 2013;**31**(1):126-7.

Boulière 2011 {published data only}

Boulière F, Crepel M, Bigot P, Pignot G, Bessede T, de la Taille A, et al. Nephron-sparing surgery is superior to radical nephrectomy in preserving renal function outcome in tumors larger than 4 cm. *Intérêt de la néphrectomie partielle pour la préservation de la fonction rénale des patients ayant une tumeur rénale de plus de 4 cm* 2011;**21**(12):842-850.

Brookman May 2013 {published data only}

Brookman-May S, May M, Shariat S, Novara G, Zigeuner R, Cindolo L, et al. Features associated with recurrence beyond 5 years after nephrectomy and nephron-sparing surgery for renal cell carcinoma: Development and internal validation of a large multi-center database (CORONA/SATURN-PROJECT). *Journal of Urology* 2013;**189**(4, Suppl. S):E305-E306.

Brookman May 2013a {published data only}

Brookman-May S, May M, Shariat SF, Xylinas E, Stief C, Zigeuner R, et al. Features associated with recurrence beyond 5 years after nephrectomy and nephron-sparing surgery for renal cell carcinoma: development and internal validation of a risk model (PRELANE score) to predict late recurrence based on a large multicenter database (CORONA/SATURN Project). *European Urology* 2013;**64**(3):472-7.

Butler 1995 {published data only}

Butler BP, Novick AC, Miller DP, Campbell SA, Licht MR. Management of small unilateral renal cell carcinomas: radical versus nephron-sparing surgery. *Urology* 1995;**45**(1):34-40; discussion 40-1.

Campbell 2012 {published data only}

Campbell SC. Re: A prospective, randomized EORTC intergroup phase 3 study comparing the oncologic outcome of elective nephron-sparing surgery and radical nephrectomy for low-stage renal cell carcinoma. *European Urology* 2012;**62**(3):564-565.

Capitanio 2015 {published data only}

Capitanio U, Terrone C, Antonelli A, Minervini A, Volpe A, Furlan M, et al. Nephron-sparing Techniques Independently Decrease the Risk of Cardiovascular Events Relative to Radical Nephrectomy in Patients with a T1a-T1b Renal Mass and Normal Preoperative Renal Function. *European Urology* 2015;**67**(4):683-689. [DOI: [10.1016/j.eururo.2014.09.027](https://doi.org/10.1016/j.eururo.2014.09.027)]

Choi 2012 {published data only}

Choi D, Yoo S, Song C, Hong JH, Kim CS, Ahn H. Risk stratification model for chronic kidney disease stage iii or greater after radical nephrectomy in t1b renal cell carcinoma: Implications for partial nephrectomy. *Journal of Urology* 2012;**1**:e579-e580.

Chung 2015 {published data only}

Chung JS, Son NH, Lee SE, Hong SK, Lee SC, Kwak C, et al. Overall survival and renal function after partial and radical nephrectomy among older patients with localised renal cell carcinoma: A propensity-matched multicentre study. *European Journal of Cancer* 2015;**51**(4):489-497. [DOI: [10.1016/j.ejca.2014.12.012](https://doi.org/10.1016/j.ejca.2014.12.012)]

Clark 2008 {published data only}

Clark AT, Breau RH, Morash C, Fergusson D, Doucette S, Cagiannos I. Preservation of renal function following partial or radical nephrectomy using 24-hour creatinine clearance. *European Urology* 2008;**54**(1):143-49.

Cooper 2015 {published data only}

Cooper CJ, Teleb M, Dwivedi A, Rangel G, Sanchez LA, Laks S, et al. Comparative Outcome of Computed Tomography-guided Percutaneous Radiofrequency Ablation, Partial Nephrectomy or Radical Nephrectomy in the Treatment of Stage T1 Renal Cell Carcinoma. *Rare Tumors* 2015;**7**(1):5583.

Cost 2012 {published data only}

Cost NG, Lubahn JD, Granberg CF, Schlomer BJ, Wickiser JE, Rakheja D. Oncologic outcomes of partial versus radical

nephrectomy for unilateral Wilms tumor. *Pediatric Blood & Cancer* 2012;**58**(6):898-904.

D'Armiento 1997 {published data only}

D'Armiento M, Damiano R, Feleppa B, Perdona S, Oriani G, De Sio M. Elective conservative surgery for renal carcinoma versus radical nephrectomy: a prospective study. *British Journal of Urology* 1997;**79**(1):15-9.

Dash 2006 {published data only}

Dash A, Vickers AJ, Schachter LR, Bach AM, Snyder ME, Russo P. Comparison of outcomes in elective partial vs radical nephrectomy for clear cell renal cell carcinoma of 4-7 cm. *BJU International* 2006;**97**(5):939-945. [DOI: [10.1111/j.1464-410X.2006.06060.x](https://doi.org/10.1111/j.1464-410X.2006.06060.x)]

Deklaj 2010 {published data only}

Deklaj T, Lifshitz DA, Shikanov SA, Katz MH, Zorn KC, Shalhav AL. Laparoscopic radical versus laparoscopic partial nephrectomy for clinical T1bN0M0 renal tumors: comparison of perioperative, pathological, and functional outcomes. *Journal of Endourology* 2010;**24**(10):1603-7.

DiBlasio 2006 {published data only}

DiBlasio CJ, Snyder ME, Russo P. Mini-flank supra-11th rib incision for open partial or radical nephrectomy. *BJU International* 2006;**97**(1):149-156. [DOI: [10.1111/j.1464-410X.2006.05882.x](https://doi.org/10.1111/j.1464-410X.2006.05882.x)]

Donin 2012 {published data only}

Donin NM, Suh LK, Barlow L, Hruby GW, Newhouse J, McKiernan J. Tumour diameter and decreased preoperative estimated glomerular filtration rate are independently correlated in patients with renal cell carcinoma. *BJU International* 2012;**109**(3):379-383.

Ganesamoni 2011 {published data only}

Ganesamoni R, Mavuduru R, Agarwal MM. Re: Hendrik Van Poppel, Luigi da Pozzo, Walter Albrecht, et al. A prospective, randomised EORTC intergroup phase 3 study comparing the oncologic outcome of elective nephron-sparing surgery and radical nephrectomy for low-stage renal cell carcinoma. *Eur Urol* 2011;**59**:543-52. *European Urology* 2011;**60**(2):e9.

Huang 2009 {published data only}

Huang WC, Elkin EB, Levey AS, Jang TL, Russo P. Partial Nephrectomy Versus Radical Nephrectomy in Patients With Small Renal Tumors-Is There a Difference in Mortality and Cardiovascular Outcomes?. *Journal of Urology* 2009;**181**(1):55-62.

Indudhara 1997 {published data only}

Indudhara R, Bueschen AJ, Urban DA, Burns JR, Lloyd LK. Nephron-sparing surgery compared with radical nephrectomy for renal tumors: current indications and results. *Southern Medical Journal* 1997;**90**(10):982-5.

Janetschek 2000 {published data only}

Janetschek G, Jeschke K, Peschel R, Strohmeyer D, Henning K, Bartsch G. Laparoscopic surgery for stage T1 renal cell

carcinoma: Radical nephrectomy and wedge resection. *European Urology* 2000;**38**(2):131-138.

Jeldres 2009 {published data only}

Jeldres C, Patard J J, Capitanio U, Perrotte P, Suardi N, Crepel M, et al. Partial Versus Radical Nephrectomy in Patients With Adverse Clinical or Pathologic Characteristics. *Urology* 2009;**73**(6):1300-1305.

Johnstonlii 2005 {published data only}

Johnston lii WK, Montgomery JS, Wolf Jr JS. Retroperitoneoscopic radical and partial nephrectomy in the patient with cirrhosis. *Journal of Urology* 2005;**173**(4):1094-1097.

Joudi 2007 {published data only}

Joudi FN, Allareddy V, Kane CJ, Konety BR. Analysis of Complications Following Partial and Total Nephrectomy for Renal Cancer in a Population Based Sample. *Journal of Urology* 2007;**177**(5):1709-1714.

Kaushik 2013 {published data only}

Kaushik D, Kim SP, Childs MA, Lohse CM, Costello BA, Chevillie JC, et al. Overall survival and development of stage IV chronic kidney disease in patients undergoing partial and radical nephrectomy for benign renal tumors. *European Urology* 2013;**64**(4):600-606.

Khoder 2009 {published data only}

Khoder WY, Stief CG, Becker AJ. Laparoscopic radical and partial nephrectomy : An overview. *Laparoskopische radikale und partielle Nephrektomie : Ein Überblick* 2009;**48**(12):1523-1533.

Kim 2003 {published data only}

Kim FJ, Rha KH, Hernandez F, Jarrett TW, Pinto PA, Kavoussi LR. Laparoscopic radical versus partial nephrectomy: assessment of complications. *Journal of Urology* 2003;**170**(2 Pt 1):408-11.

Kim 2010 {published data only}

Kim JM, Song PH, Kim HT, Park TC. Comparison of Partial and Radical Nephrectomy for pT1b Renal Cell Carcinoma. *Korean Journal of Urology* 2010;**51**(9):596-600.

Kim 2012 {published data only}

Kim SP, Thompson RH, Boorjian SA, Weight CJ, Han LC, Murad MH, et al. Comparative effectiveness for survival and renal function of partial and radical nephrectomy for localized renal tumors: a systematic review and meta-analysis. *Journal of Urology* 2012;**188**(1):51-7.

Kim 2012a {published data only}

Kim S, Thompson RH, Boorjian S, Weight C, Shippee N, Chow G, et al. Comparative effectiveness of partial and radical nephrectomy for localized renal tumors on survival and renal function: A systematic review and meta-analysis. *Journal of Urology* 2012;**1**:e679.

Kim 2013 {published data only}

Kim SH, Lee SE, Hong SK, Jeong CW, Park YH, Kim YJ, et al. Incidence and Risk Factors of Chronic Kidney Disease in Korean Patients with T1a Renal Cell Carcinoma Before and After Radical

or Partial Nephrectomy. *Japanese Journal of Clinical Oncology* 2013;**43**(12):1243-1248. [DOI: [10.1093/jjco/hyt149](https://doi.org/10.1093/jjco/hyt149)]

Klinghoffer 2013 {published data only}

Klinghoffer Z, Tarride JE, Novara G, Ficarra V, Kapoor A, Shayegan B, et al. Cost-utility analysis of radical nephrectomy versus partial nephrectomy in the management of small renal masses: adjusting for the burden of ensuing chronic kidney disease (Provisional abstract). *Canadian Urological Association Journal* 2013;**7**(3-4):108-113.

Kluth 2013 {published data only}

Kluth LA, Xylinas E, Shariat SF. Re: A prospective, randomised EORTC intergroup phase 3 study comparing the oncologic outcome of elective nephron-sparing surgery and radical nephrectomy for low-stage renal cell carcinoma. *European Urology* 2013;**63**(2):399-400.

Koo 2016 {published data only}

Koo KC, Kim JC, Cho KS, Choi YD, Hong SJ, Yang SC, et al. Oncological outcomes after partial vs radical nephrectomy in renal cell carcinomas of ≤ 7 cm with presumed renal sinus fat invasion on preoperative imaging. *BJU International* 2016;**117**(1):87-93. [DOI: [10.1111/bju.12893](https://doi.org/10.1111/bju.12893)]

Kopp 2013 {published data only}

Kopp RP, Dicks BM, Goldstein I, Mehrazin R, Silberstein JL, Colangelo CJ, et al. Does radical nephrectomy increase the risk of erectile dysfunction compared with partial nephrectomy? A cohort analysis. *BJU International* 2013;**111**(3 Pt B):E98-102.

Kopp 2015 {published data only}

Kopp RP, Liss MA, Mehrazin R, Wang S, Lee HJ, Jabaji R, et al. Analysis of Renal Functional Outcomes After Radical or Partial Nephrectomy for Renal Masses ≥ 7 cm Using the RENAL Score. *Urology* 2015;**86**(2):312-319. [DOI: [10.1016/j.urology.2015.02.067](https://doi.org/10.1016/j.urology.2015.02.067)]

Kories 2013 {published data only}

Kories C, Ubrig B. [Follow-up after radical nephrectomy and nephron sparing surgery of kidney tumors]. *Aktuelle Urologie* 2013;**44**(3):211-20; quiz 221-2.

Kowalczyk 2013 {published data only}

Kowalczyk KJ, Choueiri TK, Hevelone ND, Trinh QD, Lipsitz SR, Nguyen PL, et al. Comparative effectiveness, costs and trends in treatment of small renal masses from 2005 to 2007. *BJU International* 2013;**112**(4):E273-80.

Krabbe 2016 {published data only}

Krabbe LM, Kunath F, Schmidt S, Miernik A, Cleves A, Walther M, et al. Partial nephrectomy versus radical nephrectomy for clinically localized renal masses. *Cochrane Database of Systematic Reviews* 2016, Issue 2. [DOI: [10.1002/14651858.CD012045](https://doi.org/10.1002/14651858.CD012045)]

Laguna 2014 {published data only}

Laguna MP. Re: Renal function after nephron-sparing surgery versus radical nephrectomy: Results from EORTC randomized trial 30904. *Journal of Urology* 2014;**192**(2):369-370. [DOI: <http://dx.doi.org/10.1016/j.juro.2014.05.064>]

Lam 2005 {published data only}

Lam JS, Leppert JT, Figlin RA, Belldegrun AS. Surveillance following radical or partial nephrectomy for renal cell carcinoma. *Current Urology Reports* 2005;**6**(1):7-18.

Lane 2010 {published data only}

Lane BR, Fergany AF, Weight CJ, Campbell SC. Renal functional outcomes after partial nephrectomy with extended ischemic intervals are better than after radical nephrectomy. *Journal of Urology* 2010;**184**(4):1286-90.

Larcher 2015 {published data only}

Larcher A, Sun M, Meskawi M, Boehm K, Valdivieso R, Schiffmann J, et al. Mortality, morbidity and healthcare expenditures after local tumor ablation or partial nephrectomy for t1a kidney cancer. *Journal of Urology* 2015;**191**:e972.

Lau 2000 {published data only}

Lau WK, Blute ML, Weaver AL, Torres VE, Zincke H. Matched comparison of radical nephrectomy vs nephron-sparing surgery in patients with unilateral renal cell carcinoma and a normal contralateral kidney. *Mayo Clinic Proceedings* 2000;**75**(12):1236-42.

Lee 2002 {published data only}

Lee BR. Laparoscopic total and partial nephrectomy. *International Braz J Urol* 2002;**28**(6):504-509.

Li 2009 {published data only}

Li YS, Zhu SX, Chen SP, Xu EC, Zheng S, Cai WZ, et al. Comparing study of therapeutic effect for treating small cell carcinoma by nephron-sparing surgery and radical nephrectomy. *Chinese Journal of Cancer Prevention and Treatment* 2009;**16**(13):1033-1035.

Li 2009a {published data only}

Li QL, Zhang Y, Jiang T, Song XS, Wang FP. Mini-margin nephron sparing surgery for renal cell carcinoma 4 cm or less - a comparative study with radical nephrectomy. *Journal of Urology* 2009;**181**(4):440-441.

Lopez Garibay 2013 {published data only}

Lopez-Garibay LA, Cendejas-Gomez Jde J, Rodriguez-Covarrubias F, Gomez-Conzatti A, Gabilondo-Navarro F, Sotomayor-de-Zavaleta M. [Long-term renal function in patients with renal-cell carcinoma treated surgically: comparison between radical and partial nephrectomy]. *Revista de Investigacion Clinica* 2013;**65**(1):7-11.

MacLennan 2012 {published data only}

MacLennan S, Imamura M, Lapitan MC, Omar MI, Lam TBL, Hilvano-Cabungcal A, et al. Systematic review of perioperative and quality-of-life outcomes following surgical management of localised renal cancer. *European Urology* 2012;**62**(6):1097-1117.

Malcolm 2009 {published data only}

Malcolm JB, Bagrodia A, Derweesh IH, Mehrazin R, Diblasio CJ, Wake RW, et al. Comparison of rates and risk factors for developing chronic renal insufficiency, proteinuria and metabolic acidosis after radical or partial nephrectomy. *BJU International* 2009;**104**(4):476-81.

Manikandan 2004 {published data only}

Manikandan R, Srinivasan V, Rane A. Which is the real gold standard for small-volume renal tumors? Radical nephrectomy versus nephron-sparing surgery. *Journal of Endourology* 2004;**18**(1):39-44.

Mano 2015 {published data only}

Mano R, Kent M, Larish Y, Winer AG, Chevinsky MS, Hakimi AA, et al. Partial and Radical Nephrectomy for Unilateral Synchronous Multifocal Renal Cortical Tumors. *Urology* 2015;**85**(6):1404-10.

Mariusdottir 2013 {published data only}

Mariusdottir E, Jonsson E, Marteinson VT, Sigurdsson MI, Gudbjartsson T. Kidney function following partial or radical nephrectomy for renal cell carcinoma: a population-based study. *Scandinavian Journal of Urology* 2013;**47**(6):476-82.

Martorana 2014 {published data only}

Martorana G. Radical nephrectomy versus partial nephrectomy in localized renal cell carcinoma. *Anticancer Research* 2014;**34**(10):6052-6053.

Matin 2002 {published data only}

Matin SF, Gill IS, Worley S, Novick AC. Outcome of laparoscopic radical and open partial nephrectomy for the sporadic 4 cm. or less renal tumor with a normal contralateral kidney. *Journal of Urology* 2002;**168**(4 Pt 1):1356-9; discussion 1359-60.

McKiernan 2002 {published data only}

McKiernan JM, Teschendorf B, Katz J, Herr HW, Russo P. A comparison of hospital-based charges following partial and radical nephrectomy. *Urologic Oncology* 2002;**7**(1):3-6.

McKiernan 2002a {published data only}

McKiernan J, Simmons R, Katz J, Russo P. Natural history of chronic renal insufficiency after partial and radical nephrectomy. *Urology* 2002;**59**(6):816-20.

Medina Polo 2011 {published data only}

Medina-Polo J, Romero-Otero J, Rodriguez-Antolin A, Dominguez-Esteban M, Passas-Martinez J, Villacampa-Auba F, et al. Can partial nephrectomy preserve renal function and modify survival in comparison with radical nephrectomy?. *Scandinavian Journal of Urology & Nephrology* 2011;**45**(2):143-50.

Miller 2008 {published data only}

Miller DC, Schonlau M, Litwin MS, Lai J, Saigal CS, Urolog Diseases America Project. Renal and cardiovascular morbidity after partial or radical nephrectomy. *Cancer* 2008;**112**(3):511-520. [DOI: [10.1002/cncr.23218](https://doi.org/10.1002/cncr.23218)]

Milonas 2013 {published data only}

Milonas D, Skulcius G, Baltrimavicius R, Auskalnis S, Kincius M, Matjosaitis A, et al. Comparison of long-term results after nephron-sparing surgery and radical nephrectomy in treating 4- to 7-cm renal cell carcinoma. *Medicina (Kaunas, Lithuania)* 2013;**49**(5):223-8.

Minervini 2009 {published data only}

Minervini A, Serni S, Giubilei G, Lanzi F, Vittori G, Lapini A, Carini M. Multiple ipsilateral renal tumors: Retrospective analysis of surgical and oncological results of tumor enucleation vs radical nephrectomy. *European Journal of Surgical Oncology* 2009;**35**(5):521-526.

Minervini 2012 {published data only}

Minervini A, Serni S, Tuccio A, Siena G, Vittori G, Masieri L, et al. Simple enucleation versus radical nephrectomy in the treatment of pT1a and pT1b renal cell carcinoma. *Annals of Surgical Oncology* 2012;**19**(2):694-700.

Mitchell 2006 {published data only}

Mitchell RE, Gilbert SM, Murphy AM, Olsson CA, Benson MC, McKiernan JM. Partial nephrectomy and radical nephrectomy offer similar cancer outcomes in renal cortical tumors 4 cm or larger. *Urology* 2006;**67**(2):260-4.

Miyamoto 2012 {published data only}

Miyamoto K, Inoue S, Kajiwarra M, Teishima J, Matsubara A. Comparison of renal function after partial nephrectomy and radical nephrectomy for renal cell carcinoma. *Urologia Internationalis* 2012;**89**(2):227-232.

Mo 2014 {published data only}

Mo C, Yu Z, Tan W, Mao X, Chen X, Liu J, et al. Comparison between laparoscopic partial nephrectomy and laparoscopic ablation therapy: a meta-analysis. *Minimally Invasive Therapy & Allied Technologies: Mitat* 2014;**23**(6):317-25.

Montie 1994 {published data only}

Montie JE. Follow-up after partial or total nephrectomy for renal cell carcinoma. *Urologic Clinics of North America* 1994;**21**(4):589-592.

Morgan 2011 {published data only}

Morgan TM, Tang D, Stratton KL, Barocas DA, Anderson CB, Gregg JR, et al. Preoperative nutritional status is an important predictor of survival in patients undergoing surgery for renal cell carcinoma. *European Urology* 2011;**59**(6):923-928.

Nezakatzgoo 2013 {published data only}

Nezakatzgoo N, Colli JL, Mutter M, Aranmolate S, Wake R. Retroperitoneal hand-assisted laparoscopic nephrectomy and partial nephrectomy. *Surgical Techniques Development* 2013;**3**(1):9-12.

Nohara 2011 {published data only}

Nohara T. Editorial Comment to Postoperative renal function after partial nephrectomy for renal cell carcinoma in patients with pre-existing chronic kidney disease: A comparison with radical nephrectomy. *International Journal of Urology* 2011;**18**(6):477-477.

Ogan 2002 {published data only}

Ogan K, Cadeddu JA. Minimally invasive management of the small renal tumor: Review of laparoscopic partial nephrectomy and ablative techniques. *Journal of Endourology* 2002;**16**(9):635-643.

Pasticier 2004 {published data only}

Pasticier G, Badet L, Colombel M, Touzet S, Halila M, Fassi Fehri H, et al. [Comparative analysis of conservative surgery versus radical nephrectomy for renal cancer]. *Progres en Urologie* 2004;**14**(6):1132-9; discussion 1139.

Patel 2012 {published data only}

Patel N, Cranston D, Akhtar MZ, George C, Jones A, Leiblich A, et al. Active surveillance of small renal masses offers short-term oncological efficacy equivalent to radical and partial nephrectomy. *BJU International* 2012;**110**(9):1270-5.

Pettus 2006 {published data only}

Pettus JA, Eggener SE, Shabsigh A, Yanke B, Snyder ME, Serio A, et al. Perioperative clinical thromboembolic events after radical or partial nephrectomy. *Urology* 2006;**68**(5):988-992. [DOI: [10.1016/j.urology.2006.06.026](https://doi.org/10.1016/j.urology.2006.06.026)]

Pettus 2008 {published data only}

Pettus JA, Jang TL, Thompson RH, Yossepowitch O, Kagiwada M, Russo P. Effect of baseline glomerular filtration rate on survival in patients undergoing partial or radical nephrectomy for renal cortical tumors. *Mayo Clinic Proceedings* 2008;**83**(10):1101-1106.

Polo 2012 {published data only}

Polo G, Crouzet S, Poissonnier L, Roux A, Deculier E, Martin X, et al. Partial versus radical nephrectomy for renal cell carcinoma involving peri renal fat. Oncological and Functional Outcomes. *Néphrectomie partielle versus élargie en cas d'envahissement de la graisse périrénale. Résultats oncologiques et fonctionnels* 2012;**22**(7):388-396.

Poulakis 2003 {published data only}

Poulakis V, Witzsch U, De Vries R, Moeckel M, Becht, E. Quality of life after surgery for localized renal cell carcinoma: Comparison between radical nephrectomy and nephron-sparing surgery. *Urology* 2003;**62**(5):814-820.

Roos 2011 {published data only}

Roos FC, Brenner W, Muller M, Schubert C, Jager WJ, Thuroff JW, et al. Oncologic long-term outcome of elective nephron-sparing surgery versus radical nephrectomy in patients with renal cell carcinoma stage pT1b or greater in a matched-pair cohort. *Urology* 2011;**77**(4):803-8.

Roos 2011a {published data only}

Roos FC, Brenner W, Jager W, Albert C, Muller M, Thuroff JW, et al. Perioperative morbidity and renal function in young and elderly patients undergoing elective nephron-sparing surgery or radical nephrectomy for renal tumours larger than 4 cm. *BJU International* 2011;**107**(4):554-61.

Roos 2012 {published data only}

Roos FC, Brenner W, Thomas C, Jager W, Thuroff JW, Hampel C, et al. Functional analysis of elective nephron-sparing surgery vs radical nephrectomy for renal tumors larger than 4 cm. *Urology* 2012;**79**(3):607-13.

Scosyrev 2014 {published data only}

Scosyrev E, Messing EM, Sylvester R, Campbell S, Van Poppel H. Reply from Authors re: R. Houston Thompson. Partial Versus Radical Nephrectomy: The Debate Regarding Renal Function Ends While the Survival Controversy Continues. *Eur Urol* 2014;**65**:378-9. *European Urology* 2014;**65**(2):379-380. [DOI: [10.1016/j.eururo.2013.08.020](https://doi.org/10.1016/j.eururo.2013.08.020)]

Secil 2010 {published data only}

Secil M, Elibol C, Aslan G, Kefi A, Obuz F, Tuna B, et al. Role of intraoperative US in the decision for radical or partial nephrectomy. *Radiology* 2010;**258**(1):283-290.

Seregin 2002 {published data only}

Seregin AV. Comparative evaluation of the quality of life in patients with kidney cancer after organ-preserving operations and radical nephrectomy [Sravnitel'naia otsenka kachestva zhizni bol'nykh rakom pochki posle organosokhraniayushchikh operatsii i radikal'noi nefrektomii.]. *Urologiia* 2002;**3**:6-8.

Shekarriz 2002 {published data only}

Shekarriz B, Upadhyay J, Shekarriz H, de Assis Mendes Goes F Jr, Bianco FJ, Tiguert R, et al. Comparison of costs and complications of radical and partial nephrectomy for treatment of localized renal cell carcinoma.. *Urology* 2002;**59**(2):211-5.

Shinohara 2001 {published data only}

Shinohara N, Harabayashi T, Sato S, Hioka T, Tsuchiya K, Koyanagi T. Impact of nephron-sparing surgery on quality of life in patients with localized renal cell carcinoma. *European Urology* 2001;**39**(1):114-119. [DOI: [10.1159/000052422](https://doi.org/10.1159/000052422)]

Shvarts 2000 {published data only}

Shvarts O, Tsui KH, Smith RB, Kernion JB, Belldegrin A. Blood loss and the need for transfusion in patients who undergo partial or radical nephrectomy for renal cell carcinoma. *Journal of Urology* 2000;**164**(4):1160-3.

Simmons 2009 {published data only}

Simmons MN, Weight CJ, Gill IS. Laparoscopic radical versus partial nephrectomy for tumors >4 cm: intermediate-term oncologic and functional outcomes. *Urology* 2009;**73**(5):1077-82.

Snow 2008 {published data only}

Snow DC, Bhayani SB. Rapid communication: chronic renal insufficiency after laparoscopic partial nephrectomy and radical nephrectomy for pathologic t1a lesions. *Journal of Endourology* 2008;**22**(2):337-41.

Sun 2012 {published data only}

Sun M, Hansen J, Karakiewicz PI. Re: Hendrik Van Poppel, Luigi da Pozzo, Walter Albrecht, et al. A prospective, randomized EORTC intergroup phase 3 study comparing the oncologic outcome of elective nephron-sparing surgery and radical nephrectomy for low-stage renal cell carcinoma. *Eur Urol* 2011;**59**:543-52. *European Urology* 2012;**61**(4):e37-e38.

Sun 2013 {published data only}

Sun M, Bianchi M, Trinh QD, Hansen J, Abdollah F, Hanna N, et al. Comparison of partial vs radical nephrectomy with regard to

other-cause mortality in T1 renal cell carcinoma among patients aged >75 years with multiple comorbidities. *BJU International* 2013;**111**(1):67-73.

Szalek 2012 {published data only}

Szalek E, Polom W, Karbownik A, Grabowski T, Konkolicz A, Wolc A, et al. Effect of total and partial nephrectomy on the elimination of ciprofloxacin in humans. *Pharmacological Reports: PR* 2012;**64**(3):673-9.

Takagi 2011 {published data only}

Takagi T, Kondo T, Iizuka J, Kobayashi H, Hashimoto Y, Nakazawa H, et al. Postoperative renal function after partial nephrectomy for renal cell carcinoma in patients with pre-existing chronic kidney disease: a comparison with radical nephrectomy. *International Journal of Urology* 2011;**18**(6):472-6.

Takagi 2012 {published data only}

Takagi T, Kondo T, Iizuka J, Tomita E, Kobayashi H, Hashimoto Y, et al. Predictors for postoperative renal function after open partial nephrectomy: Including postoperative biomarkers. *International Journal of Urology* 2012;**19**(9):823-828. [DOI: [10.1111/j.1442-2042.2012.03037.x](https://doi.org/10.1111/j.1442-2042.2012.03037.x)]

Takagi 2012a {published data only}

Takagi T, Kondo T, Ikezawa E, Iizuka J, Kobayashi H, Hashimoto Y, et al. Predictors for postoperative renal function after partial nephrectomy - including postoperative biomarkers. *Journal of Urology* 2012;**187**(4, Suppl. S):E446.

Takagi 2015 {published data only}

Takagi T, Kondo T, Omae K, Iizuka J, Kobayashi H, Hashimoto Y, et al. Comparison of survival rates in stage one renal cell carcinoma between partial nephrectomy and radical nephrectomy patients according to age distribution. *Journal of Urology* 2015;**1**:e696.

Tan 2012 {published data only}

Tan H, Norton EC, Ye Z, Hafez KS, Gore JL, Miller DC. Comparative effectiveness of partial versus radical nephrectomy in the treatment of patients with early-stage kidney cancer. *Journal of Urology* 2012;**187**(4, Suppl. S):E28.

Tan 2012a {published data only}

Tan HJ, Norton EC, Ye Z, Hafez KS, Gore JL, Miller DC. Long-term survival following partial vs radical nephrectomy among older patients with early-stage kidney cancer. *JAMA* 2012;**307**(15):1629-35.

Taneja 2011 {published data only}

Taneja SS. A prospective, randomised EORTC intergroup phase 3 study comparing the oncologic outcome of elective nephron-sparing surgery and radical nephrectomy for low-stage renal cell carcinoma. *Journal of Urology* 2011;**185**(5):1637-1638.

Taneja 2011a {published data only}

Taneja SS. Re.: A prospective, randomised EORTC intergroup phase 3 study comparing the oncologic outcome of elective nephron-sparing surgery and radical nephrectomy for low-stage renal cell carcinoma. *The Journal of Urology*

2011;**185**(5):1637-1638. [DOI: <http://dx.doi.org/10.1016/j.juro.2011.01.061>]

Thompson 2008 {published data only}

Thompson RH, Boorjian SA, Lohse CM, Leibovich BC, Kwon ED, Chevillie JC, et al. Radical nephrectomy for pT1a renal masses may be associated with decreased overall survival compared with partial nephrectomy. *Journal of Urology* 2008;**179**(2):468-471.

Thompson 2009 {published data only}

Thompson RH, Siddiqui S, Lohse CM, Leibovich BC, Russo P, Blute ML. Partial Versus Radical Nephrectomy for 4 to 7 cm Renal Cortical Tumors. *Journal of Urology* 2009;**182**(6):2601-2606.

Thompson 2014 {published data only}

Thompson RH. Partial Versus Radical Nephrectomy: The Debate Regarding Renal Function Ends While the Survival Controversy Continues. *European Urology* 2014;**65**(2):378-379. [DOI: [10.1016/j.eururo.2013.07.036](https://doi.org/10.1016/j.eururo.2013.07.036)]

University Hospital Roskilde 2015 {published data only}

University Hospital Roskilde (Denmark). Nephron Sparing Renal Surgery and Total Nephrectomy - Functional Adaptation, Preservation and Prediction of Kidney Function. www.clinicaltrials.gov 30 December 2015. [NCT02646293]

Uzzo 1999 {published data only}

Uzzo RG, Wei JT, Hafez K, Kay R, Novick AC. Comparison of direct hospital costs and length of stay for radical nephrectomy versus nephron-sparing surgery in the management of localized renal cell carcinoma. *Urology* 1999;**54**(6):994-8.

VanPoppel 2011 {published data only}

Van Poppel H, Collette S, Sylvester R. Reply to Raguram Ganesamoni, Ravimohan Mavuduru, Mayank Mohan agarwal's letter to the editor re: Hendrik Van Poppel, Luigi da Pozzo, Walter Albrecht, et al. A prospective, randomised EORTC intergroup phase 3 study comparing the oncologic outcome of elective nephron-sparing surgery and radical nephrectomy for low-stage renal cell carcinoma. *Eur Urol* 2011;**59**:543-52. *European Urology* 2011;**60**(2):e10.

Vourganti 2011 {published data only}

Vourganti S, Linehan W, Bratslavsky G. Comparison of partial nephrectomy for tumors greater than 7 cm to radical nephrectomy and effect on overall survival. *Journal of Clinical Oncology* 2011;**29**(7_suppl):323.

Walsh 2015 {published data only}

Walsh LG, Nason GJ, Redmond CE, Kelly NP, McGuire BB, Sharma V, et al. Comparative effectiveness of adrenal sparing radical nephrectomy and non-adrenal sparing radical nephrectomy in clear cell renal cell carcinoma: observational study of survival outcomes. *Irish Journal of Medical Science* 2015;**184**:S175-S175.

Weight 2009 {published data only}

Weight CJ, Larson BT, Fergany AF, Campbell SC, Kaouk JH, Gao T, et al. A non-randomized comparison of overall survival

in patients with clinical T1b renal tumors treated with Radical Nephrectomy (RN) or Partial Nephrectomy (PN). *Journal of Urology* 2009;**1**:321.

Weight 2010 {published data only}

Weight CJ, Larson BT, Fergany AF, Gao T, Lane BR, Campbell SC, et al. Nephrectomy Induced Chronic Renal Insufficiency is Associated With Increased Risk of Cardiovascular Death and Death From Any Cause in Patients With Localized cT1b Renal Masses. *Journal of Urology* 2010;**183**(4):1317-1323.

Weight 2010a {published data only}

Weight CJ, Larson BT, Gao T, Campbell SC, Lane BR, Kaouk JH, et al. Elective partial nephrectomy in patients with clinical T1b renal tumors is associated with improved overall survival. *Urology* 2010;**76**(3):631-7.

Weight 2010b {published data only}

Weight CJ, Lieser G, Larson BT, Gao T, Lane BR, Campbell SC, et al. Partial nephrectomy is associated with improved overall survival compared to radical nephrectomy in patients with unanticipated benign renal tumours. *European Urology* 2010;**58**(2):293-298.

Weight 2011 {published data only}

Weight CJ, Lythgoe C, Unnikrishnan R, Lane BR, Campbell SC, Fergany AF. Partial nephrectomy does not compromise survival in patients with pathologic upstaging to pT2/pT3 or high-grade renal tumors compared with radical nephrectomy. *Urology* 2011;**77**(5):1142-6.

Woldrich 2012 {published data only}

Woldrich J, Mehrazin R, Bazzi WM, Bagrodia A, Kopp RP, Malcolm JB, et al. Comparison of rates and risk factors for development of anaemia and erythropoiesis-stimulating agent utilization after radical or partial nephrectomy. *BJU International* 2012;**109**(7):1019-25.

Woldrich 2013 {published data only}

Woldrich JM, Palazzi K, Stroup SP, Sur RL, Parsons JK, Chang D, et al. Trends in the surgical management of localized renal masses: Thermal ablation, partial and radical nephrectomy in the USA, 1998-2008. *BJU International* 2013;**111**(8):1261-1268.

Yasuda 2013 {published data only}

Yasuda Y, Yuasa T, Yamamoto S, Urakami S, Ito M, Sukegawa G, et al. Evaluation of the RENAL nephrometry scoring system in adopting nephron-sparing surgery for cT1 renal cancer. *Urologia Internationalis* 2013;**90**(2):179-183.

Zhang 2015 {published data only}

Zhang Y, Yu H, Li H. Survival analysis of surgically treated renal cell carcinoma: a single Chinese medical center experience from 2002 to 2012. *International Urology and Nephrology* 2015;**47**(8):1327-1333. [DOI: [10.1007/s11255-015-1046-5](https://doi.org/10.1007/s11255-015-1046-5)]

Zorn 2007 {published data only}

Zorn KC, Gong EM, Orvieto MA, Gofrit ON, Mikhail AA, Msezane LP, et al. Comparison of laparoscopic radical and partial nephrectomy: effects on long-term serum creatinine. *Urology* 2007;**69**(6):1035-40.

Additional references

An 2017

An JY, Ball MW, Gorin MA, Hong JJ, Johnson MH, Pavlovich CP, et al. Partial vs Radical Nephrectomy for T1-T2 Renal Masses in the Elderly: Comparison of Complications, Renal Function, and Oncologic Outcomes. *Urology* 2017;**100**:151-7.

Bell 1938

Bell ET. A classification of renal tumors with observations on the frequency of the various types. *Journal of Urology* 1938;**39**:238.

Blom 2009

Blom JH, van Poppel H, Maréchal JM, Jacqmin D, Schröder FH, de Peijck L, et al. Radical nephrectomy with and without lymph-node dissection: final results of European Organization for Research and Treatment of Cancer (EORTC) randomized phase 3 trial 30881. *European Urology* 2009;**55**(1):28-34.

Campbell 2009

Campbell SC, Novick AC, Belldegrun A, Blute ML, Chow GK, Derweesh IH, et al. Guideline for management of the clinical T1 renal mass. *Journal of Urology* 2009;**182**(4):1271-9. [PUBMED: 19683266]

Chou 2010

Chou R, Aronson N, Atkins D, Ismaila AS, Santaguida P, Smith DH, et al. AHRQ series paper 4: assessing harms when comparing medical interventions: AHRQ and the effective health-care program. *Journal of Clinical Epidemiology* 2010;**63**(5):502-12.

Cohen 2005

Cohen HT, McGovern FJ. Renal-cell carcinoma. *New England Journal of Medicine* 2005;**353**(23):2477-90. [PUBMED: 16339096]

Duque 1998

Duque JL, Loughlin KR, O'Leary MP, Kumar S, Richie JP. Partial nephrectomy: alternative treatment for selected patients with renal cell carcinoma. *Urology* 1998;**52**(4):584-90.

Endnote [Computer program]

Thomson Reuters; www.endnote.com. EndNote. Version X5 or X6 or X7. Thomson Reuters; www.endnote.com, 1988-2016.

Gartlehner 2008

Gartlehner G. Assessment of adverse effects and applicability - two areas not (yet) covered adequately in Cochrane reports. *Zeitschrift für Evidenz, Fortbildung und Qualität Im Gesundheitswesen* 2008;**102**(8):497-502.

Ghani 2014

Ghani KR, Sukumar S, Sammon JD, Rogers CG, Trinh QD, Menon M. Practice patterns and outcomes of open and minimally invasive partial nephrectomy since the introduction of robotic partial nephrectomy: results from the nationwide inpatient sample. *Journal of Urology* 2014;**191**(4):907-12.

Gill 2007

Gill IS, Kavoussi LR, Lane BR, Blute ML, Babineau D, Colombo JR Jr, et al. Comparison of 1,800 laparoscopic and open partial nephrectomies for single renal tumors. *Journal of Urology* 2007;**178**(1):41-6.

Gill 2010

Gill IS, Aron M, Gervais DA, Jewett MA. Clinical practice: Small renal mass. *New England Journal of Medicine* 2010;**362**(7):624-34. [PUBMED: 20164486]

GRADEpro GDT [Computer program]

developed by Evidence Prime, Inc.. GRADEpro GDT: GRADEpro Guideline Development Tool. McMaster University: developed by Evidence Prime, Inc., 2015.

Gu 2016

Gu LY, Ma X, Li HZ, Chen LY, Xie YP, Li XT Gao Y, Zhang Y, Zhang X. Comparison of oncologic outcome between partial and radical nephrectomy for localized renal cell carcinoma: A systematic review and meta-analysis. *Surgical Oncology-Oxford* 2016;**25**(4):385-393.

Guyatt 2008

Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Schünemann HJ, et al. GRADE: what is "quality of evidence" and why is it important to clinicians?. *BMJ* 2008;**336**(7651):995-8.

Guyatt 2011

Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *Journal of Clinical Epidemiology* 2011;**64**(4):383-94. [PUBMED: 21195583]

Hemal 2007

Hemal AK, Kumar A, Kumar R, Wadhwa P, Seth A, Gupta NP. Laparoscopic versus open radical nephrectomy for large renal tumors: a long-term prospective comparison. *Journal of Urology* 2007;**177**(3):862-6.

Herr 2005

Herr HW. A history of partial nephrectomy for renal tumors. *Journal of Urology* 2005;**173**(3):705-8. [PUBMED: 15711247]

Higgins 2011a

Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions. The Cochrane Collaboration. Vol. **Version 5.1.0 [updated March 2011]**, Available from: www.cochrane-handbook.org, 2011.

Higgins 2011b

Higgins JP, Deeks JJ. Chapter 7: Selecting studies and collecting data. Cochrane Handbook for Systematic Reviews of Interventions. In: Higgins JPT, Green S editor(s). The Cochrane Collaboration. Vol. **Version 5.1.0 [updated March 2011]**, The Cochrane Collaboration, 2011:Available from: www.cochranehandbook.org.

Higgins 2011c

Higgins JPT, Altman DG, Sterne JAC. Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Green S

editor(s). Cochrane Handbook for Systematic Reviews of Interventions. Vol. **Version 5.1.0 [updated March 2011]**, The Cochrane Collaboration, 2011:Available from: www.cochrane-handbook.org.

Kuczyk 2002

Kuczyk M, Munch T, Machtens S, Bokemeyer C, Wefer A, Hartmann J, et al. The need for routine adrenalectomy during surgical treatment for renal cell cancer: the Hannover experience. *BJU International* 2002;**89**(6):517-22. [PUBMED: 11942955]

Liberati 2009

Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Plos Medicine* 2009;**6**(7):e1000100.

Ljungberg 2015

Ljungberg B, Bensalah K, Canfield S, Dabestani S, Hofmann F, Hora M, et al. EAU guidelines on renal cell carcinoma: the 2014 update. *European Urology* 2015;**67**(5):913-24.

Mir 2016

Mir MC, Derweesh I, Propiglia F, Volpe A, Novara G, Ficarra V, et al. Partial nephrectomy versus radical nephrectomy for clinical T1B and T2 renal mass: A meta-analysis of over 9000 cases. *Journal of Urology* 2016;**1**:e985-e986.

Mir 2016a

Mir MC, Derweesh I, Propiglia F, Zargar H, Motttrie A, Autorino R. Partial nephrectomy versus radical nephrectomy for clinical T1b and T2 renal tumors: A systematic review and meta-analysis of comparative studies. *European Urology* 2016;**Sep 7**:S0302-2838(16)30533-4 [Epub ahead of print].

Review Manager 2014 [Computer program]

The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager. The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014. Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Robson 1963

Robson CJ. Radical nephrectomy for renal cell carcinoma. *Journal of Urology* 1963;**89**:37-42. [PUBMED: 13974490]

Robson 1969

Robson CJ, Churchill BM, Anderson W. The results of radical nephrectomy for renal cell carcinoma. *Journal of Urology* 1969;**101**(3):297-301. [PUBMED: 5765875]

Schunemann 2013

Schunemann H J, Tugwell P, Reeves B C, Akl E A, Santesso N, Spencer F A, et al. Non-randomized studies as a source of complementary, sequential or replacement evidence for randomized controlled trials in systematic reviews on the effects of interventions. *Res Synth Methods* 2013;**4**(1):49-62.

Schünemann 2011

Schünemann HJ, Oxman AD, Vist GE, Higgins JPT, Deeks JJ, Glasziou P, et al. Chapter 12: Interpreting results and drawing conclusions. *Cochrane Handbook for Systematic Reviews of Interventions*. Version 5.1.0 [updated March 2011]. In: Higgins JPT, Green S editor(s). *The Cochrane Collaboration*. Vol. www.cochranehandbook.org, The Cochrane Collaboration, 2011.

Shuch 2013

Shuch B, Hanley J, Lai J, Vourganti S, Kim SP, Setodji CM, et al. Overall survival advantage with partial nephrectomy: a bias of observational data?. *Cancer* 2013;**119**(16):2981-9.

Siegel 2017

Siegel RL, Miller KD, Jemal A. Cancer statistics, 2017. *CA: a Cancer Journal for Clinicians* 2017;**67**(1):7-30.

Simhan 2011

Simhan J, Smaldone MC, Tsai KJ, Canter DJ, Li T, Kutikov A, et al. Objective measures of renal mass anatomic complexity predict rates of major complications following partial nephrectomy. *European Urology* 2011;**60**(4):724-30.

Sobin 2010

Sobin LH, Gospodarowicz MK, Wittekind C. *TNM Classification of Malignant Tumours*. 7th Edition. Oxford: Blackwell Publishing, 2010.

Tobert 2014

Tobert CM, Riedinger CB, Lane BR. Do we know (or just believe) that partial nephrectomy leads to better survival than radical nephrectomy for renal cancer?. *World Journal of Urology* 2014;**32**(3):573-9. [PUBMED: 24671608]

Vermooten 1950

Vermooten V. Indications for conservative surgery in certain renal tumors: a study based on the growth pattern of the cell carcinoma. *The Journal of urology* 1950;**64**(2):200-8. [PUBMED: 15429181]

Volpe 2004

Volpe A, Panzarella T, Rendon RA, Haider MA, Kondylis FI, Jewett MA. The natural history of incidentally detected small renal masses. *Cancer* 2004;**100**(4):738-45. [PUBMED: 14770429]

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Van Poppel 2007

Methods	<p>Parallel grouped randomised controlled clinical trial (RCT)</p> <p>Randomisation ratio: 541 patients, partial nephrectomy: n = 268, radical nephrectomy: n = 273.</p> <p>Non-inferiority design: "One-sided log-rank test for non-inferiority at error rates of $\alpha = 0.05$ and $\beta = 0.20$", "Tests for both non-inferiority and superiority were carried out. The prognostic role of several variables was tested in univariate fashion with the log-rank test."</p> <p>Statistical analysis: "The primary analysis included all randomised patients based on the intention-to-treat (ITT) principle; sensitivity analyses were performed in clinically and pathologically eligible patients and in patients with RCC. Survival curves were estimated using the Kaplan-Meier method, and differences were compared with the log-rank test ($p < 0.05$ was considered statistically significant). Tests for both non-inferiority and superiority were carried out. The prognostic role of several variables was tested in univariate fashion with the log-rank test."</p>
Participants	<p>Inclusion criteria: "Eligibility criteria for entry into the study comprised patients with a solitary T1–T2 N0 M0 renal tumour, suspicious for renal adenocarcinoma, and a normal contralateral kidney. According to the 1978 TNM staging system there is in T1 patients evidence of a small tumour without enlargement of the kidney and limited caliceal distortion or deformity and circumscribed vascular deformities, surrounded by parenchyma. In T2 patients there is evidence of a large tumour with deformity or enlargement of the kidney or caliceal or pelvic involvement. The continuity of the cortex is preserved on arteriography. The tumour was single on computed tomography (CT) scanning, did not exceed 5 cm in diameter, and did not show invasion of the perirenal fat (T1–T2) on the CT scan or intravenous urography (IVU). The World Health Organization (WHO) performance status was 2."</p> <p>Exclusion criteria: "Patients with a solitary kidney, von Hippel-Lindau disease, multifocal disease, T3–T4 tumours, clinical presence of distant or lymphatic metastases, a WHO performance status > 2, and patients with another carcinoma, except for adequately treated non-melanoma skin cancer, were excluded from the study."</p>

Van Poppel 2007 (Continued)

Diagnostic criteria: "The preoperative evaluation of patients included physical examination, laboratory evaluation (erythrocyte sedimentation rate, haemoglobin, serum creatinine, alkaline phosphatase), IVU if either microscopic or gross haematuria was present, ultrasonography of the kidney and the liver, chest x-ray, and a CT scan of both kidneys. The pathologic tumour stage was determined according to the TNM classification system proposed by the Union Internationale Contre le Cancer (UICC; 1978)."

Interventions

Intervention: Partial nephrectomy versus radical nephrectomy.

Number of study centres: Multicentre, "45 institutions (17 countries)."

Run-in period: "From March 1992 to January 2003"

Extension period: no

Description of interventions: "RN consisted of removal of the entire kidney with the adrenal and perinephric fat within the intact Gerota fascia. Limited lymphadenectomy could be done separately or en bloc and includes the lymphatic tissue in the renal hilus (usually included in the RN specimen anyway) and the nodes around the vena cava at the level of the renal veins on the right side and on the aorta at the level of the artery on the left side. [...] For NSS, tumour removal was done by excavation (no enucleation), wedge resection, or partial nephrectomy after rigorous inspection of the entire renal capsule together with limited lymphadenectomy. Hilar clamping was not routinely done. [...] When there was any doubt about the margin status, a frozen section analysis of the resection margins was performed. In the case of a positive resection margin, satellite or secondary lesions, RN was done and the patient was, however, followed for recurrence and survival. When enlarged lymph nodes were found, a frozen section was done. In case of a positive lymphadenectomy, further treatment was left to the surgeon's discretion but the patient was still followed for recurrence and survival."

Follow-up: "Median follow-up was 9.3yr", "Postoperative follow-up of patients included physical examination, laboratory examinations (erythrocyte sedimentation rate, haemoglobin, creatinine, alkaline phosphatase), a chest x-ray, and a renal ultrasonography every 3 mo during the first year, every 4 mo during the second and third years, and at 6-mo intervals until the end of the fifth year. Thereafter, the patient was followed yearly until death. At each occasion, both kidneys and the renal bed were examined with renal ultrasonography. A CT scan was done within 1 month after surgery and then every year. If any suspicion of disease progression arose, a complete restaging was performed. Patients in the NSS arm who underwent a RN (for any reason) and those who had no histologically proven adenocarcinoma of the kidney after definitive pathologic examination of the surgical specimen remained in the study and were followed in accordance with the protocol."

Outcomes

Composite outcome measures reported: yes (time-to-death of any cause)

Outcomes reported: "The study was designed to assess both morbidity and cancer control.", "The primary end point was overall survival (OS). Secondary end points were disease-specific survival (DSS), progression, and surgical side-effects."

Study details

Trial terminated before regular end (for poor accrual): yes, "The study was originally designed as a randomised, non-inferiority, multicentre, phase 3 study requiring 310 patients, trying to rule out a difference of 10% in 5-yr survival from 90% on RN to 80% on PN. Accrual began in April 1992, and 300 patients were entered in 5.5 yr. In early 1998, the European Organisation for Research and Treatment of Cancer Genito-Urinary Group (EORTC-GU) decided to open the trial to other groups (Southwest Oncology Group [SWOG], Eastern Cooperative Oncology Group [ECOG], American College of Surgeons Oncology Group, National Cancer Institute of Canada [NCIC]) to redesign the study based on a more realistic difference of 3% in 5-yr survival from 90% on RN to 87% on PN (hazard ratio [HR]: 1.3). For this difference, a minimum of 1300 patients and 368 deaths were now required based on a one-sided log-rank test for non-inferiority at error rates of $\alpha = 0.05$ and $\beta = 0.20$. In January 2003, the study was prematurely closed because of poor accrual. In total, 541 patients were randomised (EORTC: 527 patients; NCIC: 11 patients; USA (ECOG/SWOG): 3 patients)."

Trial ID: EORTC-30904, ACOSOG-30904, CAN-NCIC-RE1, E-30904, SWOG-EORTC-30904, NCT00002473

Publication details

Language of publication: English

Van Poppel 2007 (Continued)

Conflict of interest: "We have no commercial relationship such as: consultancies, stock ownership or other equity interests, patents received and/or pending, or any commercial relationship which might be in any way considered related to this article."

Funding: "This publication was supported by grant nos. 5U10CA11488-20 through 2U10 CA11488-36 from the National Cancer Institute (Bethesda, MD). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the National Cancer Institute. Support also came from the Vlaamse Liga tegen Kanker, Belgium, and the Federation Belge contre le Cancer, Belgium."

Publication status: peer-reviewed journal / full article

Stated aim for study	"A large, prospective, randomised study has been conducted to compare RN and NSS for small, low-stage RCC in terms of complications and oncologic efficacy."
Notes	Abbreviation: RCC, renal cell carcinoma PN, partial nephrectomy RN, radical nephrectomy NSS, nephron-sparing surgery IVU, intravenous urography CT, computed tomography

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	We assume that randomisation was performed adequately at the EORTC Data Centre. However, information was not reported and there is therefore unclear risk of bias.
Allocation concealment (selection bias)	Low risk	Central allocation.
Blinding of participants and personnel (performance bias) Time-to-death of any cause	Unclear risk	There was no blinding. It might be conceivable that this outcome is influenced by lack of blinding. We finally judge that there is an unclear risk of bias.
Blinding of participants and personnel (performance bias) Serious adverse events	High risk	There was no blinding. We judge that this outcome is likely to be influenced by lack of blinding.
Blinding of participants and personnel (performance bias) Cancer-specific survival	High risk	There was no blinding. We judge that this outcome is likely to be influenced by lack of blinding.
Blinding of participants and personnel (performance bias) Time-to-recurrence	Unclear risk	There was no blinding. It might be conceivable that this outcome is influenced by lack of blinding. We finally judge that there is an unclear risk of bias.

Van Poppel 2007 (Continued)

Blinding of participants and personnel (performance bias) Immediate post-operative adverse events	High risk	There was no blinding. We judge that this outcome is likely to be influenced by lack of blinding.
Blinding of participants and personnel (performance bias) Longterm adverse events	High risk	There was no blinding. We judge that this outcome is likely to be influenced by lack of blinding.
Blinding of outcome assessment (detection bias) Time-to-death of any cause	Low risk	There was no blinding of outcome assessment but it could have been expected. However, we judge that it is not likely that outcome assessment for time-to-death of any cause is influenced by lack of blinding.
Blinding of outcome assessment (detection bias) Serious adverse events	High risk	There was no blinding of outcome assessment but it could have been expected. We judge that outcome assessment of serious adverse events is likely to be influenced by lack of blinding.
Blinding of outcome assessment (detection bias) Cancer-specific survival	High risk	There was no blinding of outcome assessment but it could have been expected. We judge that outcome assessment of cancer-specific survival is likely to be influenced by lack of blinding.
Blinding of outcome assessment (detection bias) Time-to-recurrence	Low risk	There was no blinding of outcome assessment but it could have been expected. However, we judge that it is not likely that outcome assessment of time-to-recurrence is influenced by lack of blinding.
Blinding of outcome assessment (detection bias) Immediate post-operative adverse events	High risk	There was no blinding of outcome assessment but it could have been expected. We judge that outcome assessment of immediate post-operative adverse events is likely to be influenced by lack of blinding.
Blinding of outcome assessment (detection bias) Longterm adverse events	High risk	There was no blinding of outcome assessment but it could have been expected. We judge that outcome assessment of long-term adverse events is likely to be influenced by lack of blinding.
Incomplete outcome data (attrition bias) Time-to-death of any cause	Low risk	Outcome analysed by intention-to-treat and all patients randomised were included in the analysis for this outcome.
Incomplete outcome data (attrition bias) Serious adverse events	Low risk	Outcome analysed by intention-to-treat and all patients randomised were included in the analysis for this outcome.
Incomplete outcome data (attrition bias) Cancer-specific survival	Low risk	Outcome analysed by intention-to-treat and all patients randomised were included in the analysis for this outcome.
Incomplete outcome data (attrition bias) Time-to-recurrence	Low risk	Outcome analysed by intention-to-treat and all patients randomised were included in the analysis for this outcome.
Incomplete outcome data (attrition bias) Immediate post-operative adverse events	High risk	This outcome was not analysed by intention-to-treat and there is substantial departure of the intervention received from that assigned at randomisation.

Van Poppel 2007 *(Continued)*

Incomplete outcome data (attrition bias) Longterm adverse events	Low risk	Outcome analysed by intention-to-treat and all patients randomised were included in the analysis for this outcome.
Selective reporting (reporting bias)	Low risk	The study protocol is available and we are sure that the published reports include all expected outcomes.
Other bias	High risk	There was substantial cross-over: Of the 268 participants randomised to partial nephrectomy, 39 received radical nephrectomy and of the 273 participants randomised to radical nephrectomy, 16 received partial nephrectomy.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Abdollah 2014	Wrong study design
Abel 2010	Wrong study design
Acar 2009	Wrong study design
Antonelli 2008	Wrong study design
Antonelli 2012	Wrong study design
Antoniewicz 2012	Wrong study design
Arnold 2013	Wrong study design
Azawi 2014	Wrong study design
Azawi 2015	Wrong study design
Badalato 2012	Wrong study design
Bagrodia 2010	Wrong study design
Bagrodia 2011	Wrong study design
Baillargeon Gagné 2010	Wrong study design
Barbalias 1999	Wrong study design
Bazzi 2012	Wrong intervention
Bensalah 2008	Wrong study design
Bianchi 2013	Wrong study design
Bigot 2010	Wrong study design
Blute 2006	Wrong study design
Bohle 2008	Wrong study design

Study	Reason for exclusion
Boorjian 2013	Other publication type
Boulière 2011	Wrong study design
Brookman May 2013	Wrong study design
Brookman May 2013a	Wrong study design
Butler 1995	Wrong study design
Campbell 2012	Other publication type
Capitanio 2015	Wrong study design
Choi 2012	Wrong study design
Chung 2015	Wrong study design
Clark 2008	Wrong study design
Cooper 2015	Wrong study design
Cost 2012	Wrong patient population
D'Armiento 1997	Wrong study design
Dash 2006	Wrong study design
Deklaj 2010	Wrong study design
DiBlasio 2006	Wrong intervention
Donin 2012	Wrong study design
Ganesamoni 2011	Other publication type
Huang 2009	Wrong study design
Indudhara 1997	Wrong study design
Janetschek 2000	Wrong study design
Jeldres 2009	Wrong study design
Johnstonlii 2005	Wrong study design
Joudi 2007	Wrong study design
Kaushik 2013	Wrong patient population
Khoder 2009	Wrong study design
Kim 2003	Wrong study design
Kim 2010	Wrong study design

Study	Reason for exclusion
Kim 2012	Wrong study design
Kim 2012a	Wrong study design
Kim 2013	Wrong study design
Klinghoffer 2013	Wrong study design
Kluth 2013	Other publication type
Koo 2016	Wrong study design
Kopp 2013	Wrong study design
Kopp 2015	Wrong study design
Kories 2013	Wrong study design
Kowalczyk 2013	Wrong study design
Krabbe 2016	Wrong study design
Laguna 2014	Other publication type
Lam 2005	Wrong study design
Lane 2010	Wrong study design
Larcher 2015	Wrong comparator
Lau 2000	Wrong study design
Lee 2002	Wrong study design
Li 2009	Wrong study design
Li 2009a	Wrong study design
Lopez Garibay 2013	Wrong study design
MacLennan 2012	Wrong study design
Malcolm 2009	Wrong study design
Manikandan 2004	Wrong study design
Mano 2015	Wrong study design
Mariusdottir 2013	Wrong study design
Martorana 2014	Wrong study design
Matin 2002	Wrong study design
McKiernan 2002	Wrong study design

Study	Reason for exclusion
McKiernan 2002a	Wrong study design
Medina Polo 2011	Wrong study design
Miller 2008	Wrong study design
Milonas 2013	Wrong study design
Minervini 2009	Wrong study design
Minervini 2012	Wrong study design
Mitchell 2006	Wrong study design
Miyamoto 2012	Wrong study design
Mo 2014	Wrong study design
Montie 1994	Wrong study design
Morgan 2011	Wrong study design
Nezakatzgoo 2013	Wrong study design
Nohara 2011	Other publication type
Ogan 2002	Wrong study design
Pasticier 2004	Wrong study design
Patel 2012	Wrong study design
Pettus 2006	Wrong study design
Pettus 2008	Wrong study design
Polo 2012	Wrong study design
Poulakis 2003	Wrong study design
Roos 2011	Wrong study design
Roos 2011a	Wrong study design
Roos 2012	Wrong study design
Scosyrev 2014	Other publication type
Secil 2010	Wrong study design
Seregin 2002	Wrong study design
Shekarritz 2002	Wrong study design
Shinohara 2001	Wrong study design

Study	Reason for exclusion
Shvarts 2000	Wrong study design
Simmons 2009	Wrong study design
Snow 2008	Other publication type
Sun 2012	Other publication type
Sun 2013	Wrong study design
Szalek 2012	Wrong study design
Takagi 2011	Wrong study design
Takagi 2012	Wrong study design
Takagi 2012a	Wrong study design
Takagi 2015	Wrong study design
Tan 2012	Wrong study design
Tan 2012a	Wrong study design
Taneja 2011	Wrong study design
Taneja 2011a	Other publication type
Thompson 2008	Wrong study design
Thompson 2009	Wrong study design
Thompson 2014	Wrong study design
University Hospital Roskilde 2015	Ongoing prospective observational study. The study is designed as an observational, longitudinal study where plasma [NT-proBNP], renal function and blood pressure is followed in patients undergoing partial or radical nephrectomy and relate this to plasma BMP. This is not a randomised controlled study. NCT02646293.
Uzzo 1999	Wrong study design
VanPoppel 2011	Other publication type
Vourganti 2011	Wrong study design
Walsh 2015	Wrong study design
Weight 2009	Wrong study design
Weight 2010	Wrong study design
Weight 2010a	Wrong study design
Weight 2010b	Wrong study design

Study	Reason for exclusion
Weight 2011	Wrong study design
Woldrich 2012	Wrong study design
Woldrich 2013	Wrong study design
Yasuda 2013	Wrong study design
Zhang 2015	Wrong study design
Zorn 2007	Wrong study design

DATA AND ANALYSES

Comparison 1. Partial nephrectomy vs. radical nephrectomy (intention-to-treat)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Time-to-death of any cause	1	541	Hazard Ratio (Random, 95% CI)	1.50 [1.03, 2.18]
2 Serious adverse events (Surgery-related mortality)	1	541	Risk Ratio (M-H, Random, 95% CI)	2.04 [0.19, 22.34]
3 Cancer-specific survival	1	541	Hazard Ratio (Random, 95% CI)	2.06 [0.62, 6.84]
4 Time-to-recurrence	1	541	Hazard Ratio (Random, 95% CI)	1.37 [0.58, 3.24]
5 Spleen damage	1	529	Risk Ratio (M-H, Random, 95% CI)	1.99 [0.18, 21.84]
6 Pleural damage	1	529	Risk Ratio (M-H, Random, 95% CI)	1.12 [0.67, 1.86]
7 Perioperative bleeding	1	529	Risk Ratio (M-H, Random, 95% CI)	1.94 [1.38, 2.73]
8 Urinary fistula	1	529	Risk Ratio (M-H, Random, 95% CI)	20.92 [1.23, 355.20]
9 Reoperation due to side-effects (due to bleeding, urinary fistula, bowel obstruction, pleuropneumonia)	1	529	Risk Ratio (M-H, Random, 95% CI)	1.83 [0.69, 4.87]
10 Cardiovascular-related mortality	1	541	Risk Ratio (M-H, Random, 95% CI)	1.27 [0.72, 2.24]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
11 Liver-related mortality	1	541	Risk Ratio (M-H, Random, 95% CI)	9.17 [0.50, 169.45]
12 Renal-related mortality	1	541	Risk Ratio (M-H, Random, 95% CI)	2.04 [0.62, 6.69]
13 Infection-related mortality	1	541	Risk Ratio (M-H, Random, 95% CI)	0.68 [0.11, 4.03]
14 Chronic pulmonary disease-related mortality	1	541	Risk Ratio (M-H, Random, 95% CI)	1.53 [0.26, 9.07]

Analysis 1.1. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 1 Time-to-death of any cause.

Analysis 1.2. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 2 Serious adverse events (Surgery-related mortality).

Analysis 1.3. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 3 Cancer-specific survival.

Analysis 1.4. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 4 Time-to-recurrence.

Analysis 1.5. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 5 Spleen damage.

Analysis 1.6. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 6 Pleural damage.

Analysis 1.7. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 7 Perioperative bleeding.

Analysis 1.8. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 8 Urinary fistula.

Analysis 1.9. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 9 Reoperation due to side-effects (due to bleeding, urinary fistula, bowel obstruction, pleuropneumonia).

Analysis 1.10. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 10 Cardiovascular-related mortality.

Analysis 1.11. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 11 Liver-related mortality.

Analysis 1.12. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 12 Renal-related mortality.

Analysis 1.13. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 13 Infection-related mortality.

Analysis 1.14. Comparison 1 Partial nephrectomy vs. radical nephrectomy (intention-to-treat), Outcome 14 Chronic pulmonary disease-related mortality.

APPENDICES

Appendix 1. Electronic Search Strategies

Medline and Medline in Process (OVIDSP)

1. exp kidney neoplasms/
2. exp carcinoma, renal cell/
3. ((kidney or renal) adj3 (cancer* or carcinoma* or neoplas* or tumor* or malignan* or adenocarcinoma* or mass*)).tw.
4. ((clear cell* or papill* or chromophil* or chromophob* or collect* duct or sacromatoid*) adj3 (kidney or renal)).tw.
5. hypernephroma*.tw.
6. nephrocarcinoma*.tw.
7. grawitz tumor*.tw.
8. RCC.tw.
9. or/1-8
10. exp Nephrectomy/
11. exp Laparoscopy/
12. ((laparoscop* or partial* or radical* or transperiton* or retroperiton*) adj3 nephrectom*).tw.
13. ((nephron or kidney* or renal) adj2 surg*).tw.
14. or/10-13
15. randomized controlled trial.pt.
16. controlled clinical trial.pt.
17. randomized.ab.
18. placebo.ab.
19. drug therapy.fs.
20. randomly.ab.
21. trial.ab.

22. groups.ab.
23. or/15-22
24. exp animals/ not humans.sh.
25. 23 not 24
26. 9 and 14
27. 25 and 26

Embase (OVIDSP)

1. exp kidney tumor/
2. exp kidney carcinoma/
3. ((kidney or renal) adj3 (cancer* or carcinoma* or neoplas* or tumo?r* or malignan* or adenocarcinoma* or mass*)).tw.
4. ((clear cell* or papill* or chromophil* or chromophob* or collect* duct* or sacromatoid*) adj3 (kidney or renal)).tw.
5. hypernephroma*.tw.
6. nephrocarcinoma*.tw.
7. Grawitz tumo?r*.tw.
8. RCC.tw.
9. or/1-8
10. exp nephrectomy/
11. exp laparoscopy/
12. exp laparoscopic surgery/
13. ((laparoscop* or partial* or radical* or transperiton* or retroperiton*) adj3 nephrectom*).tw.
14. ((nephron or kidney* or renal) adj2 surg*).tw.
15. or/10-14
16. 9 and 15
17. crossover procedure/
18. double-blind procedure/
19. randomized controlled trial/
20. single-blind procedure/
21. (random* or factorial* or crossover* or cross over* or placebo* or assign* or allocat* or volunteer*).mp.
22. ((doubl* or singl*) adj blind*).mp.
23. or/17-22
24. 16 and 23

Pubmed (National Library of Medicine)

- #24 (#13 AND #23)
- #23 (#21 NOT #22)
- #22 (animals [mh] NOT humans [mh])

#21 (#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20)

#20 trial[Title]

#19 randomly[Title/Abstract]

#18 clinical trials as topic [mesh: noexp]

#17 placebo[Title/Abstract]

#16 randomized[Title/Abstract]

#15 controlled clinical trial[Publication Type]

#14 randomized controlled trial[Publication Type]

#13 (#8 AND #12)

#12 (#9 OR #10 OR #11)

#11 (Nephrectom*[Text Word]) AND (laparoscop*[Text Word] OR partial*[Text Word] OR radical*[Text Word] OR transperiton*[Text Word] OR retroperiton*[Text Word]))

#10 laparoscopy[MeSH Terms]

#9 nephrectomy[MeSH Terms]

#8 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7)

#7 (hypernephroma*[Text Word] OR Nephrocarcinoma*[Text Word] OR Grawitz tumor*[Text Word] OR Grawitz tumour*[Text Word])

#6 (renal[Text Word]) AND (clear cell*[Text Word] OR papill*[Text Word] OR chromophil*[Text Word] OR chromophob*[Text Word] OR collect* duct[Text Word] OR sacromatoid*[Text Word]))

#5 (Kidney[Text Word]) AND (clear cell*[Text Word] OR papill*[Text Word] OR chromophil*[Text Word] OR chromophob*[Text Word] OR collect* duct[Text Word] OR sacromatoid*[Text Word]))

#4 (renal[Text Word]) AND (cancer*[Text Word] OR carcinoma*[Text Word] OR neoplas*[Text Word] OR tumor*[Text Word] OR tumour*[Text Word] OR malignan*[Text Word] OR adenocarcinoma*[Text Word] OR mass*[Text Word]))

#3 (kidney[Text Word]) AND (cancer*[Text Word] OR carcinoma*[Text Word] OR neoplas*[Text Word] OR tumor*[Text Word] OR tumour*[Text Word] OR malignan*[Text Word] OR adenocarcinoma*[Text Word] OR mass*[Text Word]))

#2 carcinoma, renal cell[MeSH Terms]

#1 kidney neoplasms[MeSH Terms]

Cochrane Library (Wiley)

#1 MeSH descriptor: [Kidney Neoplasms] explode all trees

#2 MeSH descriptor: [Carcinoma, Renal Cell] explode all trees

#3 ((kidney or renal) near/3 (cancer* or carcinoma* or neoplas* or tumor?r* or malignan* or adenocarcinoma* or mass*)):ti,ab,kw

#4 ((clear cell* or papill* or chromophil* or chromophob* or collect* duct* or sacromatoid*) near/3 (kidney or renal)):ti,ab,kw

#5 hypernephroma*:ti,ab,kw

#6 nephrocarcinoma*:ti,ab,kw

#7 Grawitz tumor?r\$:ti,ab,kw

#8 RCC:ti,ab,kw

#9 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8

#10 MeSH descriptor: [Nephrectomy] explode all trees

#11 MeSH descriptor: [Laparoscopy] explode all trees

#12 ((laparoscop* or partial* or radical* or transperiton* or retroperiton*) near/3 nephrectom*):ti,ab,kw

#13 ((nephron or kidney* or renal) near/2 surg*):ti,ab,kw

#14 #10 or #11 or #12 or #13

#15 #9 and #14

Web of Science Core Collection and Conference Proceedings Citation Index - Science (CPCI-S) (Thomson Reuters)

#27 #14 and #26

#26 #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25

#25 TS=double blind*

#24 TS=single blind*

#23 TS=placebo*

#22 TS=random*

#21 TS=prospective stud*

#20 TS=follow up stud*

#19 TS=controlled trial*

#18 TS=evaluation stud*

#17 TS=comparative stud*

#16 TS=research design*

#15 TS=clinical trial*

#14 #12 and #13

#13 #9 or #10 or #11

#12 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8

#11 TS=nephrectom*

#10 TS=((surg* NEAR/2 (nephron or kidney* or renal)))

#9 TS=((nephrectom* NEAR/2 (laparoscop* or partial* or radical* or transperiton* or retroperiton*)))

#8 TS=nephrocarcinoma*

#7 TS=hypernephroma*

#6 TS=(RCC)

#5 TS=(grawitz tumo?r*)

#4 TS=((renal NEAR/2 ("clear cell" or papill* or chromophil* or chromophob* or sacromatoid*)))

#3 TS=((kidney NEAR/2 ("clear cell" or papill* or chromophil* or chromophob* or sacromatoid*)))

#2 TS=((Renal NEAR/2 (cancer* or carcinoma* or neoplas* or tumo?r* or malignan* or adenocarcinoma* or mass*)))

#1 TS=((kidney NEAR/2 (cancer* or carcinoma* or neoplas* or tumo?r* or malignan* or adenocarcinoma* or mass*)))

BIOSIS (Thomson Reuters)

#27 #14 and #26

Partial nephrectomy versus radical nephrectomy for clinical localised renal masses (Review)

Copyright © 2017 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

#26 #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25

#25 TS=double blind*

#24 TS=single blind*

#23 TS=placebo*

#22 TS=random*

#21 TS=prospective stud*

#20 TS=follow up stud*

#19 TS=controlled trial*

#18 TS=evaluation stud*

#17 TS=comparative stud*

#16 TS=research design*

#15 TS=clinical trial*

#14 #12 and #13

#13 #9 or #10 or #11

#12 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8

#11 TS=nephrectom*

#10 TS=((surg* NEAR/2 (nephron or kidney* or renal)))

#9 TS=((nephrectom* NEAR/2 (laparoscop* or partial* or radical* or transperiton* or retroperiton*))

#8 TS=nephrocarcinoma*

#7 TS=hypernephroma*

#6 TS=(RCC)

#5 TS=(grawitz tumor?r*)

#4 TS=((renal NEAR/2 ("clear cell" or papillary* or chromophil* or chromophobe* or sacromatoid*))

#3 TS=((kidney NEAR/2 ("clear cell" or papillary* or chromophil* or chromophobe* or sacromatoid*))

#2 TS=((Renal NEAR/2 (cancer* or carcinoma* or neoplas* or tumor?r* or malignan* or adenocarcinoma* or mass*)))

#1 TS=((kidney NEAR/2 (cancer* or carcinoma* or neoplas* or tumor?r* or malignan* or adenocarcinoma* or mass*)))

LILACS (Virtual Health Library)

((kidney or rinon or rim or renal\$) and (cancer\$ or carcinoma\$ or neoplas\$ or adenocarcinoma\$ or tumor\$ or tumours\$) and (laparoscop\$ or nephrectomy\$ or nefrectom\$)) AND ((PT:"randomized controlled trial" OR PT:"controlled clinical trial" OR PT:"multicenter study" OR MH:"randomized controlled trials as topic" OR MH:"controlled clinical trials as topic" OR MH:"multicenter study as topic" OR MH:"random allocation" OR MH:"double-blind method" OR MH:"single-blind method") OR ((ensaio\$ OR ensayo\$ OR trial\$) AND (azar OR acaso OR placebo OR control\$ OR aleat\$ OR random\$ OR enmascarado\$ OR simpleciego OR ((simple\$ OR single OR duplo\$ OR doble\$ OR double\$) AND (cego OR ciego OR blind OR mask))) AND clinic\$)) AND NOT (MH:animals OR MH:rabbits OR MH:rats OR MH:primates OR MH:dogs OR MH:cats OR MH:swine OR PT:"in vitro")

Scopus (Elsevier)

((TITLE-ABS-KEY(Kidney W/3 carcinoma*)) OR (TITLE-ABS-KEY(Kidney W/3 neoplas*)) OR (TITLE-ABS-KEY(Kidney W/3 tumor?r*)) OR (TITLE-ABS-KEY(Kidney W/3 mass*)) OR (TITLE-ABS-KEY(Kidney W/3 malignan*)) OR (TITLE-ABS-KEY(Kidney W/3 adenocarcinoma*)) OR (TITLE-ABS-KEY(Renal W/3 carcinoma*)) OR (TITLE-ABS-KEY(Renal W/3 neoplas*)) OR (TITLE-ABS-KEY(Renal W/3 tumor?r*)) OR (TITLE-ABS-KEY(Renal W/3 mass*)) OR (TITLE-ABS-KEY(Renal W/3 malignan*)) OR (TITLE-ABS-KEY(Renal W/3 adenocarcinoma*)) OR (TITLE-ABS-

KEY(Kidney W/2 clear cell*) OR (TITLE-ABS-KEY(Kidney W/2 papillary*)) OR (TITLE-ABS-KEY(Kidney W/2 chromophil*)) OR (TITLE-ABS-KEY(Kidney W/2 chromophobe*)) OR (TITLE-ABS-KEY(Kidney W/2 collect duct*)) OR (TITLE-ABS-KEY(Kidney W/2 sacromatoid*)) OR (TITLE-ABS-KEY(Renal W/2 clear cell*)) OR (TITLE-ABS-KEY(Renal W/2 papillary*)) OR (TITLE-ABS-KEY(Renal W/2 chromophil*)) OR (TITLE-ABS-KEY(Renal W/2 chromophobe*)) OR (TITLE-ABS-KEY(Renal W/2 collect duct*)) OR (TITLE-ABS-KEY(Renal W/2 sacromatoid*)) OR (TITLE-ABS-KEY(hypernephroma*)) OR (TITLE-ABS-KEY(nephrocarcinoma*)) OR (TITLE-ABS-KEY(Grawitz tumor*)) AND ((TITLE-ABS-KEY(nephrectom* W/3 laparoscop*)) OR (TITLE-ABS-KEY(nephrectom* W/3 partial*)) OR (TITLE-ABS-KEY(nephrectom* W/3 radical*)) OR (TITLE-ABS-KEY(nephrectom* W/3 transperiton*)) OR (TITLE-ABS-KEY(nephrectom* W/3 retroperiton*))) AND ((TITLE-ABS-KEY(clinical trial*)) OR (TITLE-ABS-KEY(research design*)) OR (TITLE-ABS-KEY(comparative stud*)) OR (TITLE-ABS-KEY(evaluation stud*)) OR (TITLE-ABS-KEY(controlled trial*)) OR (TITLE-ABS-KEY(follow up stud*)) OR (TITLE-ABS-KEY(prospective stud*)) OR (TITLE-ABS-KEY(random*)) OR (TITLE-ABS-KEY(placebo*)) OR (TITLE-ABS-KEY(single blind*)) OR (TITLE-ABS-KEY(double blind*)))

Biomed Central

((nephrectom* AND (laparoscop* OR partial* OR radical* OR transperiton* OR retroperiton*)) [TIAB])) AND (((kidney AND (cancer* OR carcinoma* OR neoplas* OR tumor* OR tumour* OR malignan* OR adenocarcinoma* OR mass*)) [TIAB])) OR (((renal AND (cancer* OR carcinoma* OR neoplas* OR tumor* OR tumour* OR malignan* OR adenocarcinoma* OR mass*)) [TIAB])) OR (((kidney AND (clear and cell* OR papillary* OR chromophil* OR chromophobe* OR collect* and duct OR sacromatoid*)) [TIAB])) OR (((renal AND (clear and cell* OR papillary* OR chromophil* OR chromophobe* OR collect* and duct OR sacromatoid*)) [TIAB])) OR (((hypernephroma* OR nephrocarcinoma* OR grawitz and tumor* OR grawitz and tumour*) [TIAB]))

WHO Int. Clin Trials Registry Search Portal

Kidney or Renal in Condition and Nephrectomy in Intervention

ClinicalTrials.gov

Kidney or Renal in Condition and Nephrectomy in Intervention

Appendix 2. Leading experts in the field of renal cell carcinoma treatment

Name	Affiliation
Prof. Dr. med. B. Wullich	Department of Urology; University Hospital Erlangen
PD Dr. med. PJ Goebell	Department of Urology; University Hospital Erlangen
Prof. Allan Pantuck, MD	Department of Urology; David Geffen School of Medicine at the University of California, Los Angeles

CONTRIBUTIONS OF AUTHORS

Concept and design: Kunath, Kroeger, Krabbe, Walther

Study selection: Kunath, Schmidt, Kroeger, Miernik

Data extraction and management: Kunath, Schmidt, Kroeger

Analysis and interpretation: Kunath, Dahm, Schmidt, Kroeger, Walther, Miernik

Statistical analysis: Walther, Dahm, Kunath

Drafting of the protocol: Kroeger, Krabbe, Kunath, Schmidt

Drafting of the review: Kunath, Dahm, Schmidt, Kroeger

Critical review of the manuscripts: all authors

DECLARATIONS OF INTEREST

Kunath: none known

Schmidt reports employment by the German Society of Urology (DGU). Schmidt reports that none of the sponsors or funding institutions had any role in gathering, analysing, or interpreting the data and they have no right to approve or disapprove any submitted paper

Krabbe: none known

Miernik reports the following relevant financial activity outside the submitted work: received support from Schölly Fiberoptic GmbH, Denzlingen, Germany, for consultations related to research and development activities in the field of urological endoscopy, which were unrelated to the submitted work

Cleves: none known

Walther: none known

Kroeger reports the following financial activities related to the submitted work: received support from Pfizer Oncology for travel to the 2013/2014 German Society of Urology meeting, RCC circle 2014; received support from Astellas for travel to the AUA meeting in 2014; received support from GlaxoSmithKline for travel to AUA and EAU meetings in 2013; received support from Novartis for travel to a Kidney Cancer Association meeting in 2010. Kroeger reports the following relevant financial activities outside the submitted work: institution received a pending research grant from Pfizer Oncology for a basic science project that investigates the influence of BAP1 on response to Axitinib

Dahm: none known

SOURCES OF SUPPORT

Internal sources

- Deutsche Gesellschaft für Urologie (DGU), Germany.

S. Schmidt receives salary by the German Society of Urology (DGU) but the DGU had no role in gathering, analysing, or interpreting the data and has no right to approve or disapprove any submitted paper.

External sources

- New Source of support, Other.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

This review is based on a published protocol ([Krabbe 2016](#)), with differences as described here.

We defined surgery-related mortality as a serious adverse event because no adverse event was reported that was named serious by the authors.

We initially planned inclusion of the following immediate adverse events: need for temporary haemodialysis, urinary tract infection, urinary leakage after partial nephrectomy, hemorrhage as well as need for re-operation or transfusion. However, we included the following reported immediate post-operative adverse events: spleen damage, pleural damage, perioperative bleeding, urinary fistula, reoperation due to side-effects.

We initially planned inclusion of the following long-term adverse events: cardiovascular events, hypertension, need for permanent haemodialysis, development of chronic kidney disease (CKD). However, we included in the evaluation of this review the following reported long-term adverse events: cardiovascular-related mortality, liver-related mortality, renal-related mortality, infection-related mortality, chronic pulmonary disease-related mortality.

We reworded the outcomes 'all-cause survival' and 'recurrence-free survival' to 'time-to-death of any cause' and 'time-to-recurrence' to make clear that the presented events are death and recurrence and the increased hazard is the hazard of that event.

NOTES

We based parts of the Methods section of the protocol for this review on a standard template developed by the Cochrane Metabolic and Endocrine Disorders Group, which has been modified and adapted for use by the Cochrane Urology Group.

INDEX TERMS

Medical Subject Headings (MeSH)

Carcinoma, Renal Cell [mortality] [pathology] [*surgery]; Cause of Death; Kidney Neoplasms [mortality] [pathology] [*surgery]; Neoplasm Recurrence, Local [mortality]; Nephrectomy [*methods] [mortality]; Randomized Controlled Trials as Topic; Time Factors

MeSH check words

Humans