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Nephron-Sparing Surgery for Wilms Tumor: a Systematic Review

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Abstract

Introduction—Radical nephrectomy (RN, or total nephrectomy) is the current gold-standard surgical treatment for children with Wilms' tumors (WT). However, nephron-sparing surgery (NSS, or partial nephrectomy) has recently been gaining increasing attention. The objective of this systematic review is to compare the effectiveness of NSS as compared to RN for the treatment of children with WT.

Methods—We searched the Cochrane Controlled Trials Register, clinicaltrials.gov, MEDLINE, EMBASE, Google Scholar, and recently presented meeting abstracts for reports in English. The bibliographies of included studies were then hand-searched for any missed articles. The protocol was prospectively registered. Manuscripts were assessed and data abstracted in duplicate with differences resolved by the senior author. Due to high heterogeneity among the final included studies, only a qualitative systematic review was performed; no formal meta-analysis was undertaken.

Results—We identified 694 articles, 118 of which were selected for full-text review and 66 of which were included in the final analysis. Most studies were single- or multi-institution retrospective case series (60, 91%), with a small number of prospective cohort studies (6, 9%) and 1 administrative database analysis. The majority of studies were from Europe (27, 41%) or North America (21, 32%). Nearly half (32, 48%) of included studies dated from 2010 or later. In total, data on 4,002 patients were included, of whom 1,040 (26%) underwent NSS and 2,962 (74%) underwent RN. Reported rupture rates were similar between RN and NSS (13 vs. 7%), as were

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recurrence rates (12 vs. 11%) and survival rates (85 vs. 88%). However, these comparisons are limited by inherent biases in the design and reporting of most included studies.

Conclusions—Most contemporary studies reporting the use of NSS in children with WT report similar long-term outcomes to RN. However, most existing studies are limited by their small numbers, inconsistent reporting, and methodological biases. There are significant opportunities for future research on the use of NSS in children with WT, including issues related to surgical quality, optimal technique, timing and duration of chemotherapy, and variation in the use of NSS among centers.

Keywords

Pediatric; renal tumor; Wilms tumor; partial nephrectomy; radical nephrectomy; nephron-sparing surgery

INTRODUCTION

Wilms' tumor (WT) is the most common solid renal malignancy in children; the estimated annual incidence rate is 7 to 10 cases per million for children younger than 15 years. The Children's Oncology Group (COG) identifies approximately 600 children per year in the United States with a renal tumor, more than 90% of which are WT. Bilateral WT are relatively uncommon, accounting for 5-7% of children with renal tumors.^{1, 2}

Multimodality therapy, including radical nephrectomy via a transperitoneal approach is the mainstay of WT management.³ Historically, nephron-sparing surgery (NSS) was generally reserved for bilateral WT or children with a solitary kidney in whom preservation of renal function was mandatory.⁴ The major challenge in these children is to preserve renal function while adequately treating the tumors. Most commonly, bilateral WT is managed by radical nephrectomy (RN) of the more involved kidney and NSS on the less involved contralateral kidney following neoadjuvant chemotherapy. However, bilateral WT patients have been noted to have a significant risk of ESRD due to perioperative renal insults in addition to tumor recurrence and subsequent nephrectomy.^{5, 6}

In contrast to adult renal malignancies, children with WT often present with very large tumors relative to the size of the normal renal parenchyma and relative to the child as well. Modern management of bilateral WT incorporates neoadjuvant chemotherapy along with NSS as first-line treatment.⁷⁻⁹ The current bilateral and/or syndromic WT protocol for COG (AREN0534) recommends 6 to 12 weeks of vincristine, dactinomycin, and doxorubicin prior to resection. Following surgery, adjuvant chemotherapy and radiation therapy regimen depend on tumor histology and staging.^{10, 11, 12}

Data on NSS in preserving long-term renal function, cardiovascular function, and overall health provide an insight of the potential wider applicability of NSS in children with WT.^{13, 14} The AREN0534 trial of COG encourages NSS in children with bilateral WT or for unilateral WT in children with syndromes which predispose to renal failure or metachronous development of WT in the contralateral kidney. Although contemporary data on NSS seems

promising, data on NSS outcomes in children with WT remain scarce outside of high-volume centers.¹⁵⁻¹⁸

The objective of this systematic review was to examine the accumulated literature on the use of NSS among children with WT, both unilateral and bilateral. Specifically, the aims of this study are to assess the reported outcomes of NSS and to compare these to the current gold standard surgical treatment of WT, RN.

METHODS

Search strategy

The initial literature search was designed and executed by a reference librarian at our institution (MVN). We searched MEDLINE, EMBASE, the Cochrane Controlled Trials Register, Google Scholar, and Scopus electronic databases for studies published 1980-2014 based upon PRISMA guidelines.¹⁹ The exploded search terms were: “nephron-sparing surgery,” “partial nephrectomy,” or “nephron sparing surgery,” restricted to “tumor,” “mass,” “Wilms,” “cancer,” or “renal cell carcinoma.” These were then restricted to articles retrieved under a second search for the exploded search terms “pediatric” or “child” or “children”. Reference lists of included studies were manually screened for any additional studies. We also manually searched for unpublished abstracts presented at relevant scientific meetings: the American Urological Association, the American Academy of Pediatrics Section on Urology, the Pediatric Academic Societies, the American Pediatric Surgical Association, and the European Society of Pediatric Urology. The exact search strategy for each database is detailed in **Appendix 1**. Prior to the formal literature search, the protocol was prospectively registered at the international registry of systematic reviews, PROSPERO (registration number CRD42015016420).

Selection criteria

We included English-language studies of children (aged 18 years or younger) diagnosed with Wilms tumor that compared the outcomes or effects of NSS vs. RN. No manuscript was excluded based on method of analysis, definition of success, perceived quality, or susceptibility to bias. In cases of ambiguity or where study reporting made evaluation difficult, we attempted to err on the side of inclusiveness.

Data Abstraction

Two reviewers (RNWV and ENB) independently reviewed all study abstracts in duplicate with disagreements resolved by the senior author (JCR). Full text articles appearing to meet selection criteria were reviewed, and study data was abstracted in the same manner.

Statistical methods

Our preparatory surveys of the literature demonstrated a large number of case series and a dearth of randomized trials comparing NSS and RN. We therefore anticipated a high level of inter-study heterogeneity, leading us to *a priori* plan not to proceed with data pooling or meta-analysis. Instead, we planned to perform only a qualitative, non-pooled systematic review. All studies were tracked and analyses were performed using EndNote version X7.3

(Thomson Reuters, New York, NY), SAS version 5.4 (SAS Institute, Cary, NC), and RevMan version 5.3.5 (Nordic Cochrane Centre of the Cochrane Collaboration, Copenhagen, Denmark).

RESULTS

Search Results

A total of 694 publications were identified using our search criteria, with an additional 3 reports identified by hand-searching bibliographies of included studies and/or conference abstracts. Of these, 118 studies were selected for full text review. We excluded 15 studies due to a focus on disease other than Wilms' tumor; 5 due to inability to extract out pediatric-specific data; 18 due to duplicate reporting or review of previous reports; and 15 due to insufficient reporting of data on RN and NSS patients. A total of 66 studies met all criteria for inclusion and were included in the final review (**Figure 1**).

Of the 66 included studies, most (60, 91%) were retrospective cohorts or case series, including 1 administrative database analysis that also met inclusion criteria. Only 6 (9%) studies reported prospective data. The complete list of included studies is in **Table 1**.

Most studies were from Europe (29, 41%) or North America (22, 31%), although studies were also reported from Africa (12, 17%), Asia (5, 7%), and South America (3, 4%). Of individual countries, the USA (20, 28%) and Italy (10, 14%) were the most frequently represented. The majority of studies were published relatively recently, with nearly half (34, 48%) published since 2010 (**Figure 2**).

Patient Cohort

In total, 4,022 patients were included. Of these, 1,632 children (41%) were male. Reported ages ranged from <1 month to 18 years. Bilateral tumors were present in 1,153 (29%) patients, including at least 4 metachronous contralateral tumors. The reported mean size of excised tumors ranged from 5-14 cm for RN and 1.5-9 cm for NSS. NSS was performed in 1,040 (26%) patients and 1,311 (32%) kidneys, while RN was performed in 2,962 (74%) patients and 2,844 (68%) kidneys. Preoperative chemotherapy was reported as being given to 195 (7%) of the RN patients and 248 (24%) of the NSS patients.

Histology and Staging

Histology and staging were not universally collected and were variably reported. Few studies differentiated between NSS and RN cohorts. Bilateral Wilms Tumor added further complexity as local stage was infrequently reported and a distinction between discordant local staging per kidney was often not noted. Histology was reported in aggregate for NSS and RN in 24 studies (86% favorable; 14% unfavorable), reported for NSS in 8 studies (mean 94% favorable; 6% unfavorable), and reported for RN in 2 studies (mean 92% favorable; 8% unfavorable). Tumor stage was reported in aggregate for NSS and RN in 21 studies (mean Stage I 33%, Stage II 37%, Stage III 19%, Stage IV 5%, Stage V 7%), reported for NSS in 14 studies (mean Stage I 49%, Stage II 32%, Stage III 18%, Stage IV

0.6%, Stage V 1%), and reported for RN in 7 studies (mean Stage I 34%, Stage II 31%, Stage III 20%, Stage IV 15%, Stage V 0.0%).

Outcomes

Surgical and oncologic outcomes data were presented in highly variable ways among the included studies. Due to these differences in reporting among studies in conjunction with a lack of individual patient data, direct comparisons of outcomes data (e.g., overall or event-free survival rates after RN and NSS) was not performed.

Tumor rupture data was reported for RN patients in 3 studies (mean 13%, range 0-40%), and for NSS patients in 7 studies (mean 7%, range 0-25%). Tumor recurrences were reported for RN in 14 studies (mean 12%, range 0-38%) and for NSS patients in 33 studies (mean 11%, range 0-60%). End-stage renal disease (ESRD) data were reported for RN in 12 studies (mean 8%, range 0-50%) and for NSS in 28 studies (mean 3%, range 0-18%). Overall survival data were reported for RN in 24 studies (mean 85%, range 50-100%) and for NSS in 35 studies (mean 88%, range 38-100%). Because survival data was given using various endpoints in various studies, the figures cited above are crude survival data as reported in the original studies at those various time points.

Across all categories, there was a marked trend towards improved outcomes over time (e.g., mean overall survival for RN and NSS was 61 and 87% among the studies from the 1980s, but increased to 99 and 93%, respectively, for studies from the 2010s).

DISCUSSION

In this study, we found that most studies detailing outcomes of surgical techniques for resection of WT were retrospective cohorts and case series. Differences in reporting and cohort heterogeneity among the included studies negated the possibility of meaningful, pooled comparisons of RN and NSS outcomes. Nevertheless, most current studies of RN and NSS patients appear to show similar tumor rupture, recurrence, ESRD, and overall survival outcomes between the 2 techniques. However, current studies are also likely to be subject to significant selection bias, as patients chosen for NSS are likely to be different than the average RN patient. Further, these studies are also likely to be subject to significant reporting bias, as poor results with a new or controversial technique (such as NSS) are less likely to be reported than poor results with a well-established technique (such as RN). Coupled with a relative lack of well-designed, well-reported data, we interpret these data to mean that a formal head-to-head comparison of RN and NSS would be worthwhile. An RCT of RN vs. NSS would thus be likely to have a significant impact on modern management of WT. We eagerly await and will continue to press for such a study being performed, despite the logistical hurdles that would doubtless be required to bring it to fruition.

The general principle of RN as the mainstay surgical management for Wilms tumor has not significantly changed since the 1800s.²⁰ By contrast, NSS for Wilms tumor is a more modern innovation that was first described in the 1970s. For the first several decades following its introduction, NSS was reserved for indications such as bilateral WT or WT in a solitary kidney as a means to prevent immediate postoperative renal failure.^{1, 21} More

recently, NSS has been reported for children with unilateral WT in the absence of these absolute indications.^{14, 22}

Investigators have reported that NSS in adults with renal cell carcinoma and other renal tumors provides significant benefit in terms of long-term renal and cardiovascular function, which in turn provides overall survival benefits.²³ A recent European Organisation for Research and Treatment of Cancer (EORTC) RCT comparing RN and NSS suggested similar outcomes between the two surgeries.²⁴ However, there were methodological limitations in this RCT. Recent publications suggest that NSS provides a risk reduction in all cause mortality, cancer specific mortality, and severe chronic kidney disease²⁵, which was also supported by a systematic review which drew the same conclusion regarding malignant renal tumors less than 4.0 cm.²⁶⁻²⁸ These data, coupled with the increased familiarity with NSS among surgeons and urologists, have led to increased use of NSS in children with WT in recent years.^{29, 30}

The potential benefits of NSS for WT are significant. Due to their anticipated long lifespan, children with kidney cancer may be at long-term risk of renal insufficiency and ESRD-related morbidity. This premise is supported by a recent study which noted that ESRD was the second most common cause of death among WT survivors in a recent long-term study; only cardiovascular causes occurred (albeit slightly) more frequently.³¹

However, such risks are only relevant in the context of successful cancer treatments; this necessarily implies that the theoretical benefits of NSS must be considered against any potential risks in terms of cancer recurrence and/or event-free survival from tumor spill or positive margins. These risks are also not trivial, as demonstrated by a recent analysis by Green and colleagues; patients in the 4th National Wilms' Tumor Study with intraoperative tumor spill nearly doubled their risk of death (HR 1.94) as compared to patients without tumor spill.³² Similarly, recent reports from SEER,³⁰ SIOP,³³ and COG³⁴ have indicated that relatively few patients currently undergo NSS, and that the benefits of NSS clearly need to be weighed against the potential downside risks of compromised oncologic outcomes in the name of improved nephron counts.

Thus, it is important to realize that NSS use in children poses several significant challenges. First, the technical considerations of removing a large tumor from a small kidney are not inconsequential, particularly if one is attempting to preserve a functional renal remnant. Importantly, the included studies did not report sufficient data on surgical technique to allow for any comment on the superiority (or inferiority) of any particular technique; for example, is tumor enucleation alone sufficient, or is a margin of normal parenchyma required (and, if the latter, how large of a margin is required)? Recently, Longo and colleagues found that when comparing simple enucleation and partial nephrectomy for T1 renal masses, enucleation was associated with similar warm ischemia time but lower intraoperative blood loss, shorter operative time, and a decreased risk of positive surgical margins.³⁵ Interestingly, Kieran and colleagues recently reported that positive margins did not impact survival in patients with bilateral WT undergoing NSS; however, it should be noted that this was a relatively small study (21 patients total, only 5 of whom had positive margins).

Further, those patients with positive margins also underwent additional confounding therapy in the form of flank irradiation.³⁶

Second, there are important training issues to be considered in the use of NSS as well; namely, most WT are treated by pediatric surgeons who may or may not have been trained in the use of NSS during their residency or fellowship.³⁷ Ritchey and colleagues previously reported that there were significant quality differences between pediatric surgeons and general surgeons in terms of WT surgical management.³⁸ Differences between pediatric urologists and pediatric surgeons have recently been studied for RN, with few clinically significant differences noted.³⁷ Differences between specialties and their use of NSS have, to the best of our knowledge, not yet been assessed. At the authors' institution, we routinely perform any surgical management of WT in a multidisciplinary manner, with both a pediatric urologist and a pediatric surgeon participating as co-surgeons. We also actively share all patient care duties and management decisions in conjunction with pediatric oncology.

Similarly, the role of neoadjuvant chemotherapy is an important issue to consider. The current COG protocol (AREN0534) calls for 6-12 weeks of preoperative chemotherapy for children with bilateral tumors or syndromic associations, without biopsy, prior to surgical removal of the tumor. Similarly, multiple centers have reported their results with preoperative chemotherapy as a means of reducing tumor volume, of improving the technical feasibility of NSS), and of improving surgical positive margin rates.^{22, 39-41}

Perhaps the most important issue to consider is that of patient selection. The authors were unable to extract enough data regarding tumor size, tumor location, or residual amount of healthy parenchyma to tease out their affects on patient selection. Previous studies by Cost¹⁵ and Ferrar⁴² suggest that only 25% of children with unilateral WT are candidates for NSS; however, only 1% of these children actually undergo NSS.³⁴ Thus, one of the goals of future research efforts should be to determine which children can safely undergo NSS. In a recent abstract, Ehrlich and colleagues reported on 39 patients with unilateral WT who underwent NSS. The authors found that 9/39 (23%) were found to have positive margins or intraoperative tumor spill; these patients thus would have received additional chemotherapy and radiation due to surgical factors. Despite this, the 5-year overall survival in those patients was 96%. Although this study has to date only been reported in abstract form, the presented data seems to imply that at least some of these tumors may not have been appropriate candidates for NSS. Preoperative tumor weights in these patients ranged from 133 to 1,870 gm, while 13 patients had Stage II or III disease. Further, based on the fact that 13/39 (33%) patients did not undergo staging lymphadenectomy as recommended, one can perhaps conclude that the surgeons involved in those cases may not have been fully up to date on standard COG guidelines.³⁴ NSS feasibility, however, can be aided by preoperative imaging and was associated with a sensitivity of 87%, specificity of 97%, and accuracy of 93%.⁴³ As noted previously, NSS is a technically demanding procedure that requires significant expertise both in terms of patient selection and technical ability and experience.

Tumor histology and staging are two important factors that cannot be overlooked as their variable and incomplete reporting did not allow for proper analysis of their potential impact

on patient selection and subsequent outcome measures. When reported, the histological typing of WT was similar between NSS and RN groups. It is unfortunate that differential outcomes by histological type were unable to be determined. As for staging, it appeared that patients chosen for NSS were more likely to have a lower-staged tumor than those undergoing RN with 80.5% being Stage I or II in the NSS group, compared to 65.2% in the RN group. This is similar to what Cost and colleagues found in one of the few studies that reported WT stage by NSS or RN; in said study, 80% of patients undergoing NSS were Stage I or II compared to 57% of RN patients.⁴⁴ More uniform reporting standards would help elucidate the extent to which histology and stage impact outcome, and how they should be implemented in patient selection.

All told, the accumulated literature strongly supports further study of this issue. Given the overall excellent results of RN, it is apparent that a trial of RN and NSS would be technically challenging to plan and to accomplish. One option would be to consider a voluntary moratorium for centers considering NSS, similar to what was performed in the MOMS trial.⁴⁵ Such an arrangement would likely boost the accrual and feasibility of a trial.

This study should be interpreted in light of its limitations. Most included studies were retrospective case series with highly variable reporting quality; this made data abstraction particularly challenging. This level of evidence is generally recognized as suboptimal for inclusion in meta-analyses, which is why we *a priori* chose not to pool any study data. Instead of pursuing a meta-analysis, we instead limited this study to a qualitative, non-pooled, systematic review. It is important to note that any comparisons of these studies will be significantly limited by their small numbers, inconsistent reporting, and the inherent methodological biases of their study design. As with any systematic review, the reader must be wary of a “garbage in, garbage out” phenomenon, whereby the systematic review serves only to amplify the limitations of an initial study. Nevertheless, we hope that these limitations have been mitigated by the authors’ relative caution in amplifying significant findings (and significant non-findings).

In summary, most contemporary studies reporting the use of NSS in children with WT report similar long-term outcomes to RN in regards to ESRD, tumor recurrence, tumor rupture and overall survival. However, these studies are significantly limited by their inherent methodological flaws; notably, to the best of our knowledge there is no randomized controlled trial of NSS and RN use in children with WT. Thus there are significant opportunities for future research on the use of NSS in children with WT, and it is incumbent upon clinicians and researchers who care for children with WT to continue to attempt to answer these questions. The short- and long-term risks and benefits of NSS and RN as “gold standard” treatments for all children, and for each individual child, are ripe areas for future comparative effectiveness research.

CONCLUSIONS

Most contemporary studies reporting the use of NSS in children with WT report similar long-term outcomes to RN; specifically, reported rates of ESRD, tumor recurrence, tumor rupture and overall survival are, on average, relatively similar. However, most existing

studies are relatively small, non-randomized, retrospective studies. As such, it is important to note that any comparisons of these studies will be significantly limited by their small numbers, inconsistent reporting, and the inherent methodological biases of their study design. There are significant opportunities for future research on the use of NSS in children with WT, including issues related to what children are most (and least) likely to benefit from NSS, what is the optimal surgical technique, whether or not preoperative chemotherapy plays a role in NSS, and what is acceptable variation in the use of NSS among centers and among providers.

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Appendix 1: Systematic review literature search strategy

PubMed Search:

Search	Query	Items found
#1	Search "Kidney Neoplasms"[Mesh] OR "kidney neoplasm"[tiab] OR "kidney neoplasms"[tiab] OR "kidney tumor"[tiab] OR "kidney tumors"[tiab] OR "kidney tumour"[tiab] OR "kidney tumours"[tiab] OR "kidney cancer"[tiab] OR "kidney cancers"[tiab] OR "cancer of kidney"[tiab] OR "cancer of the kidney"[tiab] OR "renal tumor"[tiab] OR "renal tumors"[tiab] OR "renal tumour"[tiab] OR "renal tumours"[tiab] OR "renal neoplasm"[tiab] OR "renal neoplasms"[tiab] OR "renal cancer"[tiab] OR "renal cancers"[tiab] OR "wilms tumor"[MeSH Terms] OR "wilms tumor"[tiab] OR "wilms tumors"[tiab] OR "wilm's tumor"[tiab] OR "wilm's tumors"[tiab] OR "wilms tumour"[tiab] OR "wilms tumours"[tiab] OR "wilm's tumour"[tiab] OR "wilm's tumours"[tiab] OR "Nephroblastoma"[tiab] OR "Nephroblastomas"[tiab]	66229
#2	Search (((("nephrectomy"[MeSH Terms] OR "nephrectomy"[tiab]) AND ("partial"[tiab] OR "minimally invasive" [tiab])) OR "nephron sparing"[tiab] OR "nephron-sparing"[tiab]) OR "Nephrons/surgery"[Mesh])	6882
#3	Search "Child"[Mesh] OR "Children"[tiab] OR "child"[tiab] OR "childhood"[tiab] OR "teen"[tiab] OR "teenager"[tiab] OR "teenagers"[tiab] OR "Pediatrics"[Mesh] OR "pediatric"[tiab] OR "pediatrics"[tiab] OR "Paediatric"[tiab] OR "Paediatrics"[tiab] OR "Adolescent"[Mesh] OR "Adolescent"[tiab] OR "Adolescents"[tiab] OR "Adolescence"[tiab] OR "infant"[Mesh] OR "infant"[tiab] OR "youth"[tiab]	3167975
#4	Search #1 AND #2 AND #3	443
#5	Search #4 NOT (Editorial[ptyp] OR Letter[ptyp] OR "Case Reports"[ptyp] OR Comment[ptyp])	317
#6	Search #4 NOT (Editorial[ptyp] OR Letter[ptyp] OR "Case Reports"[ptyp] OR Comment[ptyp]) Filters: Publication date from 1980/01/01	310

EMBASE:

#1	'kidney cancer'/exp OR 'kidney neoplasm':ab,ti OR 'kidney neoplasms':ab,ti OR 'kidney tumor':ab,ti OR 'kidney tumors':ab,ti OR 'kidney tumour':ab,ti OR 'kidney tumours':ab,ti OR 'kidney cancer':ab,ti OR 'kidney cancers':ab,ti OR 'cancer of kidney':ab,ti OR 'cancer of the kidney':ab,ti OR 'renal neoplasm':ab,ti OR 'renal neoplasms':ab,ti OR 'renal tumor':ab,ti OR 'renal tumors':ab,ti OR 'renal tumour':ab,ti OR 'renal tumours':ab,ti OR 'renal cancer':ab,ti OR 'renal cancers':ab,ti OR 'wilms tumor':ab,ti OR 'wilms tumors':ab,ti OR 'wilm's tumour':ab,ti OR 'wilm's tumours':ab,ti OR 'nephroblastoma':ab,ti OR 'nephroblastomas':ab,ti	86,867

#2	'partial nephrectomy'/exp OR 'partial nephrectomy':ab,ti OR 'nephron sparing surgery'/exp	9,508
#3	#1 AND #2	5,107
#4	'juvenile'/exp	2,929,761
#5	#3 AND #4	337
#6	#5 AND [humans]/lim AND [1980-2015]/py	308

Cochrane:

ID	Search	Hits
#1	kidney cancer:ti,ab,kw (Word variations have been searched)	106
#2	kidney neoplasm or "kidney neoplasms" or "kidney tumor" or "kidney tumors" or "kidney tumour" or "kidney tumours" or "kidney cancers" or "cancer of kidney" or "cancer of the kidney" or "renal tumor" or "renal tumors" or "renal tumour" or "renal tumours" or "renal neoplasm" or "renal neoplasms" or "renal cancer" or "renal cancers" or "wilms tumor" or "wilms tumors" or "wilm's tumor" or "wilm's tumors" or "wilms tumour" or "wilms tumours" or "wilm's tumour" or "wilm's tumours" or "Nephroblastoma" or "Nephroblastomas"	879
#3	#1 or #2	951
#4	partial nephrectomy:ti,ab,kw (Word variations have been searched)	47
#5	partial nephrectomies:ti,ab,kw (Word variations have been searched)	4
#6	nephron sparing surgery:ti,ab,kw (Word variations have been searched)	14
#7	nephron sparing surgeries:ti,ab,kw (Word variations have been searched)	14
#8	{or #4-#7}	58
#9	nephron sparing or "nephron-sparing":ti,ab,kw (Word variations have been searched)	18
#10	#8 or #9	62
#11	#10 and #3	36

Analogous search terms used in Google Scholar and Scopus.

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Highlights

- Most nephron-sparing surgery reports are small, single-institution case series
- Reporting is often inconsistent and may be subject to significant bias
- NSS is more commonly used in lower stage, smaller tumors
- With that caveat, reports show similar recurrence and survival rates for RN and NSS
- This is significant opportunity for future research on NSS use in children with WT

Figure 1.
PRISMA Flow Diagram

Figure 2.
Number of included publications per year

Table 1**Included Studies**

Author	Year	Country	Total WT patients	NSS patients	RN patients
Agarwala	2014	India	11	10	3
Alfer	1991	Brazil	1	1	0
Amel	2003	Tunisia	35	1	33
Apoznanski	2008	Poland	10	10	3
Aronson	2011	The Netherlands	25	8	17
Auber	2009	France	15	6	11
Barrantes	1993	England	175	3	154
Bishop	1985	USA	1	1	0
Blute	1987	USA	145	144	1
Boglino	2004	Italy	98	7	91
Brozyna	2012	Poland	24	12	24
Cost	2012	USA	203	82	121
Cost	2014	USA	30	15	15
Cozzi	2013	Italy	59	12	49
Cozzi	2012	Italy	20	10	15
Cozzi	2001	Italy	4	4	-
Cozzi	2012	Italy	10	10	-
Davidoff	2008	USA	12	11	2
Ehrlich	2014	USA	39	39	0
Erginel	2014	Turkey	71	6	65
Fuchs	2011	Germany	5	5	0
Fuchs	1999	Germany	14	13	5
Giel	2007	USA	17	17	9
Glick	2004	USA	3	0	3
Gordon	1996	USA	1	1	0
Guglielmi	2000	Italy	11	0	11
Hadley	2013	South Africa	20	-	-
Hamilton	2011	USA	188	101	116
Horwitz	1996	USA	98	-	-
Hubertus	2015	Germany	22	22	12
Indolfi	2013	Italy	93	71	44
Kay	1986	USA	11	11	0
Kieran	2013	USA	21	21	3
Kubiak	2004	England	23	23	18
Laberge	1987	Canada	9	7	8
Labonia	2012	Brazil	15	11	4
Lago	1985	Spain	1	1	0

Author	Year	Country	Total WT patients	NSS patients	RN patients
Linni	2003	Austria	11	11	2
Manchanda	2011	India	27	1	18
Millar	2005	South Africa	19	9	7
Mittal	2012	Indian	11	-	-
Moorman-Voestermans	1998	Netherlands	90	7	83
Nawaz	1999	UAE	6	4	4
Nerli	2013	India	9	9	0
Oue	2014	Japan	31	25	18
Paulino	1996	USA	38	-	-
Paya	2000	Austria	7	6	4
Qureshi	2007	Saudi Arabia	20	1	19
Raffoul	2013	France	9	9	-
Ramao	2012	Canada	8	5	3
Salem	2013	Egypt	10	10	0
Sarhan	2010	Egypt	22	17	17
Sayed	2011	Egypt	16	1	14
Sen	1998	Saudi Arabia	71	10	66
Shaul	1992	USA	15	13	13
Streif	1997	Austria	1	1	0
Sudour	2012	France	49	48	20
Sulkowski	2012	USA	12	12	2
Szymik-Kantorowicz	2012	Poland	43	8	35
Tucker	1986	USA	10	8	5
Urban	1995	Austria	3	3	0
Vaughan	1995	USA	10	1	9
Verga	1986	Italy	1	1	0
Wang	2014	USA	1832	114	1720
Warmann	2014	Germany	24	0	24
Zani	2005	Italy	52	10	42
Zekri	2014	Egypt	25	-	-