

INPLASY PROTOCOL

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None declared.

Comparison of Efficacy and Late Kidney Effects Between Nephron Sparing Surgery and Radical Nephrectomy in Unilateral Wilms Tumor: A Systematic Review and Meta-Analysis

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Review question / Objective: Compare the efficacy and late kidney effects between Nephron Sparing Surgery (NSS) and Radical Nephrectomy (RN) in the management of unilateral Wilms Tumor (WT) patients. Studies were either randomized controlled trials, quasi-randomized controlled trials, controlled clinical trials, prospective observational trials with control groups, or retrospective trials.

Condition being studied: Wilms tumor (WT) is the most common solid renal malignancy in children and 93% to 95% of WT happens unilaterally. Although radical nephrectomy (RN) has always been the gold standard for the treatment of unilateral WT and has a good survival rate, its damage to renal function is substantial and may lead to further dysfunction of cardiovascular system. Therefore, another surgery method of nephron-sparing surgery (NSS) has gained much attention as a possible substitute for RN in unilateral WT. NSS is helpful to preserve renal parenchyma as much as possible and prevent long-term renal failure while it has the possible risks of positive surgical margins and recurrence. We compare differences of efficiency and long-term kidney function between patients undergoing either RN or NSS in unilateral WT, respectively.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 15 February 2023 and was last updated on 15 February 2023 (registration number INPLASY202320064).

INTRODUCTION

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METHODS

Search strategy: We searched five databases (Pubmed, Embase, Scopus, Web of Science and Cochrane) for studies in English with no date restrictions. A text search with the following keywords singly or in combination was conducted: “Wilm’s Tumor,” “Wilms Tumor,” “Wilms’ Tumor,” “Wilm Tumor,” “Wilms tumor 1,” “Nephroblastoma,” “Nephroblastomas,” “Nephron Sparing Surgery,” “Partial Nephrectomy,” “Radical Nephrectomy,” and “Total Nephrectomy.” The final search was conducted on February 10, 2023.

Participant or population: Patients of unilateral wilms tumor (WT) undergoing nephron sparing surgery (NSS) or radical nephrectomy (RN).

Intervention: Patients of unilateral wilms tumor (WT) undergoing nephron sparing surgery (NSS).

Comparator: Patients of unilateral wilms tumor (WT) undergoing radical nephrectomy (RN).

Study designs to be included: Studies were either randomized controlled trials, quasi-randomized controlled trials, controlled clinical trials, prospective observational trials with control groups, or retrospective trials.

Eligibility criteria: Inclusion criteria:(a) Studies evaluated the efficacy or late kidney effects of radical nephrectomy and/or nephron sparing surgery on unilateral WT patients.(b) Studies evaluated pediatric population, i.e., <18 years old.(c) Studies evaluated survival rate, relapse rate, hypertension and/or renal disease insufficiency [e.g., eGFR, creatinine, proteinuria, chronic kidney disease (CKD) or end-stage renal disease (ESRD) outcome ratio].(d) Studies measured the outcomes at least 12 months after radical nephrectomy or nephron sparing surgery. (e) Studies were either randomized controlled trials, quasi-randomized controlled trials, controlled clinical trials, prospective observational trials with control groups, or retrospective trials.(f) Studies published in peer-reviewed scientific journals and conferences.(g) Studies published in the English language. (h) Studies evaluated more than 5 patients during the research.Exclusion criteria: (a) Non-human studies.(b) Studies that did not include patients of unilateral wilms tumor (WT).(c) Studies without available data can be extracted.(d) Non-original studies (letters, reviews, editorials).

Information sources: We searched five databases (Pubmed, Embase, Scopus, Web of Science and Cochrane) for studies in English with no date restrictions. We searched the references of published studies and hand-searched corresponding full-text articles from gray literature to identify additional studies. In the articles where quantitative data outcomes were not mentioned, the reviewers made attempts to contact respective corresponding authors for additional data.

Main outcome(s): Survival rate, relapse rate, estimated glomerular filtration rate (eGFR) at diagnosis and follow-up, rate of renal dysfunction (presence of estimated

GFR (eGFR) 1.5 mg/dl or kidney failure), rate of hypertension.

Additional outcome(s): rate of patients received chemotherapy or radiation therapy, percent with low-risk cancer (stage I and II), follow-up time after surgery.

Quality assessment / Risk of bias analysis:

The risk of bias in the included studies was assessed by Cochrane's risk of bias assessment tool for randomized controlled trials and non-randomized controlled trials. ROBINS-I (Risk of Bias in Non-randomized Studies of Interventions) tool was used in appraisal of nonrandomized trials and randomized controlled trials were appraised using the RoB 2.0 tool. Meanwhile, quality control of cross-sectional studies was also evaluated using the assessment tool involving 11 items recommended by the Agency for Healthcare Research and Quality (AHRQ). For cohort and case-control studies, we also utilized the Newcastle-Ottawa Scale (NOS) to evaluate.

Strategy of data synthesis: Odds ratios (OR) were estimated to evaluate the relation of these dichotomous outcomes with nephrectomy group. Means and standard deviations (SMD) for continuous measures were estimated to allow for pooling of continuous outcomes or estimated from error bars if information was solely provided in figures, when required. A random-effects model was chosen for all meta-analyses. The random-effects meta-analysis was conducted using an inverse-variance method. Cochran' S Q test and Higgins I-squared statistic were undertaken to assess the heterogeneity of the included trials, and between-study heterogeneity was calculated using the DerSimonian and Laird method. We defined significant heterogeneity as P heterogeneity < 0.05 or I² > 50%. All meta-analyses were performed using Stata/SE 12.0 software (Stata Corporation, College Station, TX, USA).

Subgroup analysis: A subgroup analysis was applied to explore the origin of heterogeneity for comparisons with high heterogeneity (P heterogeneity < 0.05 or I²

> 50%), including mean follow-up duration (<7.5 years, 7.5-15 years and ≥15 years), study design (randomized or non-randomized), size of the study (≤10, 11-49 or ≥50 participants), year of publication (<2015 or ≥2015) and protocols guiding the treatment (SIOP or COG/NWTS). Meanwhile, subgroup analysis of SIOP and COG/NWTS subgroups was applied to every comparison in our study.

Sensitivity analysis: A sensitivity analysis was conducted post hoc to explore the impact of zero-event studies and the origin of heterogeneity. We used Stata 12.0 software to confirm the robustness and reliability of pooled results through the one-study-out method.

Language restriction: English.

Country(ies) involved: China.

Keywords: nephroblastoma, Wilms tumor, nephrectomy, nephron sparing surgery, renal tumor, pediatric cancer, renal insufficiency.

Contributions of each author:

Author 1 - Shan Li - Author 1 contributed to study design, search strategy formulation, study selection, quality assessment, data extraction, data analysis, writing original draft, and manuscript preparation.

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