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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 with 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. Owing 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. Most studies were from Europe (27, 41%) or North America (21, 32%). Nearly half (32, 48%) of studies those were included were 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 NSS. Reported rupture rates were similar between RN and NSS (13% vs. 7%), as were 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% to 7% of children with renal tumors [1,2].

Multimodality therapy, including radical nephrectomy (RN) 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

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function was mandatory [4]. The major challenge in these children is to preserve renal function whereas adequately treating the tumors. Most commonly, bilateral WT is managed by RN of the more involved kidney and NSS on the less involved contralateral kidney following neoadjuvant chemotherapy. However, patients with bilateral WT have been noted to have a significant risk of end-stage renal disease (ESRD) owing 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 before resection. Following surgery, adjuvant chemotherapy and radiation therapy regimen depend on tumor histology and staging [10–12].

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 that 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 with 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 (M.V.N.). We searched MEDLINE, EMBASE, the Cochrane Controlled Trials Register, Google Scholar, and Scopus electronic databases for studies published between 1980 and 2014 based on Preferred Reporting Items for Systematic reviews and Meta-Analyses (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," "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. Before 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 y or younger) diagnosed with WT 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

The 2 reviewers, R.N.W.V. and E.N.B. independently reviewed all study abstracts in duplicate with disagreements resolved by the senior author (J.C.R.). 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 conference abstracts. Of these, 118 studies were selected for full-text review. We excluded 15 studies owing to a focus on disease other than WT; 5 studies owing to inability