

Development of Hypertension is Less Frequent after Bilateral Nephron Sparing Surgery for Bilateral Wilms Tumor in a Long-Term Survey

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Abbreviations and Acronyms

MRI = magnetic resonance imaging
NSS = nephron sparing surgery
OS = overall survival
PN = partial nephrectomy
SIOP = International Society of Pediatric Oncology
TN = total nephrectomy
WT = Wilms tumor

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Purpose: The option of nephron sparing surgery for unilateral Wilms tumor has been debated in the recent literature. This procedure is being used increasingly to preserve kidney tissue and function. However, nephron sparing surgery is feasible only for selected cases, and a higher local relapse rate has been observed. Moreover, a significant reduction of nephrons is associated with development of renal hypertension and progressive renal failure. We analyzed outcomes after bilateral partial nephrectomy and unilateral partial plus contralateral total nephrectomy in patients with bilateral Wilms tumor.

Materials and Methods: We analyzed data from the Society of Pediatric Oncology and Hematology database on 22 patients with bilateral Wilms tumor. Kidney size was measured using volumetric analysis of magnetic resonance imaging. Patients were matched with children who had undergone magnetic resonance imaging of the abdomen for other malignancies.

Results: Mean kidney volumes after unilateral partial plus total contralateral nephrectomy (66.9 cm³) were significantly greater than the reference kidneys ($p = 0.028$), whereas controls were equal to the bilateral partial nephrectomy group (49.7 cm³, $p = 0.959$). Total kidney volume was significantly larger after bilateral partial nephrectomy (102.1 cm³) vs unilateral partial plus total contralateral nephrectomy (66.9 cm³, $p = 0.0338$). Eight patients (66.7%) had renal hypertension after unilateral partial plus total contralateral nephrectomy but only 2 (20%) after bilateral partial nephrectomy ($p = 0.043$). Overall survival and relapse rates were equal between the groups and did not correlate with unfavorable histology.

Conclusions: Our findings suggest that patients with bilateral Wilms tumor benefit from bilateral nephron sparing surgery. Hypertension is less common after bilateral partial nephrectomy, and rates of local relapse or disease associated death are distributed equally between the groups.

Key Words: kidney neoplasms, nephrons, organ sparing treatments, Wilms tumor

THE option of nephron sparing surgery for unilateral Wilms tumor has been a subject of debate in the recent literature.^{1–5} This procedure is being used increasingly to preserve kidney tissue and function, since 1.6% of all Wilms tumors evolve into a metachronous contralateral malignancy. This issue is particularly relevant in patients genetically predisposed to renal malignancies.⁶ Another negative predictive factor for renal failure is the nephrotoxicity from chemotherapy, radiation and intrinsic renal diseases, which makes preserving kidney tissue a favorable management strategy.^{7–9} However, nephron sparing surgery is feasible only for select patients with peripheral tumors, unaffected collecting systems and sufficient healthy tissue. Finally, the rate of recurrence is as high as 10%, especially for tumors larger than 4 cm in diameter.³ Local relapse may be associated with surgical technique and surgeon experience. Haecker et al reported a higher local relapse rate after nephron sparing surgery.⁵

Preserving a healthy kidney is mandatory in patients with bilateral WT to prevent renal insufficiency and the need for hemofiltration. However, this strategy is frequently complicated in tumors greater than 4 cm in diameter and multifocal nephroblastomatosis. Moreover, a significant decrease in nephrons is associated with development of renal hypertension and progressive renal failure, known as the Brenner-Barker hypothesis.¹⁰ Usually in a patient with bilateral WT both kidneys are affected to varying degrees. Typically TN is performed in the kidney with the larger mass, while PN is attempted in the other kidney. However, the final decision is based on the feasibility of PN. Stehr et al described equal overall survival after bilateral PN compared to partial plus total nephrectomy (86% vs 89%).¹¹ Nevertheless, the 5-year event-free survival after partial plus total nephrectomy (85%) is superior to that after bilateral PN (60%). This disadvantage has been attributed to a higher rate of local relapse after bilateral PN.¹¹ Thus, we need to balance the advantages and disadvantages of PN/TN and bilateral PN to optimize the surgical treatment of patients with bilateral Wilms tumor.

We analyzed outcomes after PN/TN and bilateral PN regarding renal function and hypertension. According to the Brenner-Barker hypothesis, we postulated better outcomes for patients after bilateral PN regarding the mentioned parameters. This approach might also be useful for evaluating patients with unilateral WT for PN.

MATERIALS AND METHODS

Patients

Data on 24 patients with bilateral WT were derived from the Society of Pediatric Oncology and Hematology

database (Homburg/Saar, Germany). Patients underwent surgery at Dr. von Hauner Children's Hospital between 2000 and 2012. Data were matched and completed based on documentation in the medical charts. Inclusion criteria were partial nephrectomy of at least 1 kidney and partial or total nephrectomy of the contralateral kidney due to bilateral WT, and oncologic therapy according to the SIOP protocols. Data obtained included gender, age at diagnosis, histological stage, histology, (neo)adjuvant chemotherapy, surgical procedure, radiation, kidney size, creatinine, proteinuria, albuminuria, blood pressure and OS.

All patients were categorized as having stage V disease according to the SIOP staging criteria for WT. Only 1 patient did not undergo neoadjuvant chemotherapy. All others received preoperative chemotherapy consisting of actinomycin D and vincristine for 6 weeks. Patients with advanced disease additionally received doxorubicin. After neoadjuvant chemotherapy the treatment response was assessed via MRI, and resection of the primary tumor was performed. All cases of NSS were attempted as partial nephrectomy with inclusion of a rim of grossly uninvolved renal parenchyma along with the resected tumor rather than enucleation. NSS was performed using the off-clamp technique to ensure kidney perfusion during the entire operation. Generally the operations were performed in 2 stages, starting with the most affected kidney. Bilateral PN was selected when technically feasible, including cases with peripherally located tumors without invasion of the pylon and sufficient remnant of healthy renal tissue. After achieving local control of primary and metastatic disease adjuvant chemotherapy and diagnostic followup were performed according to histological risk stratification based on the appropriate SIOP protocol.¹²

Diagnostic Followup

After PN kidney size was measured using contrast enhanced (0.5 mmol/ml gadoteric acid) MRI. Dosage of contrast material was adapted to renal function. Volumetry was conducted by 1 experienced observer using a 32-bit DICOM™ viewer (version 5.8.2). Comparing the measured data with data from the literature was not feasible because there are no standard kidney volumes available. Instead, we matched our patients with children who underwent abdominal MRI for other malignancies (neuroblastoma, hepatoblastoma) and children with healthy kidneys who had not previously undergone kidney surgery (controls). Oncologic subjects were chosen as controls to measure for effect of chemotherapy on kidney size. Patients and controls were matched regarding age at MRI, gender and ethnicity. All patients and controls were matched pairwise.

Blood pressure values were measured at the upper right extremity, and arterial hypertension was considered repeated blood pressure measurements above the 95th percentile according to the Fourth Report on the Diagnosis, Evaluation and Treatment of High Blood Pressure in Children and Adolescents.¹³ Hypertension was diagnosed by nephrologists based on repeated measurements of blood pressure. This parameter at MRI was relevant for our analysis.

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