Renal Function Outcomes in Patients Treated With Nephron Sparing Surgery for Bilateral Wilms Tumor

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Purpose: Management of bilateral Wilms tumor represents a particular challenge in the consideration of long-term renal function for affected patients. Aggressive surgical resection to prevent recurrence must be balanced with the desire to preserve renal function. We evaluated our institutional experience with nephrological outcomes in patients treated with nephron sparing surgery for bilateral Wilms tumor.

Materials and Methods: We identified all patients with synchronous bilateral Wilms tumors presenting to St. Jude Children's Research Hospital between October 1987 and February 2004. We also included patients with Wilms tumor involving a solitary kidney presenting during the same period. A total of 17 patients were identified who underwent nephron sparing surgery, including 16 with bilateral tumors and 1 with tumor in a solitary kidney. Institutional review board approval was obtained to retrospectively review records and analyze outcomes based on long-term renal function, hypertension, proteinuria, need for dialysis and indications for renal transplantation.

Results: Eight of the 17 patients initially underwent bilateral nephron sparing surgery and 9 initially underwent a combination of nephrectomy and contralateral nephron sparing surgery. Two patients were eventually rendered anephric following further resections secondary to local recurrence. Before the initiation of therapy all patients had normal baseline creatinine clearance, which was calculated using the Schwartz formula. At a median followup from diagnosis of 72 months (range 15 to 207) 1 patient had renal insufficiency and another 3 had renal failure requiring dialysis. One of the 3 patients on dialysis died of metastatic Wilms and 2 await renal transplantation. None of the remaining patients had evidence of proteinuria. Ten of the 17 patients (58.8%) had hypertension at diagnosis and 9 (52.9%) required antihypertensive medications at the most recent followup. The overall survival rate in this group of patients was 88.2% with no evidence of disease in survivors at the most recent followup.

Conclusions: When combined with adjuvant radiation and/or chemotherapy, nephron sparing surgery provides an opportunity to preserve renal function, while maintaining excellent long-term oncological outcomes for patients with bilateral Wilms tumor.

Key Words: kidney, nephrectomy, Wilms tumor

Management of BWT represents a distinct challenge of maintaining long-term renal function while not compromising overall cure rates. Since establishing that tumor control and resection is more manageable following preoperative chemotherapy, thereby allowing NSS and the preservation of renal function without sacrificing cure,[1] patients with BWT have been successfully treated with a more conservative approach. Recent reports from NWTS indicate that the incidence of renal failure in patients with BWT without associated anomalies is 11.5% at 20 years.[2] While single institution series cannot replicate the number of patients identified in larger cooperative group trials, these series provide the benefits of consistency in surgical approach and completeness of followup. We evaluated our institutional experience with long-term renal function outcomes in patients treated with NSS for BWT.

MATERIALS AND METHODS

Following approval by the institutional review board we identified all patients presenting to St. Jude Children's Research Hospital with a diagnosis of synchronous BWT between October 1987 and February 2004. Patients presenting with WT involving a solitary kidney in this period were also identified. All patients included in this study underwent NSS of at least 1 renal unit. Medical records, operative reports and pathology findings were reviewed. Patient age at diagnosis, associated congenital syndromes or anomalies, hypertension at diagnosis and initial renal function were documented. Renal function was determined by estimating the glomerular filtration rate using the Schwartz formula, creatinine clearance = (k × height in cm)/serum creatinine, where k equals 0.55 and 0.45 for children older and younger than 18 months, respectively.[3] Clinical outcomes based on most recent followup data were further analyzed. The variables assessed included long-term renal function, hyperten-

Study received institutional review board approval.

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sion, proteinuria, need for dialysis and indications for renal transplantation.

All patients were categorized as having stage V tumors according to the NWTS staging system. However, each individual renal unit was assigned a local tumor stage by the treating oncologist. All patients received preoperative chemotherapy with vincristine and dactinomycin with or without doxorubicin based on the highest stage assigned to either kidney. Details regarding the chemotherapy regimens used at our institution were previously described.[4] Following initial treatment with preoperative chemotherapy patients underwent surgical excision with NSS performed on at least 1 renal unit. All cases of NSS were attempted partial nephrectomies rather than enucleation when possible, with inclusion of a rim of grossly uninvolved renal parenchyma along with the resected tumor. However, the challenging size and multifocality of many tumors led to marginal resection in some patients. Further postoperative treatment, consisting of continued chemotherapy with or without radiation, was documented. Any additional surgical procedures performed for recurrence were also documented.

RESULTS

A total of 17 patients were identified, including 16 with BWT and 1 with WT in a solitary kidney (33 affected renal units). Table 1 lists demographic data on the study population. Median patient age at diagnosis was 22 months (range 5 to 54). Of the renal units 69.7% were staged as I or II, although 2 children presented with distant metastases.

All patients were initially treated with 2 or 3-drug chemotherapy depending on the assigned stage. Following neoadjuvant chemotherapy all children underwent NSS of at least 1 renal unit. Eight of the 17 patients initially underwent bilateral NSS and 9 initially underwent a combination of nephrectomy and contralateral NSS. As mentioned, the tumors that we observed in this patient population were often quite large, especially radiographically, and in our experience patients who presented with smaller tumors also presented with multifocal lesions throughout the affected kidney. Because of these factors, estimating the percent of parenchymal involvement was not attempted as we considered this method to be highly subjective and not reproducible for documentation purposes. However, for NSS to be attempted all surgeons had to agree that at least a third of the uninvolved parenchyma could be spared. Formal occlusion of the renal vasculature was not routinely performed, although temporary manual compression was used when needed. Two patients were eventually rendered anephric following further resections/completion bilateral nephrectomies secondary to local recurrence. Notably patients who experienced recurrence had negative surgical margins following the initial surgical resection. Importantly NSS was not done when tumor histology was discovered to be unfavorable. Table 1 lists a breakdown of tumor histology in our patients. Following all surgical resections 23 of 33 renal units were ultimately spared for a 70% renal salvage rate for this patient population.

Before the initiation of any therapy all patients had normal baseline renal function, as estimated using the Schwartz formula. At diagnosis 10 of 17 patients (58.8%) presented with hypertension and all with hypertension required medications to control blood pressure. Although it was not statistically significant, there was a trend toward an increased incidence of hypertension at diagnosis in male patients and in black patients. Six patients (35.3%) were diagnosed with at least 1 GU anomaly, including WAGR in 1 and a *WT1* abnormality in 1 that was not classified as WAGR or Denys-Drash syndrome (table 1).

At a median followup from diagnosis of 72 months (range 15 to 207) 3 of 17 patients had ESRD requiring dialysis, including the 2 rendered anephric. One of these patients died of metastatic disease and the other 2 await renal transplantation. Another patient had mild renal insufficiency with a serum creatinine of 1.6 mg/dl. Notably he was an adolescent on creatine supplements and the nephrologists seemed to think that this may have falsely elevated creatinine levels.

Table 2 lists the clinical details of patients with renal function abnormalities. In all patients who had ESRD the condition developed within 5 years of initial surgery. In addition, all 3 patients with renal failure received abdominal radiation secondary to tumor stage or histology. Notably patient 11 had discordant histology with focal anaplasia only on the side of complete nephrectomy. The tumor resected via NSS was diagnosed with favorable histology on careful review. All of the remaining 13 patients had normal renal function using the Schwartz formula and none had any evidence of proteinuria (see figure).

At most recent followup 10 of 17 patients (58.8%) had hypertension, although this group with hypertension at followup did not consist of the same 10 patients who initially presented with hypertension. In patients with hypertension at followup there was no difference in gender or race with regard to the incidence of hypertension. Nine of the 10 children with hypertension required medications to control blood pressure.

Two of the 3 patients (66.6%) with ESRD presented with GU anomalies, including the child with the *WT1* anomaly. When specifically considering the subset with GU anomalies, ESRD developed in 2 of the 6 patients (33.3%) with GU anomalies in our study. Notably the child with WAGR has

TABLE 1

	No. Pts (%)
Sex:	
M	10 (59)
F	7 (41)
Race:	
White	8 (47)
Black	9 (53)
Age (mos):	
0–12	6 (35.3)
13–24	4 (23.5)
25–36	3 (17.6)
37–48	2 (11.8)
49–60	2 (11.8)
Stage (individual renal units):	
I	2 (6.1)
II	21 (63.6)
III	10 (30.3)
Histology:	
Favorable	14 (82.4)
Anaplasia	3 (17.6)
Anomalies:	
WAGR	1 (5.9)
Cryptorchidism	5 (29.4)
Hypospadias	1 (5.9)
Hemihypertrophy	1 (5.9)
Other	1 (5.9)