Repeat nephron-sparing surgery for children with bilateral Wilms tumor

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A B S T R A C T

Background: Renal insufficiency is a significant complication of Wilms tumor treatment in the 5% with bilateral disease. Nephron-sparing surgery (NSS) is recommended after neoadjuvant chemotherapy initially. However, the role of NSS in recurrent disease is unknown. We reviewed our experience to assess the feasibility and oncologic and functional outcomes of repeat NSS for children with recurrent disease.

Methods: A retrospective review was performed of all children treated at our institution for bilateral, favorable histology (FH) Wilms tumor. Patients undergoing repeat NSS for locally recurrent disease were identified. The outcomes evaluated included tumor recurrence, renal function, and patient survival.

Results: Since 2001, 36 children with bilateral FH Wilms tumor have been treated at our institution. Eight patients (22%) underwent repeat NSS for locally recurrent disease. Two patients had a second local recurrence and underwent a third NSS. Six patients are alive without disease (75%) with an average follow-up of 4.5 years. Two patients have died, each with blastemal-predominant histology at repeat NSS. The surviving patients have normal renal function, although two patients require medical management of hypertension.

Conclusions: Our experience suggests that repeat NSS for local recurrence of FH bilateral Wilms tumor is feasible and affords acceptable oncologic outcome with preservation of renal function. However, more aggressive therapy may be required for patients whose recurrence has blastemal-predominant histology, given the poor outcome for these patients in our series.

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Wilms tumor (WT) is the most common renal cancer in children, with about 600 cases in the United States each year. Approximately 5% of these children will have disease in both kidneys [1]. In these patients with bilateral Wilms tumor (BWT), successful treatment must achieve oncologic control while preserving maximal renal parenchyma to ensure sufficient renal function. Renal insufficiency may adversely affect both overall health outcomes as well as quality of life [2]; this impact may be especially pronounced in children with BWT, who are often younger than their counterparts with unilateral disease and may also be afflicted with syndromes associated with poor renal function at baseline [3,4].

Upfront chemotherapy and nephron-sparing surgery (NSS) provide a safe and effective means of providing oncologic control while optimizing renal function [5,6]. BWT is an independent risk factor for the development of renal insufficiency, due in large part to the loss of renal parenchyma, especially in children who had not undergone upfront chemotherapy or initial nephron-sparing surgery [7,8].

Overall, about 15% of children with BWT who were enrolled in National Wilms Tumor Studies 1–4 developed renal insufficiency in the two decades following diagnosis; children with metachronous disease and those with underlying syndromes such as WAGR or Denys–Drash had increased risks of renal failure, with up to 50% of children affected [9]. With the addition of upfront chemotherapy, children who have undergone NSS have similar rates of hypertension (52.9%) before and after surgery and a low risk of renal insufficiency (13.3%, excluding two patients rendered anephric by completion nephrectomies) [5,10]. These favorable outcomes, as well as the ability to successfully perform NSS on technically challenging tumors owing to size or location, have enabled many children with BWT to delay or avoid hemodialysis, renal transplantation, and other adverse sequelae of renal insufficiency.

One risk of renal parenchymal preservation is the development of recurrent disease; the estimated recurrence rate after treatment of WT is between 8.5% and 13.9% [11,12]. Although all patients with WT must be monitored closely for local tumor recurrence, the multifocality of BWT, the young age at which patients develop primary tumors, and the increased prevalence of syndromes associated with renal compromise make treatment of tumor recurrence in patients
with BWT especially challenging. Recurrent disease is typically treated with a combination of chemotherapy and surgical excision; balancing oncologic control with parenchymal preservation may be technically difficult in kidneys that have previously undergone surgery. Further renal parenchymal loss may increase the risk of renal insufficiency, particularly in the setting of the need for additional chemotherapy and/or radiation. To date, neither oncologic outcomes nor renal functional assessments have been reported in patients who have undergone treatment for tumor recurrence after NSS for BWT. We undertook this study to determine whether repeat NSS in patients with recurrent disease was associated with an increased risk of renal insufficiency or changes in overall survival.

1. Methods

After obtaining Institutional Review Board approval, ICD-9 codes were utilized to identify all patients who had undergone NSS for BWT at St. Jude Children’s Research Hospital between January 2001 and August 2012. Patients without at least 3 months of postsurgical follow-up were excluded, as were patients with focal or diffuse anaplasia on histopathologic analysis at initial NSS. Data were collected on demographics, tumor characteristics, histopathologic findings including margin status, neoadjuvant and adjuvant therapy, locoregional and distant recurrence, development of hypertension, renal functional assessments, and event-free and overall survival. Demographic variables were described using measures of central tendency. Renal function was assessed using glomerular filtration rates calculated in technetium-99m renal clearance studies. Patients were classified as hypertensive if the medical record specifically noted a diagnosis of hypertension or if daily antihypertensive medication was required to maintain blood pressure within the normal range for age.

We approach all nephron-sparing surgeries similarly, whether or not the patient has previously undergone renal surgery. We have previously described our surgical technique in detail [5]. NSS is considered in all patients with WT involving all renal units, with the only absolute contraindications being venous involvement with tumor thrombus and anaplastic histology. All families are counseled that nephrectomy will be considered when the tumor precludes preservation of the renal hilar vessels or when less than 25% of the renal parenchyma can be salvaged; in our experience, this is the case in very few patients. Since renal parenchymal loss is the most common cause of end-stage renal disease in children with WT [9], patients who are not candidates for NSS are at increased risk of requiring dialysis and/or renal transplantation in the future.

We employ a transverse upper abdominal incision to maximize exposure to the peritoneal cavity, and each renal unit is approached sequentially. The colon is reflected medially and the renal hilar vessels as well as the ureter are identified and isolated. The renal hilum is compressed manually; we do not employ clamps in order to minimize the risk of crush injury to delicate pediatric vessels, nor do we employ topical ice slush or other cooling agents. With the aid of preoperative cross-sectional imaging as well as intraoperative ultrasound, we identify all intrarenal masses and excise them sequentially with a small surrounding rim (<1 cm) of normal renal parenchyma, when possible. Hemostasis is obtained with suture ligation of localized bleeding points and argon beam electrocautery of raw surfaces. Careful inspection determines if the collecting system has been entered; if so, the defect is oversewn with absorbable suture. A double J ureteral stent is placed antegrade to maximize drainage when a complex closure is required. Parenchymal defects are closed with a separate layer of mattress silk sutures, where feasible. A percutaneous Penrose drain may be placed on the side where the collecting system has been entered; a Foley catheter is placed to dependent drainage and left in place for at least 48 h or until the Penrose drain output is minimal. The drains are removed if the output does not increase following Foley catheter removal. Ureteral stents are left in place until completion of chemotherapy and are removed cystoscopically.

2. Results

Thirty-six patients with favorable histology BWT met the inclusion criteria, of whom 8 (22.2%) patients had a local recurrence. Of these eight patients, seven had initial bilateral NSS procedures after neoadjuvant chemotherapy while one patient (#6) underwent an initial unilateral nephrectomy with subsequent contralateral NSS for a metachronous Wilms tumor. Patient demographics and characteristics of the initial NSS are summarized in Table 1. Six (75%) patients were male and the mean age was 1.34 (range: 0.54–3.37) years at initial NSS. One patient (#8) had Beckwith–Wiedemann syndrome; the others had no known syndromes associated with the development of Wilms tumor, although patient #2 had bilateral undescended testes for which he underwent bilateral orchiopexies at the time of initial NSS. The 7 patients undergoing bilateral NSS were treated with upfront chemotherapy prior to initial NSS: all patients received three-drug chemotherapy consisting of vincristine, actinomycinD and doxorubicin; one patient (#3), initially treated at another institution, had etoposide and cyclophosphamide added due to poor initial tumor response. All patients had FH at initial NSS although patient #3 had blastemal-predominant histology in one of the tumors from the right kidney and positive margins in tumors from both kidneys, for which he received bilateral flank irradiation. All other patients had negative margins at initial resection.

Following initial NSS, 6 patients received histology-directed chemotherapy per the contemporaneous COG protocol; one patient (#7) did not receive any postoperative chemotherapy following initial NSS, and the aforementioned patient (#3) with an alternative chemotherapy regimen continued receiving those additional agents.

Seven of these patients initially recurred in one kidney; each patient underwent repeat NSS as part of local control for the recurrence. Six recurrences were on the right side and one on the left. One patient (#3) had bilateral disease at initial recurrence and underwent bilateral repeat NSS. Initial repeat NSS was performed a mean of 1.39 (range: 0.13–2.59) years after the initial surgery. Table 2 summarizes the treatment course of the recurrent tumors. Favorable histology tumor was found in all eight patients undergoing redo NSS; one patient (#4) had a cystic lesion obstructing the ureteropelvic junction which was suspicious for cystic WT and underwent a pyeloplasty and NSS with final pathology being equivocal for Wilms tumor. At redo NSS, two patients (#3, #8) had blastemal-predominant histology. Postoperatively, five patients again received chemotherapy with vincristine, doxorubicin, and actinomycinD. One patient (#3) subsequently received ifosfamide, carboplatin, and etoposide. After he developed progressive disease, he was transitioned to a topotecan-based chemotherapy regimen, but had continued disease progression. Patient #7 was treated with carboplatin/cyclophosphamide/etoposide postoperatively. Three patients (#1, #3, #7) underwent flank irradiation for positive margins at redo NSS. One patient (#4) received no further therapy.

Three patients had a second recurrence. One patient (2) developed a retroperitoneal recurrence that was successfully excised and treated with adjuvant chemotherapy and radiotherapy. Two patients (#3, #8) underwent a third NS for recurrent disease, a mean of 0.96 (range: 0.81–1.11) years after the first redo NSS (Table 3). Patient #3 developed a right renal mass for which he underwent right NSS; pathology showed diffuse anaplasia with negative margins. He underwent stem cell apheresis and was treated with high-dose consolidation chemotherapy with busulfan and melphalan. He continued to have disease progression with hepatic metastases and ultimately died of disease. Patient #8 developed a second recurrent tumor in the left kidney (the first recurrence had been in the right kidney) and underwent repeat left NSS; pathology showed diffuse
**Table 1**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Race</th>
<th>Age at Initial NSS (years)</th>
<th>Surgery Type</th>
<th>Pathology</th>
<th>Margin Status</th>
<th>Chemotherapy</th>
<th>Radiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>White</td>
<td>1.23</td>
<td>Bilateral partial</td>
<td>FH</td>
<td>Negative</td>
<td>VAD</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>Male</td>
<td>White</td>
<td>0.96</td>
<td>Bilateral partial</td>
<td>FH</td>
<td>Negative</td>
<td>VAD</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>Male</td>
<td>Black</td>
<td>1.28</td>
<td>Bilateral partial</td>
<td>FH (blastemal predominant)</td>
<td>Positive</td>
<td>VAD, cyclophosphamide, etoposide</td>
<td>Yes (bilateral flanks, 10.5 Gy)</td>
</tr>
<tr>
<td>4</td>
<td>Male</td>
<td>White</td>
<td>3.37</td>
<td>Bilateral partial</td>
<td>FH</td>
<td>Negative</td>
<td>VAD</td>
<td>No</td>
</tr>
<tr>
<td>5</td>
<td>Male</td>
<td>White</td>
<td>0.54</td>
<td>Bilateral partial</td>
<td>FH</td>
<td>Negative</td>
<td>VAD</td>
<td>No</td>
</tr>
<tr>
<td>6</td>
<td>Male</td>
<td>White</td>
<td>0.64</td>
<td>Right partial s/p left nephrectomy</td>
<td>FH</td>
<td>Negative</td>
<td>VAD</td>
<td>No</td>
</tr>
<tr>
<td>7</td>
<td>Female</td>
<td>White</td>
<td>0.84</td>
<td>Bilateral partial</td>
<td>FH</td>
<td>Negative</td>
<td>VA/VAD</td>
<td>No</td>
</tr>
<tr>
<td>8</td>
<td>Female</td>
<td>White</td>
<td>0.61</td>
<td>Bilateral partial</td>
<td>FH</td>
<td>Negative</td>
<td>VAD</td>
<td>No</td>
</tr>
</tbody>
</table>

VAD, vinblastine, Adriamycin, actinomycinID; FH, Favorable histology.

Anaplasia with negative margins. She underwent flank irradiation as well as treatment with cyclophosphamide/carboplatin/cyclophosphamide, but has developed recurrent disease in the left kidney and chest, and recently died of disease.

Thus, of the eight patients with recurrence following NSS, six (75%) are alive without evidence of disease, a mean of 4.5 (range 0.6–11.4) years after initial repeat NSS. Four of the six surviving patients have undergone technetium-99m renal clearance studies demonstrating normal renal glomerular filtration rates (mean GFR = 86.7 ± 12.5 ml/min/1.73 m²) a mean of 6.7 years (range: 4–9 years) after surgery; in addition, all seven patients have a normal serum creatinine level (mean = 0.4 ± 0.1 mg/dL). Two patients have elevated blood pressure, which is well controlled with oral antihypertensive agents (one patient requires one agent and the other requires two medications).

Four patients (50%) developed partial small bowel obstructions during the course of their follow-up. All four patients failed conservative management and required exploratory laparotomy with lysis of adhesions a mean of 3.9 (range: 0.18–7.6) years after initial surgery.

3. Discussion

In our experience, most patients undergoing repeat NSS for BWT have excellent oncologic outcomes, as well as renal function (as assessed by normal serum creatinine levels and glomerular filtration rates). A minority of patients require antihypertensive medication to control blood pressure. Our data suggest that, in the majority of patients with recurrent disease after BWT, redo NSS achieves oncologic control while preserving renal parenchyma adequate to maintain normal renal function and blood pressure. However, two patients developed diffuse anaplasia and visceral metastases refractory to chemotherapy and radiation therapy, despite favorable histology at the time of initial tumor resection; both of these patients have died of disease. The outcomes of these two patients underscore the important role of histology in determining oncologic outcome, and that redo NSS may not offer adequate oncologic control for all patients with favorable histology tumors.

In our overall series, tumors recurred in 22% of patients, a rate that is higher than the 8.2% reported in NWTS-4 [13] or prior reports from our institution in patients with unilateral disease [11]. One large study of recurrence after treatment for BWT noted a 15.4% recurrence rate [14]; however, because of the large number of patients in this series, there was significant variation in treatment, including whether or not upfront chemotherapy was given as well as the actual surgical procedure performed. On retrospective review of the diagnostic imaging, our two earliest “recurrent” tumors (patients #1 and #2) may have actually been present but not resected at the time of initial surgery. This conclusion is further supported by the very short interval before their detection after surgery on the first post-operative imaging studies six and nine weeks after initial NSS. This may reflect a learning curve with NSS; we now routinely employ intraoperative ultrasound to ensure resection of less visible lesions, and have had no “early recurrences” since. Both patients completed primary chemotherapy with VAD (vincristine, Adriamycin, actinomycin), and one patient (#1) underwent flank irradiation for a positive surgical margin at re-resection. In both patients, the most recent recurrence was over 8 years ago; both have been clinically well without evidence of disease since, despite the fact that no additional chemotherapy was given. The absence of new tumors in these patients argues for missed primary tumors with similar chemosensitivities as the initially resected lesions, rather than selection of a chemoresistant population of tumor cells.

Another consideration in this patient population predisposed to multiple tumors, when evaluating for the possibility of disease recurrence, is whether a new lesion detected on follow-up imaging

<table>
<thead>
<tr>
<th>Patient</th>
<th>Time Since Initial NSS (years)</th>
<th>Laterality</th>
<th>Surgery Type</th>
<th>Pathology</th>
<th>Margin Status</th>
<th>Chemotherapy</th>
<th>Radiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.24</td>
<td>Left</td>
<td>Partial</td>
<td>FH</td>
<td>Positive</td>
<td>VAD</td>
<td>Yes (left flank, 10.8 Gy)</td>
</tr>
<tr>
<td>2</td>
<td>0.13</td>
<td>Right</td>
<td>Partial</td>
<td>FH</td>
<td>Negative</td>
<td>VAD</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>1.75</td>
<td>Bilateral</td>
<td>Partial</td>
<td>FH (blastemal predominant)</td>
<td>Positive</td>
<td>ICE, then topotecan</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td>0.58</td>
<td>Right</td>
<td>Partial</td>
<td>Equivocal for WT</td>
<td>Negative</td>
<td>None</td>
<td>No</td>
</tr>
<tr>
<td>5</td>
<td>2.33</td>
<td>Right</td>
<td>Partial</td>
<td>FH</td>
<td>Negative</td>
<td>VAD</td>
<td>No</td>
</tr>
<tr>
<td>6</td>
<td>1.22</td>
<td>Right</td>
<td>Partial</td>
<td>FH</td>
<td>Negative</td>
<td>Cyclophosphamide, carboplatin, etoposide</td>
<td>Yes (right flank, 10.8 Gy)</td>
</tr>
<tr>
<td>7</td>
<td>2.59</td>
<td>Right</td>
<td>Partial</td>
<td>FH</td>
<td>Positive</td>
<td>Cyclophosphamide, carboplatin, etoposide</td>
<td>No</td>
</tr>
<tr>
<td>8</td>
<td>1.85</td>
<td>Right</td>
<td>Partial</td>
<td>FH (blastemal predominant)</td>
<td>Negative</td>
<td>VAD, then cyclophosphamide, carboplatin, etoposide</td>
<td>No</td>
</tr>
</tbody>
</table>

ICE, ifosfamide, carboplatin, etoposide.

a Considered “missed” rather than recurrent (e.g. chemoresistant) WT.
b Considered “new” rather than recurrent (e.g. chemoresistant) WT.
c Additional chemotherapy given when end-of-study evaluation showed recurrent disease.
after the completion of planned therapy is really a local recurrence or a new tumor arising in a background of precursor lesions such as nephrogenic rests. This distinction has both prognostic as well as therapeutic implications, as new lesions might still be sensitive to the three-drug chemotherapy that was routinely used to treat the original bilateral Wilms tumors. This distinction and approach were used in patients #4 and #8.

Renal insufficiency is a known complication of BWT, affecting about 1 in 8 patients in the National Wilms Tumor Study [9] and 1 in 12 patients in a smaller series [15]; the prevalence of renal insufficiency in patients with BWT is 9–18 times that seen in patients with unilateral disease [9]. In NWTS, the increased risk of renal insufficiency was attributed to both the loss of renal parenchyma associated with surgical resection and the nephrotoxic effects of chemotherapeutic agents and radiotherapy. The former was associated with earlier development of renal insufficiency while the latter predominated in patients developing later renal failure; this likely reflects the fact that many of the children with BWT in earlier NWTS studies were rendered anephric by removal of both affected renal units [9]. Recent NWTS data report that a minority of patients developing renal insufficiency have a history of radiotherapy, whereas a majority had received two or more courses of chemotherapy, suggesting that chemotherapy may be more influential than radiotherapy in the development of renal failure [14]; another NTWS study found no dose–response effect between radiation therapy and the development of renal insufficiency [16]. In our series, all four patients who underwent radionuclide scans have GFR in the normal range, all six surviving patients have normal serum creatinine levels, and only two patients require pharmacological management of hypertension. These patients will continue to be followed carefully, as previous research has demonstrated that renal insufficiency may develop up to two decades following treatment for WT [9].

Of the two patients with hypertension, one (#6) initially presented with unilateral WT and was treated with nephrectomy prior to undergoing two subsequent NSS for contralateral recurrences; since renal insufficiency may be exacerbated by hyperfiltration injury, this patient’s solitary renal unit may have been at increased risk for development of adverse nephrologic outcomes. Both patients received flank irradiation for positive margins at redo NSS, and both have received extensive chemotherapy regimens: cyclophosphamide, etoposide, and carboplatin. This protocol is employed in children who relapse after standard three-drug chemotherapy and radiotherapy, although at least one study noted no significant nephrotoxicity from this regimen [17]. Although the ability to draw conclusions is limited with only two patients, our experience would suggest that the development of hypertension in this cohort may reflect sensitivity of the renal unit to selected chemotherapeutic agents rather than nephron loss alone.

When performing NSS, the surgeon must balance the need for oncologic control with the desire to preserve maximal renal parenchyma. Although Wilms tumor is exquisitely radiosensitive, local treatment with radiation is associated with an increased risk of complications such as small bowel obstruction (SBO) for decades after therapy [18,19]; however, in patients undergoing nephrectomy for unilateral disease, flank irradiation was not found to increase the risk of small bowel obstruction [20]. In our series, three of the four patients who developed partial small bowel obstructions presented after flank irradiation; the three patients who did undergo XRT presented with symptoms of SBO as a late complication (1.8–7.75 years after initial surgery). These patients may have been at risk for SBO owing to the comparatively extensive intraoperative bowel mobilization during bilateral partial nephrectomies, the transperitoneal approach, or the effects of local irradiation. Regardless of the etiology, surgeons should be aware of the possibility of SBO even years after therapy has been successfully completed.

Previous studies have suggested that preoperative chemotherapy may facilitate surgery and reduce the likelihood of intraoperative spill [21]. In redo NSS, achievement of a negative margin may be technically more difficult, owing to prior scarring, limited volume of renal parenchyma compared with tumor, and local changes secondary to prior chemotherapy and radiation. In our series, patients with recurrent disease (with the exception of those who were receiving chemotherapy when the recurrence was discovered) did not routinely receive preoperative chemotherapy prior to excision of recurrent tumor. Our greater positive margin rate at redo NSS likely reflects the increased technical difficulty of redo surgery, and surgeons should be cognizant of this risk when the decision is made to pursue redo NSS.

Our overall survival rate compares favorably with that reported for recurrent unilateral WT at our institution: for patients with recurrent WT treated after 1984, 63.6% survived [11]. That high success rate was attributed to the routine use of effective chemotherapy for recurrent tumors; as we also found, the authors reported that patients with high-risk disease, such as anaplastic histology and those who required autologous stem cell rescue after high-dose chemotherapy continued to have universally poor outcomes. Although our follow-up period is short, the mean follow-up is 4.5 years in our series; all of our patients with recurrences presented within two years of initial NSS, consistent with the timing of recurrences reported by other authors [11]. More recently, review of the NWTS data has found an overall 8-year event-free survival rate of 74% and overall survival rate of 89% for patients with FH BWT [14]; had we recognized the “recurrent” tumors in patients #1 and #2 at the time of initial surgery, our event-free and overall survival rates would be 77.8% and 97.2% respectively, consistent with these results.

The development of diffuse anaplasia in recurrent tumor in two patients initially presenting with FH BWT is a phenomenon worth noting. Patients undergoing NSS who are found to have diffuse anaplasia have universally poor outcomes despite adjuvant therapy [22,23]. In both cases in our series, the patients had undergone aggressive tumor resection and neoadjuvant chemotherapy, with negative surgical margins at initial resection, but rapid development of recurrent local tumor and distant visceral metastases despite off-protocol chemotherapy. One patient (#3) had blastemal–predominant histology at initial resection, while the other (#8) had blastemal–predominant histology in the specimen obtained at NSS for initial recurrence. Blastemal–predominant histology is known to portend a poor prognosis with higher recurrence rates than other WT subtypes even though it is a subset of favorable histology tumors, particularly when it is present in chemotherapy-treated tissue [22–24]. Recent research has suggested

<table>
<thead>
<tr>
<th>Patient</th>
<th>Time Since First Redo NSS (years)</th>
<th>Laterality</th>
<th>Surgery Type</th>
<th>Pathology</th>
<th>Margin Status</th>
<th>Chemotherapy</th>
<th>Radiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>1.11</td>
<td>Right</td>
<td>Partial</td>
<td>Diffuse anaplasia</td>
<td>Negative</td>
<td>Busulfan, melphalan; autologous stem cell rescue</td>
<td>Yes (to liver only)</td>
</tr>
<tr>
<td>8</td>
<td>0.81</td>
<td>Left</td>
<td>Partial</td>
<td>Diffuse anaplasia</td>
<td>Negative</td>
<td>None</td>
<td>Yes (left flank, 21.6 GY)</td>
</tr>
</tbody>
</table>

NB: Patient #2 had an extrarenal recurrence which was excised with positive margins and treated with right flank irradiation (10.5 Gy), as well as cyclophosphamide, carboplatin, and etoposide.

Table 3
Characteristics of second redo nephron-sparing surgery.
that genetic changes associated with the development of anaplasia and of blastemal-predominant histology may be linked [25,26]. The presence of diffuse anaplasia in patients initially presenting with blastemal-predominant favorable histology tumors may reflect devo-
lution of the initial blastemal component into anaplasia, or creation of a local environment in which replication of a population of anaplastic
cells is favored owing to the chemosensitivity of the favorable histology
tumors [26,27]. In either case, the progression of disease despite aggressive measures in these two patients underscores the limitations of primary and redo NSS in certain histologic populations. Selected patients may benefit from completion nephrectomy if histology at initial or redo NSS suggests they are at high risk of recurrence.

NSS enables preservation of renal parenchyma while achieving good local oncologic control for patients with both primary and recurrent BWT. Patients must be monitored carefully for tumor recurrence following NSS. Patients with blastemal-predominant histology appear to be at increased risk for development of diffuse anaplasia and metastatic disease, and consideration should be given to completion nephrectomy rather than redo NSS in this population. Renal insufficiency may be more common in patients with significant renal parenchymal loss as well as those undergoing chemotherapy with agents other than actinomycinD, adriamycin, and vinblastine. Although most patients with recurrence after NSS for BWT can safely be treated with redo NSS without a significantly increased risk of hypertension or renal insufficiency, some patients may not benefit from renal parenchymal preservation in obtaining oncologic control. Surgeons should be cognizant of the potential additive nephrotoxicity of surgical and medical therapies in patients with recurrent tumors, as well as the histologic predictors of poor oncologic outcome, when considering candidates for redo NSS.

References