Hypertension after Bilateral Nephron Sparing Surgery for Bilateral Wilms

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Received: 28 May 2016; Received in revised form: 18 July 2016; Accepted: 20 Nov. 2016

Abstract

Background: Nephron sparing surgery (NSS) for unilateral Wilms tumor (WT) has been debated recently and is being used to preserve kidney tissue and function. However, NSS is feasible only for selected cases with higher local relapse rates. There is a significant reduction of nephrons with the development of renal hypertension and progressive renal failure. In this paper, we have analyzed outcomes after bilateral partial nephrectomy (PN) and unilateral partial plus contralateral total nephrectomy in our patients with bilateral WT.

Methods: We have analyzed our four patients (8 kidneys) with bilateral WT and 8 unilateral complete resection. Kidney size was measured using volumetric analysis computed tomography scan imaging. The patients were matched with children who had undergone imaging of the abdomen for other malignancies.

Results: Mean kidney volumes after unilateral partial plus total contralateral nephrectomy (60.9 cm³) were significantly greater than the reference kidneys. Total kidney volume was significantly larger after bilateral PN (98.1 cm³) versus unilateral partial plus total contralateral nephrectomy (60.9 cm³).

Conclusions: Our findings suggest that patients with bilateral WT benefit from bilateral PN. Hypertension is less common after bilateral PN. However, rates of local relapse or disease associated death are separately between the groups.

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Keywords: Wilms’ tumor; Hypertension; Nephron-sparing surgery

Introduction

Wilms tumor (WT) is the most common renal cancer in children. About 5% of children who live with WT disease have it in both kidneys (1). Although WT have been a life-threatening tumor for years, by new investigations in treatment and new methods of surgery, WT has an excellent survival rate compared with other pediatric malignancies and adult renal tumors (2); however, bilateral WT management is a particular challenge because preserving kidney function to prevent end-stage renal failure and dialysis in patients with such tumors, is mandatory, so we have to balance the aggressive surgical resection to prevent recurrence with our desire to preserve renal function (3).

The current gold-standard surgical treatment for children with unilateral WT’s is radical nephrectomy (RN, or total nephrectomy) and regional lymph node sampling. Investigations are being carried out to reduce treatment mortality and morbidity; accordingly, there is some debate on nephron sparing surgery (NSS) as one of these strategies to preserve kidney tissue and function.

On the other hand, NSS is feasible only in certain conditions such as presence of a functioning kidney, no invasion of the collecting system or renal vein, clear margins between the tumor, kidney, and surrounding structures, and tumor involving only one pole occupying less than one-third of the kidney (4).

However, as Uzzo and Novick (5) reported, the rate of recurrence, especially for tumors larger than 4 cm in diameter, is about 10%. Furthermore, higher local relapse rate has been observed with nephron sparing surgeries; it can be lowered depending on surgery’s technique and surgeon’s experience (6).

One of the frequent findings in patients presenting with WT is hypertension. It seems to be the result of increased renin production secondary to renal ischemia produced by the pressure of the tumor on hilar or intrarenal vessel, and also the tumor can even be directly responsible for hypertension by producing
renin itself. In addition, as the Brenner-Barker hypothesis noted, there is a significant reduction of nephrons with the development of renal hypertension and progressive renal failure (7,8).

We analyzed outcomes after bilateral partial nephrectomy (PN) and unilateral partial plus contralateral total nephrectomy in our patients with bilateral WT.

Materials and Methods

We studied our four patients (8 kidneys) with bilateral WT for volumetric changes after two methods as mentioned, respectively, in comparison to 8 unilateral kidney resections as control groups for nonmalignant disease with correlated age and weight. Criteria for selection of patients eligible for this study were PN of at least one kidney and partial or total nephrectomy of the contralateral kidney due to bilateral WT. The data contained age at diagnosis, gender, histology, histological stage, kidney size, creatinine, proteinuria, albuminuria, and blood pressure.

We have done NSS by using the off-clamp technique making sure that kidney perfusion is enough during the entire operation. Total nephrectomy has been done in the kidney with the larger mass, while PN has attempted in the other kidney. In cases with enough remnant of healthy renal tissue, peripherally located tumors without invasion of the pylon; bilateral PN was selected follow-up was performed, after gaining local control of the primary and metastatic disease.

Kidney size was measured using volumetric analysis computed tomography scan imaging. Dosage of contrast material was adapted to renal function. Due to the fact that there are no standard kidney volumes available, comparing the measured data with data from the literature was not feasible. Instead, the patients were matched with children who had undergone imaging of the abdomen for other malignancies. We considered blood pressures (BPs) above the 95th percentile in repeated BP measurements according to the fourth report on the diagnosis, evaluation, and treatment of high BP in children and adolescents as arterial hypertension (9). It was diagnosed, based on repeated measurements of BP by nephrologists.

The differences between the kidney volumes and BP were evaluated using Mann–Whitney U-test via SPSS software (version 21; SPSS Inc., Chicago, IL, USA) at the significant level of P < 0.0500.

Results

Three female patients (75%) and one male (25%) were evaluated. The mean and standard deviation of age of the patients was 1.80 ± 0.57 years.

Mean kidney volumes after unilateral partial plus total contralateral nephrectomy (60.9 cm³) were significantly greater than the reference kidneys (P = 0.0010), whereas controls were equal to the bilateral PN group (40.7 cm³). Total kidney volume was significantly larger after bilateral PN (98.1 cm³) versus unilateral partial plus total contralateral nephrectomy (60.9 cm³, P = 0.0001). Two patients (4 kidneys) with WT in (Group I) resection had renal hypertension. However, only one patient in (Group II) resection for WT developed hypertension and subsequently 1 (kidney) in (Group II) underwent resection due to recurrence (Table 1).

Overall, survival and relapse rates were not equal between the groups, and they were better in the group with complete resection (75% during follow-up time). Accordingly, incidence of hypertension in unilateral partial plus contralateral total nephrectomy was more (P = 0.0200) in the area that both groups were homogenous.

<table>
<thead>
<tr>
<th>N = 8</th>
<th>WT groups</th>
<th>Nephrectomy in control groups</th>
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<tbody>
<tr>
<td>1</td>
<td>Unilateral partial (Group I)</td>
<td>Volume after surgery 40.5</td>
</tr>
<tr>
<td>2</td>
<td>Unilateral partial (Group I)</td>
<td>55</td>
</tr>
<tr>
<td>3</td>
<td>Unilateral partial (Group I)</td>
<td>35</td>
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<tr>
<td>4</td>
<td>Unilateral partial (Group I)</td>
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<td>Bilateral partial (Group II)</td>
<td>65</td>
</tr>
<tr>
<td>8</td>
<td>Bilateral partial (Group II)</td>
<td>95</td>
</tr>
</tbody>
</table>

WT: Wilms tumor
Discussion

The treatment of bilateral WT is still challenging. Although there is a likelihood of local recurrence of the tumor after treatment with NSS, number of surgeons who tend to perform these surgeries is on the rise. Reviewing literature revealed that there is a trend toward kidney preservation worldwide, similar to that of other solid malignancies, such as breast cancer and soft tissue sarcoma. As an example, during the past decade, at specialized medical centers in the United States, a paradigm shift has been occurred, where elective PN now accounts for up to 60% of all nephrectomies. This can be a result of improvements in surgical techniques, advances in the understanding of the biology of renal tumors and an increasing awareness of the importance of preserving long-term kidney function (10,11). Furthermore, when we preserve the normal kidney tissue by doing NSS instead of RN in cases with bilateral tumors, we subtract disability-adjusted life years and increase life-efficiency which are two major goals of WHO.

As we recognized, the pressure of WT to the adjacent tissue, result in loosing nephrons, and is associated with high risk of hypertension and end-stage renal disease. Since the number of nephrons is determined at the birth and cannot be altered, this condition is exacerbated.

Knowing this, we analyzed our patients who have undergone bilateral PN for WT, and we compared them to those who were treated with unilateral partial plus contralateral total nephrectomy.

In this context, several studies have been done. A retrospective review on 36 children with bilateral favorable history WT who undergo repeated NSS for locally recurrent disease found that two patients require medical management of hypertension (12). Mavinkurve-Groothuis et al. (13) have also demonstrated a 0% incidence of hypertension in 12 survivors of their increased inception cohort of 23 patients. Moreover, renal function of 31 WT survivors at a follow-up of 15 years has been studied. During follow-up, BP Z-scores remained stable on average, and none of the survivors used renoprotective drugs during follow-up (14). Similarly, Hadley et al. reported that only one patient required long-term antihypertensive medication in a 10-year period experience of treatment of 20 patients (14). In addition, In a study by Aronson et al., 25 patients with a follow-up more than 5 years have been observed; three patients developed mild renal insufficiency (creatinine levels 1.3, 1.8, and 2.8 mg/100 ml, respectively; N/4 0.5-1.2), combined with hypertension in one (15). Furthermore, Giel et al. (3) have identified a total of 17 patients who underwent NSS, including 16 with bilateral tumors and 1 with tumor in a solitary kidney; they noted that the prevalence of hypertension after NSS decreased slightly (from 58.8% preoperatively to 41.2% postoperatively).

It has been explained that there is a lack of relevance between renal hypertension and unilateral nephrectomy and thus, the increase in glomerular filtration rate, is the compensatory mechanism, in the remaining kidney (8-18). Moreover, Brenner and Chertow (18) have demonstrated that renal hypertension does not seem to be the result of nephrectomy alone. Similarly, Cozzi et al. (19) have supported the view that there is an “inverse relationship between nephron number and BP, irrespective of whether nephron number is reduced congenitally or in postnatal life” (20). In agreement with this concept, we found that patients who have undergone bilateral PN demonstrated less hypertension than patients who have undergone unilateral partial plus contralateral total nephrectomy.

Hubertus et al. (21) reported that 66.7% of their patients had hypertension after unilateral partial plus contralateral total nephrectomy and 20% after bilateral PN. This study is in agreement with ours. In contrast to our research Davidoff et al. (20) stated that 70% of their patients had hypertension after bilateral PN. However, the rate of hypertension might be related to factors such as high rate of post-operative radiotherapy in their series.

Other parameters such as increased serum creatinine, proteinuria, and albuminuria were less frequent in our population and were not correlated with the type of operation.

In conclusion, our findings recommend that patients with bilateral WT gain from bilateral NSS. Although hypertension is less common after bilateral PN, nevertheless, rates of local relapse or disease associated death are distributed evenly between the groups. Studies in a greater number of children are clearly needed to confirm our data, and to determine whether some children who have undergone NSS will experience hypertension after several decades.

Conflict of Interests

Authors have no conflict of interests.

Acknowledgments

The authors would like to thank the pediatric and neonatal surgical ward staff of the Bandar Abbas Sick Hospital for Children for their devotion and care.

References


