

## Hypertension after Bilateral Nephron Sparing Surgery for Bilateral Wilms

Seyed Mohammad Vahid-Hosseini<sup>1</sup>, Seyedeh Narges Tabatabaee<sup>2</sup>, Babak Sabet<sup>3</sup>,  
Manuchehr Kamali<sup>4</sup>, Sakieneh Falahi<sup>5</sup>

<sup>1</sup> Pediatric Surgeon, Department of Surgery, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

<sup>2</sup> Medical Student, Department of Surgery, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>3</sup> Associate Professor, Department of Surgery, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>4</sup> Anesthesiologist, Member of the Research Center for Anesthesiology AND Department of Pain and Critical Care, School of Medicine, Hormozgan University of Medical Sciences, Hormozgan, Iran

<sup>5</sup> Head Nurse of Surgical Ward, Pediatric Hospital, Hormozgan University of Medical Sciences, Hormozgan, Iran

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 cm<sup>3</sup>) were significantly greater than the reference kidneys. Total kidney volume was significantly larger after bilateral PN (98.1 cm<sup>3</sup>) versus unilateral partial plus total contralateral nephrectomy (60.9 cm<sup>3</sup>).

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

© 2016 Tehran University of Medical Sciences. All rights reserved.

**Citation:** Vahid-Hosseini SM, Tabatabaee SN, Sabet B, Kamali M, Falahi S. Hypertension after Bilateral Nephron Sparing Surgery for Bilateral Wilms. *Acad J Surg*, 2016; 3(3-4): 50-3.

**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 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

**Corresponding Author:** Babak Sabet

Department of Surgery, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran  
Tel: +98 9131009078/Fax: +98 21 223 60 635, E-mail: sabet@crc.mui.ac.ir

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 95<sup>th</sup> 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  $1.80 \pm 0.57$  years.

Mean kidney volumes after unilateral partial plus total contralateral nephrectomy ( $60.9 \text{ cm}^3$ ) were significantly greater than the reference kidneys ( $P = 0.0010$ ), whereas controls were equal to the bilateral PN group ( $40.7 \text{ cm}^3$ ). Total kidney volume was significantly larger after bilateral PN ( $98.1 \text{ cm}^3$ ) versus unilateral partial plus total contralateral nephrectomy ( $60.9 \text{ cm}^3$ ,  $P = 0.0001$ ). 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 1.** Demographic and volumetric data of patients with WT and unilateral nephrectomy in control groups

N = 8	WT groups			Nephrectomy in control groups		
	Type of surgery	Volume after surgery	Hypertention	Reresection	Causes of nephrectomy	Volumetric
1	Unilateral partial (Group I)	40.5	+		Reflux	30
2	Unilateral partial (Group I)	55	+		Reflux	35
3	Unilateral partial (Group I)	35	+		Infection	40
4	Unilateral partial (Group I)	60	+		Duplication	35
5	Bilateral partial (Group II)	55			Up to	40
6	Bilateral partial (Group II)	60		+	Neurogenic bladder	30
7	Bilateral partial (Group II)	65	+		Neurogenic Bladder	35
8	Bilateral partial (Group II)	95	+		Reflux	30

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; N¼ 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

1. Davidoff AM, Interiano RB, Wynn L, Delos Santos N, Dome JS, Green DM, et al. Overall survival and renal function of patients with synchronous bilateral wilms tumor undergoing surgery at a single institution. *Ann*

- Surg 2015; 262(4): 570-6.
2. Romao RL, Lorenzo AJ. Renal function in patients with Wilms tumor. *Urol Oncol* 2016; 34(1): 33-41.
  3. Giel DW, Williams MA, Jones DP, Davidoff AM, Dome JS. Renal function outcomes in patients treated with nephron sparing surgery for bilateral Wilms tumor. *J Urol* 2007; 178(4 Pt 2): 1786-9.
  4. Ritchey ML, Green DM, Thomas PR, Smith GR, Haase G, Shochat S, et al. Renal failure in Wilms' tumor patients: a report from the National Wilms' Tumor Study Group. *Med Pediatr Oncol* 1996; 26(2): 75-80.
  5. Uzzo RG, Novick AC. Nephron sparing surgery for renal tumors: Indications, techniques and outcomes. *J Urol* 2001; 166(1): 6-18.
  6. Haecker FM, von Schweinitz D, Harms D, Buerger D, Graf N. Partial nephrectomy for unilateral Wilms tumor: results of study SIOP 93-01/GPOH. *J Urol* 2003; 170(3): 939-42.
  7. Sukarochana K, Tolentino W, Kiesewetter WB. Wilms' tumor and hypertension. *J Pediatr Surg* 1972; 7(5): 573-6.
  8. Kieran K, Williams MA, McGregor LM, Dome JS, Krasin MJ, Davidoff AM. Repeat nephron-sparing surgery for children with bilateral Wilms tumor. *J Pediatr Surg* 2014; 49(1): 149-53.
  9. Scherr DS, Ng C, Munver R, Sosa RE, Vaughan ED Jr, Del Pizzo J. Practice patterns among urologic surgeons treating localized renal cell carcinoma in the laparoscopic age: technology versus oncology. *Urology* 2003; 62(6): 1007-11.
  10. Luyckx VA, Shukha K, Brenner BM. Low nephron number and its clinical consequences. *Rambam Maimonides Med J* 2011; 2(4): e0061.
  11. Huang WC, Elkin EB, Levey AS, Jang TL, Russo P. Partial nephrectomy versus radical nephrectomy in patients with small renal tumors--is there a difference in mortality and cardiovascular outcomes? *J Urol* 2009; 181(1): 55-61.
  12. Millar AJ, Davidson A, Rode H, Numanoglu A, Hartley PS, Desai F. Nephron-sparing surgery for bilateral Wilms' tumours: a single-centre experience with 23 cases. *Afr J Paediatr Surg* 2011; 8(1): 49-56.
  13. Mavinkurve-Groothuis AM, van de Kracht F, Westland R, van Wijk JA, Loonen JJ, Schreuder MF. Long-term follow-up of blood pressure and glomerular filtration rate in patients with a solitary functioning kidney: a comparison between Wilms tumor survivors and nephrectomy for other reasons. *Pediatr Nephrol* 2016; 31(3): 435-41.
  14. Hadley GP, Mars M, Ramdial PK. Bilateral Wilms' tumour in a developing country: a descriptive study. *Pediatr Surg Int* 2013; 29(5): 419-23.
  15. Aronson DC, Slaar A, Heinen RC, de Kraker J, Heij HA. Long-term outcome of bilateral Wilms tumors (BWT). *Pediatr Blood Cancer* 2011; 56(7): 1110-3.
  16. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Pediatrics* 2004; 114(2 Suppl 4th Report): 555-76.
  17. Brenner BM, Garcia DL, Anderson S. Glomeruli and blood pressure. Less of one, more the other? *Am J Hypertens* 1988; 1(4 Pt 1): 335-47.
  18. Brenner BM, Chertow GM. Congenital oligonephropathy and the etiology of adult hypertension and progressive renal injury. *Am J Kidney Dis* 1994; 23(2): 171-5.
  19. Cozzi F, Schiavetti A, Morini F, Zani A, Gambino M, Donfrancesco C, et al. Renal function adaptation in children with unilateral renal tumors treated with nephron sparing surgery or nephrectomy. *J Urol* 2005; 174(4 Pt 1): 1404-8.
  20. Davidoff AM, Giel DW, Jones DP, Jenkins JJ, Krasin MJ, Hoffer FA, et al. The feasibility and outcome of nephron-sparing surgery for children with bilateral Wilms tumor. The St Jude Children's Research Hospital experience: 1999-2006. *Cancer* 2008; 112(9): 2060-70.
  21. Hubertus J, Gunther B, Becker K, Graf N, Furtwangler R, Ferrari R, et al. Development of hypertension is less frequent after bilateral nephron sparing surgery for bilateral Wilms tumor in a long-term survey. *J Urol* 2015; 193(1): 262-6.