Synchronous Bilateral Wilms Tumor: Surgical Evaluation and Survival

doi: https://doi.org/10.32635/2176-9745.RBC.2018v64n3.33

Tumor de Wilms Bilateral Sincrônico: Avaliação Cirúrgica e Sobrevida

Tumor de Wilms Bilateral Sincrónico: Evaluación Quirúrgica y Sobrevida

Pablo Baptista Oliveira[1]; Marilia Fornaciari Grabois[2]; Fernanda Ferreira da Silva Lima[3]; Paulo Antônio Silvestre de Faria[4]; Vanessa do Nascimento Santos[5]; Francisca Norma Albuquerque Girão Gutierrez[6]; Sima Esther Ferman[7]; Ricardo Vianna de Carvalho[8]

Abstract

Introduction: Kidney tumors account for about 7% of all childhood malignancies. Synchronous bilateral Wilms tumor corresponds to 5-7% of all nephroblastomas. The treatment consists of preoperative chemotherapy, followed by conservative surgery, postoperative chemotherapy and, when indicated, radiotherapy. **Objective:** To analyze the type of surgery and the overall survival of patients with synchronous bilateral Wilms tumor. **Method:** This retrospective cohort study included 18 pediatric patients from the Hospital do Cancer I, from the National Cancer Institute José Alencar Gomes da Silva, in Rio de Janeiro, from January 2000 to december 2017. Survival curves were calculated using the Kaplan-Meier method. **Results:** The median age at diagnosis was 19 months, and 10 patients were female. It was possible to perform conservative surgery in 62.5% of the kidneys, and in 41.2% (7/17) of patients in both kidneys. The 5-year overall survival according to the type of surgery was 87.5% for conservative surgery and 62.8% for radical nephrectomy (p=0.0001). The 5-year overall survival of the entire cohort was 70.8%. **Conclusion:** Conservative surgery in pediatric synchronous bilateral Wilms tumor is feasible and can be performed safely in reference centers.

Key words: Wilms Tumor Bilateral; Child; Adolescent; Nephrectomy; Survival Analysis.

Resumo

Introdução: Os tumores renais representam cerca de 7% de todas as neoplasias malignas da infância. O tumor de Wilms bilateral sincrônico corresponde a 5-7% de todos os nefroblastomas. O tratamento consiste em quimioterapia pré-operatória, seguida de cirurgia conservadora, quimioterapia pós-operatória e, quando indicada, radioterapia. **Objetivo:** Analisar o tipo de cirurgia e a sobrevida global dos pacientes com tumor de Wilms bilateral sincrônico. **Método:** Este estudo de coorte retrospectivo incluiu 18 pacientes pediátricos do Hospital do Câncer I, do Instituto Nacional de Câncer José Alencar Gomes da Silva, no Rio de Janeiro, de janeiro de 2000 a dezembro de 2017. Curvas de sobrevida foram calculadas pelo método Kaplan-Meier. **Resultados:** A idade mediana ao diagnóstico foi de 19 meses, sendo dez casos do sexo feminino. Em 62,5% dos rins operados, foi possível realizar cirurgia conservadora e, em 41,2% (7/17) dos pacientes, em ambos os rins. A sobrevida global em cinco anos, segundo o tipo cirurgia, foi de 87,5% para cirurgia conservadora e de 62,8% para nefrectomia total (p=0,0001). A sobrevida global em cinco anos para a coorte inteira foi de 70,8%. **Conclusão:** A cirurgia preservadora de tecido renal em crianças com o tumor de Wilms bilateral sincrônico é viável e pode ser realizada com segurança em centros de referência.

Palavras-chave: Tumor de Wilms Bilateral; Criança; Adolescente; Nefrectomia; Análise de Sobrevida.

Resumen

Introducción: Los tumores renales representan alrededor del 7% de todas las neoplasias malignas de la infancia. El tumor de Wilms bilateral sincrónico corresponde al 5-7% de todos los nefroblastomas. El tratamiento consiste en quimioterapia preoperatoria, seguida de cirugía conservadora, quimioterapia postoperatoria y, cuando indicada, la radioterapia. **Objetivo:** Analizar el tipo de cirugía y la supervivencia global de los pacientes con un tumor de Wilms bilateral sincrónico. **Método:** Este estudio de cohorte retrospectivo incluyó 18 pacientes pediátricos del Hospital del Cáncer I, del Instituto Nacional de Cáncer José Alencar Gomes da Silva, nel Río de Janeiro, de enero de 2000 a diciembre de 2017. Las curvas de sobrevida fueron calculadas por el método Kaplan-Meier. **Resultados:** La edad media al diagnóstico fue de 19 meses, siendo diez casos del sexo femenino. En el 62,5% de los riñones operados fue posible realizar cirugía conservadora, siendo en el 41,2% (7/17) de los pacientes en los dos riñones. La supervivencia global en cinco años según el tipo de cirugía fue de 87,5% para cirugía conservadora y de 62,8% nefrectomía total (p=0,0001). La supervivencia global en cinco años para la cohorte entera fue del 70,8%. **Conclusión:** La cirugía conservadora en niños con el tumor de Wilms bilateral sincrónico es viable y puede ser realizada con seguridad en centros de referencia.

Palabras clave: Tumor de Wilms Bilateral; Niño; Adolescente; Nefrectomía; Análisis de Supervivencia.

[1] Instituto Nacional de Câncer José Alencar Gomes da Silva (INCA). Rio de Janeiro (RJ), Brazil. Orcid iD: https://orcid.org/0000-0003-4677-8873
[2] INCA. Rio de Janeiro (RJ), Brazil. Orcid iD: https://orcid.org/0000-0002-9368-1030
[3] INCA. Rio de Janeiro (RJ), Brazil. Orcid iD: https://orcid.org/0000-0002-6658-3101
[4] INCA. Rio de Janeiro (RJ), Brazil. Orcid iD: https://orcid.org/0000-0003-1817-4888
[5] INCA. Rio de Janeiro (RJ), Brazil. Orcid iD: https://orcid.org/0000-0003-38434085
[6] INCA. Rio de Janeiro (RJ), Brazil. Orcid iD: https://orcid.org/0000-0002-8107-0136
[7] INCA. Rio de Janeiro (RJ), Brazil. Orcid iD: https://orcid.org/0000-0002-7076-6779
[8] INCA. Rio de Janeiro (RJ), Brazil. Orcid iD: https://orcid.org/0000-0002-3768-8289
Corresponding Author: Ricardo Vianna de Carvalho. Hospital do Câncer I. INCA. Praça Cruz Vermelha, 23 - 5º andar (chefia da pediatria) - Centro. Rio de Janeiro (RJ), Brazil. CEP 20230-130. E-mail: cir_oncologica.pediatrica@inca.gov.br.

INTRODUCTION

Renal tumors represent some 7% of all malignant neoplasms in childhood[1]. Incidence of Wilms tumor in children 0-14 years of age was 8.3 per million[2] in the United States and 6.01 per million in Brazil[1]. Wilms tumor or nephroblastoma is the most frequent form, accounting for 95% of cases[3], affecting either one kidney (unilateral) or both kidneys simultaneously (bilateral), also called synchronous bilateral Wilms tumor.

Synchronous bilateral Wilms tumor accounts for 5-7% of all nephroblastomas[4,5]. It generally occurs in younger children (mean age 2.5 years) when compared to age in unilateral tumors, in addition to being an important risk factor for the development of renal failure[4]. According to data from the *National Wilms Tumor Study* (NWTS 1-4), 12% of patients with synchronous bilateral Wilms tumor developed renal failure, due mainly to the aggressive surgical approach[6].

Modern therapy for synchronous bilateral Wilms tumor consists of preoperative chemotherapy followed by nephron-sparing surgery (NSS), postoperative chemotherapy, and radiotherapy when indicated. In these patients, successful treatment should achieve oncological control, preserving the renal parenchyma insofar as possible to guarantee renal function[7]. End-stage renal disease negatively affects the patient's overall health status and quality of life, and these effects are more pronounced in small children[8]. Children with end-stage renal disease require dietary and lifestyle modifications, in addition to renal replacement therapy, frequent hospitalizations, and increased use of medications[9].

This study aims to present the clinical characteristics and evolution of patients with synchronous bilateral Wilms tumor, with emphasis on surgical aspects, in a referral hospital for treatment of pediatric cancer. The approach to these patients should be multidisciplinary (pediatric surgeons, pediatric oncologists, pathologists, radiologists, and radiation therapists). The treatment protocol for these patients was standardized by the International Society of Pediatric Oncology (SIOP) 2001 and by the Brazilian Society of Pediatric Oncology (SOBOPE).

METHOD

This retrospective cohort consisted of all children with synchronous bilateral Wilms tumor enrolled in the Pediatric Oncology Service at Cancer Hospital I of the Brazilian National Cancer Institute José Alencar Gomes da Silva (HC I/INCA) in Rio de Janeiro from January 2000 to December 2017. A total of 259 patients with Wilms tumor were identified, of whom 18 (7%) presented imaging tests suggestive of bilateral renal tumor. Eligibility criteria were: age up to 15 years, synchronous bilateral renal disease at diagnosis defined by imaging studies (ultrasound, computerized tomography, and/or magnetic resonance), and absence of metastatic disease. Imaging tests allowed identifying multicentric tumor distribution in each kidney. All the data were collected from print or electronic patient charts.

The target variables were: age at diagnosis, sex, initial clinical presentation, associated malformations, preoperative chemotherapy, surgical procedures (biopsy, NSS, partial nephrectomy, and/or total nephrectomy), histopathology, surgical stage, follow-up time, and clinical status at the end of observation. Conservative surgery was defined as NSS alone, NSS associated with partial nephrectomy, or partial nephrectomy alone.

All 18 patients received neoadjuvant chemotherapy, initiated with two drugs: dactinomycin 0.045 mg/kg/day, (D1 and D15 - total of two doses) and vincristine 1.5 mg/m^2/week (total of four doses). After the first four weeks of treatment, new imaging tests were performed to assess the disease response. The third chemotherapy drug, doxorubicin (50 mg/m^2/dose), was added in cases of lack of tumor reduction or disease progression. All patients received at least eight weeks of neoadjuvant chemotherapy. One patient received carboplatin rather than dactinomycin due to the temporary shortage of the latter drug in Brazil.

The decision as to surgical procedure was based on radiological assessment after eight weeks of preoperative chemotherapy and was made jointly by the multidisciplinary team. Each kidney was treated individually, beginning with the less affected kidney, followed by the kidney with more advanced disease. The objective was to perform the most conservative surgical approach possible to maintain the best renal function and with oncological criteria (disease-free margins).

The surgical approach was wide supraumbilical transverse incision. The entire abdominal cavity was inspected for associated lesions not detected by preoperative tests. After isolation of the affected kidney, vascular control was obtained by isolation of the corresponding renal artery and vein, and the surgical bed was maintained in hypothermia with sterile ice. An electrocautery was used to mark on the kidney a borderline between the tumor and macroscopic free margin before the surgical incision in the respective kidney's parenchyma. The surgical margin was assessed by the pathologist via intraoperative frozen section.

Potential complications assessed during surgical procedures were: capsular violation, ischemia of the

remaining parenchyma due to surgical manipulation, extension of tumoral thrombi into large vessels, and extensive injury of renal calyces and adjacent anatomical structures.

Postoperative chemotherapy was based on abdominal surgical staging and histology, classified according to the side affected by the most advanced and more aggressive stage, respectively. In the postoperative period, patients received at least 27 weeks of chemotherapy with dactinomycin and vincristine. Radiotherapy was indicated in selected cases according to guidelines in the SIOP protocol (2001).

Patient follow-up was done with serial chest x-rays and abdominal ultrasound. Renal function was monitored with laboratory tests and renal scintigraphy.

Two- and five-year overall survival rates were calculated. Baseline observation was defined for each individual (T_0) as date of enrollment in the specialized hospital. Survival analysis defined the occurrence of death from any cause as the event. Patients that did not present the event were classified as "censure", and time was counted until the date of the last observation recorded on the medical chart or until the study's final date. Survival functions were estimated by the Kaplan-Meier method. Log-rank test was applied to test whether the curves differed between categories of the same variable. Exploratory analysis of the variables and survival analysis was done in R, which is a free software environment for statistical and graphic computation, using the *Chron* and *Survival* statistical packages (R Core Team 2016)[10].

The study was approved by the Institutional Review Board of INCA, protocol number CAAE 82799618.9.0000.5274.

RESULTS

Table 1 shows the characteristics of the 18 patients with synchronous bilateral Wilms tumor. There were ten female patients and eight males (F/M=1.25/1). Median age at diagnosis was 19 months, ranging from 3.4 to 63.1 months.

All 18 patients presented non-metastatic disease at diagnosis. Increased abdominal volume, alone or associated with other clinical complaints, was the most frequent sign/symptom, accounting for 77.8% (n=14) of the total. Five patients (29.4%) presented associated constitutional anomalies: Denys-Drash (n=1), Beckwith-Wiedemann (n=1), Frasier (n=1), hemihypertrophy (n=1), and Von Willebrand disease (n=1).

All patients received preoperative chemotherapy with two or three drugs, with a median duration of 15 weeks (range: 7 to 29 weeks).

Surgical procedures were performed in 17 patients, totaling 32 kidneys: 4/32 biopsies (12.5%); 8/32 NSS (25%); 3/32 partial nephrectomies associated with NSS (9.4%); 9/32 partial nephrectomies (28.1%), and 8/32 total nephrectomies (25%) (Figure 1). In 8/17 patients (47.1%) it was possible to perform NSS in one or both kidneys per patient. In addition, in 3/17 patients (17.6%) with multicentric tumors it was possible to proceed to partial nephrectomy combined with NSS in the same kidney. In all, it was possible to perform bilateral conservative surgery in 7/17 patients (41.2%). Two patients were not submitted to surgery in one of the kidneys since they presented punctiform residual lesions following preoperative chemotherapy, and thus did not have histopathological results for these kidneys. One child with Denys-Drash syndrome evolved to death due to severe renal failure during preoperative chemotherapy, and thus also had no histopathological results.

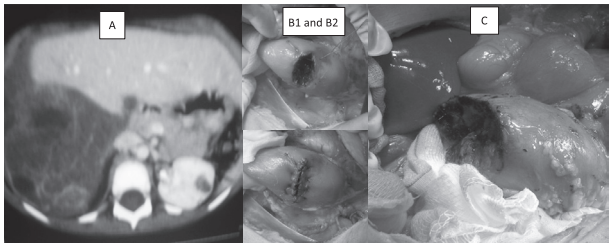


Figure 1. A Figure 1A shows the preoperative abdominal computerized tomography. Figures 1B1 and 1B2 show the NSS procedure in the posterior pole of the left kidney. Figure 1C shows the NSS procedure in the upper third of the right kidney

Of the 17 patients submitted to surgery, the surgical stages were: seven stage I (39%), five stage II (27.8%), and five stage III (27.8%). Among the patients with surgical stage III (ID 4, 6, 7, 9, and 10 in Table 1), one patient presented surgical margin compromised by neoplastic infiltration of the renal capsule and leakage of the perirenal adipose tissue, two patients presented tumor rupture and positive peritoneal liquid for neoplastic cells, and the other two patients presented implantation on the peritoneal surface.

In relation to histology, nephrogenic remnants were present in 13/17 of the patients (76.5%), favorable histology in 14/17 patients (82.4%), and unfavorable histology in 3/17 patients (17.6%).

Complications during the first surgical stage in each patient were: ruptured tumor capsule (n=2), ischemia of the remaining parenchyma due to surgical manipulation (n=1), and injury to the renal vein (n=1).

During follow-up, eight patients (47.1%) presented disease relapse: lung and kidney (n=3), abdomen (n=2),

Table 1. Clinical characteristics of patients with bilateral Wilms tumor, 2000-2017

ID	Sex	Age (months)	Associated malformations	Preoperative chemotherapy	Initial surgical approaches		Histology		Highest surgical stage	Relapse	*Status*	Last creatinine (mg/dL)	Time in follow-up (in years)
					right kidney	Left kidney	Right kidney	Left kidney					
1	F	3.4		AV	NSS	NSS	WT, FH and NR	WT, FH and NR	I		AWOD	0.8	14.4
2	M	14.9	Beckwith--Wiedmann	AV	Total nephrectomy	NSS	WT, FH	WT, FH and NR	I	Lung and kidney	Death&	6.8	15.4
3	F	16.3		AV	Biopsy	Total nephrectomy	WT, FH	WT, FH and NR	I		AWOD	0.6	16.6
4	M	48.6		AV and AVD	Partial nephrectomy	Partial nephrectomy and NSS	WT, FH (IR)	WT, HD (HR DA) and NR	III	Lung and kidney	Death	0.4	2.0
5	F	33.5		AV and AVD	Total nephrectomy	without surgery	WT, FH (IR epithelial)	Unknown	I		AWOD	0.6	14.1
6	M	38.8	Hemihypertrophy	AV	Biopsy	Partial nephrectomy	NR	WT, FH (IR mixed type)	III	Lung	AWOD	0.9	11.7
7	F	63.1		AV and AVD	Partial nephrectomy	NSS	WT, FH (IR stromal)	WT, FH (IR epithelial and stromal)	III		AWOD	0.5	12.0
8	F	5.5	Von Willebrand	AV and AVD	Biopsy	Total nephrectomy	WT, FH (IR stromal and epithelial)	WT, FH (IR mixed type)	I	Lung and kidney	Death&	2.3	2.4
9	M	49.7		AV	Partial nephrectomy	Partial nephrectomy	WT, FH (IR FA) and NR	WT, FH (IR regressive type)	III	Liver	AWOD	0.7	9.3
10	M	61.1		AV and AVD	Total nephrectomy	Partial nephrectomy	WT, FH (IR mixed type) and NR	WT, FH (IR mixed type) and NR	III	Abdomen	Death	0.4	2.0
11	M	11.2		AV and AVD	NSS	Partial nephrectomy	NR	WT FH (IR mixed type)	II		AWOD	0.5	8.2
12	F	31.8		AV and AVD	Total nephrectomy	NSS	WT, UH (HR DA)	NR	I	Abdomen	Death	1.4	1.4
13	M	5.0	Denys-Drash	AV	without surgery	without surgery	Unknown	unknown	unknown		Death*	1.3	82*
14	M	21.1	Frasier	AV and AVD	Total nephrectomy	Partial nephrectomy	WT, FH (IR stromal) and NR	NR	II		AWOD	0.5	6.0
15	F	11.9		AV	Biopsy	Partial nephrectomy	NR	WT, FH (IR epithelial) and NR	II		AWOD	0.6	6.5
16	F	17.0		AV	Partial nephrectomy and NSS	NSS	WT, FH (IR epithelial) and NR	NR	I		AWOD	0.3	5.1
17	F	6.3		AV and AVD	without surgery	Total nephrectomy	Unknown	WT, FH (IR mixed)	II	Kidney	AWOD	0.5	4.2
18	F	31.0		CDV	Partial nephrectomy and NSS	NSS	WT, UH (HR blastemal) and NR	WT, FH (IR epithelial)	II		AWOD	0.3	1.4

ID: patient; NSS: nephron-sparing surgery; WT: Wilms tumor; FH: favorable histology; UH: unfavorable histology; NR: nephrogenic remnants; DA diffuse anaplasia; FA: focal anaplasia; IR: intermediate risk, HR: high risk; AV: actinomycin D and vincristine; AVD: actinomycin D, vincristine, and doxorubicin; CDV: carboplatin, doxorubicin, and vincristine; AWOD: alive without disease; 82*: 82 days; death*: from toxicity; death&: anephric.

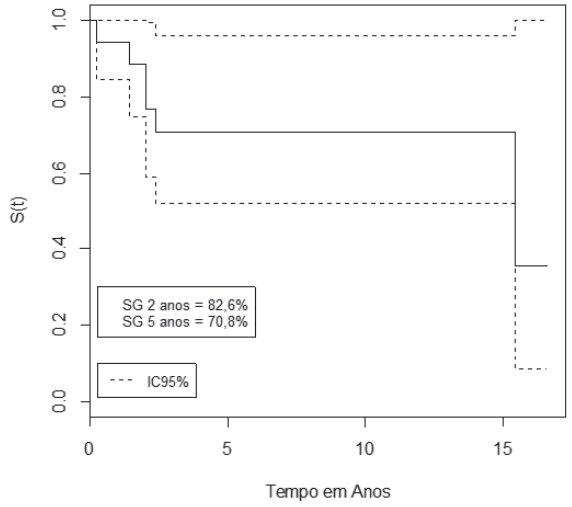
liver (n=1), lung (n=1), and kidney (n=1). Five of these patients (ID 2, 4, 8, 10, and 12) evolved to death from disease progression, and the others (ID 6, 9, and 17) remained alive without evidence of disease.

Following relapse, two patients (11%) became anephric. Patient ID 2 presented Beckwith-Wiedmman syndrome and was submitted to total right nephrectomy and biopsy of a small lesion in the left kidney. Histology evidenced Wilms tumor with favorable histology and nephrogenic remnants. The patient remained in control for 12 years, after which he presented relapse in the left kidney with diffuse anaplasia. He was treated with various rounds of chemotherapy and abdominal radiotherapy, without success. Resection of the remaining kidney was necessary, and the patient evolved to death from disease progression 2.6 years after relapse. Patient ID 8 presented

Von Willebrand disease. She was submitted to total left nephrectomy and biopsy of a small lesion in the mid third of the right kidney. Histology showed Wilms tumor with favorable histology in both kidneys. She presented relapse in the right kidney nine months after the first surgery. She received various rounds of chemotherapy and abdominal radiotherapy, plus the need for total right nephrectomy. She evolved to death from disease progression 1.3 years after relapse (Table 1).

There were six deaths in all: five from disease progression and one from toxicity (patient with Denys-Drash syndrome).

All the surviving patients presented normal renal function at the last assessment. Median follow-up time in the study cohort was 6.3 years (0.22 to 16.6 years) and two and five-year overall survival rates for all 18 patients, including favorable and unfavorable histology, were 82.6% and 70.8%, respectively (Graph 1). For patients with favorable histology, two- and five-year overall survival rates were 92.9% and 85.7%, respectively, a statistically significant result (p-value <0.0001). For patients with unfavorable histology, two-year overall survival was 50%. Five-year overall survival according to type of surgery was 87.5% for NSS and/or partial nephrectomy (conservative surgery) and 62.8% for total nephrectomy (p=0.0001) (Graph 2).

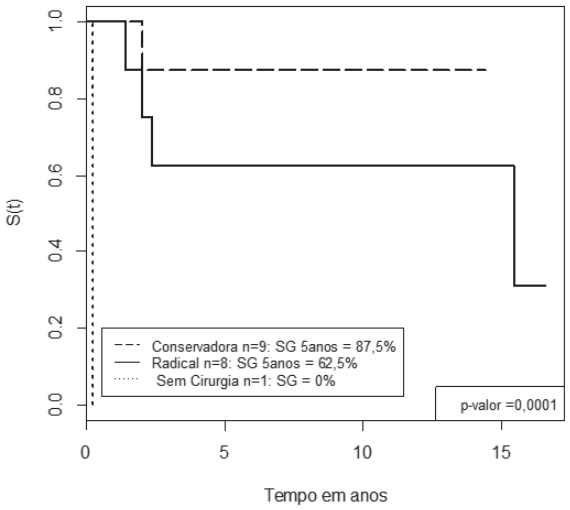


Graph 1. Two- and five-year overall survival for synchronous bilateral Wilms tumor (n=18), 2000-2017

Key: CI: confidence interval; OS: overall survival.

DISCUSSION

In keeping with the literature, the current retrospective study found 7% of WT patients with synchronous bilateral Wilms tumor during the study period[4]. Five-



Graph 2. Five-year overall survival for synchronous bilateral Wilms tumor according to type of surgery, 2000-2017

Key: OS: overall survival.

year overall survival for all 18 patients with synchronous bilateral Wilms tumor was 70.8%. According to type of surgery, five-year overall survival was 87.5% for patients submitted to NSS and partial nephrectomy. These rates are similar to those of the studies by NWTS-5 and *Associazione Italiana di Ematologia Oncologia Pediatrica* (AIEOP), which report four-year overall survival rates for all patients with synchronous bilateral Wilms tumor at 80.8%[11] and 80%[12], respectively, although lower than the overall survival reported by the *Children's Oncology Group* (COG), namely 94.16%[11].

Bilateral Wilms tumor tends to manifest more in infants[7]. In the current study, median age at diagnosis was 19 months, affecting children at younger ages than reported in the literature, which range from 24 months[12] to 30 months[4]. Nephrogenic remnants were found in 76.5% of patients, similar to results in the literature[8]. Synchronous bilateral Wilms tumor is more commonly associated with genetic syndromes that frequently correlate with intrinsic renal disease. The tumors can be multifocal and present increased risk of developing renal failure as a result of aggressive surgery, as the most common cause of surgical removal of nephrons and bilateral nephrectomy in some cases [6-8]. In the current study, two children underwent bilateral nephrectomy due to disease progression, corroborating the international literature[5].

In the attempt to avoid renal failure, the role of NSS for children with synchronous bilateral Wilms tumor has become increasingly important, although bilateral NSS is still not widely used. Davidoff et al.[6] report that it was possible to perform bilateral NSS in 92.9% of patients (39/42) with synchronous bilateral Wilms

tumor, achieving good oncological results. According to the authors, preoperative chemotherapy with three drugs (AVD) in this series may have contributed to greater ease in performing NSS.

However, the study by AIEOP in 90 patients with synchronous bilateral Wilms tumor did not find a higher proportion of bilateral NSS in the 37 patients (32%) that received AVD preoperative chemotherapy when compared to the group of 43 patients (58%) that received two drugs (AV)[12]. In addition, the multicenter prospective study on treatment of children with bilateral Wilms tumor coordinated by the Children's Oncology Group (COG) achieved 39% of bilateral NSS in the sample of 242 patients[11].

The current study reported NSS in 47.1% of patients and the combination of NSS with partial nephrectomy in the same kidney in 17.6% of patients, achieving good oncological and renal function results. In all, it was possible to perform bilateral conservative surgery in 41.2% of patients (7/17). In our series, unlike Davidoff et al.[6], preoperative chemotherapy was initiated with AV, and doxorubicin was only added in cases with lack of tumor reduction after the first four weeks of treatment. This may have contributed to the lower percentage of bilateral NSS.

Even in cases of synchronous bilateral Wilms tumor with involvement of the renal hilus, it is possible to perform NSS safely using the longitudinal partial nephrectomy technique described by Fuchs[13]. Surgical success is essential for a favorable outcome in these patients, and it is crucial to perform the surgery in referral centers with pediatric oncologists and surgeons with great expertise, as recommended by the SIOP protocol of 2001.

Another important aspect is the duration of preoperative chemotherapy, that is, time between initiation of chemotherapy and the first surgical resection. Preoperative chemotherapy aims at tumor downstaging and facilitating conservative surgery. In the current study, preoperative chemotherapy lasted a median of 15 weeks. Various authors have reported that extending the time on neoadjuvant chemotherapy beyond three months (12 weeks) did not increase the proportion of bilateral NSS. In addition, various studies have reported that maximum tumor reduction occurred in the first 12 weeks of preoperative chemotherapy. Besides, the lack of response to neoadjuvant chemotherapy assumes two histological conditions: differentiation in mature stromal tissue or anaplastic transformation[11,12,14].

One of the study's limitations was its retrospective design, potentially leading to selection and information bias.

Patients with synchronous bilateral Wilms tumor need to be followed indefinitely to assess treatment-related complications, the possibility of tumor recurrence, and long-term monitoring of renal function[15].

CONCLUSION

Treatment of synchronous bilateral Wilms tumor is complex and requires joint multidisciplinary action aimed at optimal oncological outcomes. NSS in children with synchronous bilateral Wilms tumor is feasible and can be performed safely in specialized centers. Surgical preservation of the renal parenchyma is essential for controlling the disease and conserving renal function in these children, who are at significant risk of renal insufficiency.

CONTRIBUTIONS

All the authors participated equally in the research, data collection, interpretation of the results, critical analysis of the content, development of the manuscript, and analysis and revision of the article in its final form for submission to publication.

ACKNOWLEDGMENTS

The authors wish to thank the staffs of Pediatric Oncology and Pediatric Surgery, the medical archives, and the Department of Pediatrics at HCI/INCA/RJ.

CONFLICT OF INTEREST

None.

FUNDING SOURCES

None.

REFERENCES:

1. Instituto Nacional de Câncer José Alencar Gomes da Silva. Incidência, mortalidade e morbidade hospitalar por câncer em crianças, adolescentes e adultos jovens no Brasil: informações dos registros de câncer e do sistema de mortalidade. Rio de Janeiro: INCA, 2016.
2. Doganis D, Panagopoulou P, Tragiannidis A, Georgakis MK, Moschovi M, Polychronopoulou S, et al. Childhood nephroblastoma in Southern and Eastern Europe and the US: incidence variations and temporal trends by human development index. Cancer Epidemiol. 2018;54:75-81.
3. Chu A, Heck JE, Ribeiro KB, Brennan P, Boffetta P, Buffler P, et al. Wilms' tumour: a systematic review of risk factors and meta-analysis. Paediatr Perinat Epidemiol. 2010;24(5):449-469.

4. Ehrlich PF. Bilateral Wilms tumor: the need to improve outcomes. Expert Rev Anticancer Ther. 2009;9(7):963-973.
5. 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 Urology 2007;118(4):1786-1790.
6. Davidoff AM, Interiano RB, Wynn L, Delo 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):570-576.
7. 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):149-153.
8. Kieran K, Davidoff AM. Nephron-sparing surgery for bilateral Wilms tumor. Pediatr Surg Int. 2015;31(3):229-236.
9. McKenna AM, Keating LE, Vigneux A, Stevens S, Williams A, Geary DF. Quality of life in children with chronic kidney disease: patient and caregiver assessments. Nephrol Dial Transplant. 2006;21(7):1899-1905.
10. R Foundation for Statistical Computing. The R Project for Statistical Computing. [computer program]. R version 3.3.2. [Internet]. [place unknown]: The R foundation; 2016. [cited 2016 Out 31]. Available from: https://www.R-project.org.
11. Ehrlich P, Chi YY, Chintagumpala MM, Hoffer FA, Perlman EJ, Kalapurakal JA, et al. Results of the first prospective multi-institutional treatment study in children with bilateral Wilms tumor (AREN0534): a report from the Children's Oncology Group. Ann Surg. 2017;266(3):470-478.
12. Indolfi P, Jenkner A, Terenziani M, Crocoli A, Serra A, Collini P, et al. Synchronous bilateral Wilms tumor: a report from the Associazione Italiana Ematologia Oncologia Pediatrica (AIEOP). Cancer. 2013;119(8):1586-1592.
13. Fuchs J, Szavay P, Seitz G, Handgretinger R, Schäfer JF, Warmann SW. Nephron sparing surgery for synchronous bilateral nephroblastoma involving the renal hilus. J Urol. 2011;186(4):1430-36.
14. Shamberger RC, Haase GM, Argani P, Perlman EJ, Cotton CA, Takashima J, et al. Bilateral Wilms' tumors with progressive or nonresponsive disease. J Pediatr Surg. 2006;41(4):652– 657.
15. Sarhan OM, El-Baz M, Sarhan MM, Ghali AM, Ghoneim MA. Bilateral Wilms' tumor: single-center experience with 22 cases and literature review. Urology 2010;76(4):946-951.

Recebido em 5/9/2018
Aprovado em 20/12/2018