ASSESSMENT OF SURGICAL TREATMENT OF WILMS TUMORS IN CHILDREN ACCORDING TO SIOP 2001

Dang Huu Chien[1], Truong Dinh Khai [2]

SUMMARY

Objective: *To assess the results of surgical treatment of Wilms tumors in children according to SIOP 2001.*

Study method: *A descriptive and retrospective study of cases diagnosed of Wilms tumors by age, according to Algorithm of Diagnosis and Treatment of Wilms Tumors (SIOP 2001).*

RESULTS: There were 47 pediatric patients of nephroblastoma treated in accordance with SIOP 2001 algorithm who had survival rate, no relapse for 1 year of 82.9%. The overall survival rate was 91.5%. Accidents during surgery include tumor ruptures (8.51%), injuries to colon and jejunum (8.51%) and lacerations of inferior vena cava (4.26%).

Conclusion: *The results of surgical treatment of nephroblastoma in accordance of the SIOP 2001 algorithm are relatively good despite the fact that the follow-up is short-term and small in numbers to compare with other research groups in the world.*

Key words: *Wilms tumor or nephroblastoma, surgical treatment, SIOP 2001 algorithm.*

I. INTRODUCTION

Wilms tumor or nephroblastoma is the most common type of cancer that accounts for 95% of all kidney tumors in children [10]. Nearly 1,000 children are diagnosed of having Wilms tumors each year in Europe. The Wilms tumors are mostly diagnosed in the age of 2 to 4 years, in one kidney and large in size. The survival rate without relapse after 5 years for the patients with tumors treated in the localized stage was 91% in the 2004 SIOP study [10].

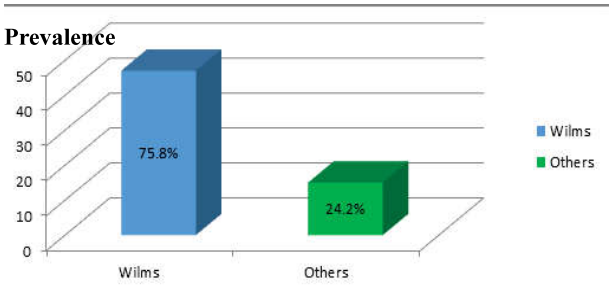
II. STUDY METHOD

Descriptive and retrospective study was performed in a series of cases treated from June 2013 to June 2017 at Children's Hospital 2. We enrolled 62 pediatric patients with kidney tumors in the study sample of 2001 SIOP. Wilms tumors are diagnosed in 47 cases (76%) and other tumors diagnosed in the rest.

III. RESULTS AND DISCUSSIONS

3.1. Wilms tumors and other kidney tumors

Chart 1. Prevalence of Wilms tumors and other kidney tumors



The prevalence of Wilms tumors is high, up to two-thirds of all kidney tumors

1. Pediatric Hospital Gia Lai
2. Medicine and Pharmacy of University at HCM City

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- Corresponding author: Dang Huu chien
- Email: thientrangduc@hotmail.com , Tel: 0914009090

Table 1. Percentage of kidney tumors in the study sample

Percentage of kidney tumors		
Tumor types	**Prevalence**	**Percentage %**
Wilms tumor	47	75.8
Congenital Mesoblastic nephroma	4	6.5
Kidney epithelial cell cancers	3	4.9
Clear cell sarcoma	2	3.2
Rhabdoid tumor	2	3.2
Renal cell carcinoma	2	3.2
Cystic renal tumor	1	1.6
Neuroblastoma	1	1.6
Total	62	100

3.2. Age and Gender

The mean age of the study sample was less than 5 years (26.9 ± 25.9), ranged 1-80 months. The age of males was lower than that of females, but the difference was not statistically significant (p = 0.52). The cases in each age group are unevenly distributed, mostly in the age group of 6 months to 5 years old (38/47, 80.85%).

- In the study, Wilms tumors were found in female infants more than in male (female / male = 1:1.14). This result is similar to that of 1: 11 of Nguyen Huu Dung [1]; 1: 1.22 of North American studies [10] and 1: 1 of SIOP study in Europe [10].

3.3. Genetic syndromes

Most of cases have no accompanying congenital abnormalities. There is a case of absence of iris and a case of hemihypertrophy disorder.

All cases have normal family history.

3.4. Ultrasound, CT scans and MRI

+ Ultrasound

In 62 cases of renal tumors, ultrasonography accurately identified 59 cases (95%) and diagnosed incorrectly 3 cases (5%). Doppler ultrasound is a good tool to investigate invasion to renal veins and inferior vena cava, with sensitivity and specificity comparable to CT and MRI [6], [7], [3]. However, in our study, we did not collect sufficient information to evaluate the role of Doppler ultrasound.

+ CT scans, MRI

In Table 1, 15/62 cases (24.2%) of other cancers were diagnosed as nephroblastoma on imaging studies and received chemotherapy before surgical treatment. According to SIOP, a falsely positive diagnosis is of 5% [10]. However, this 5% rate does not include other kidney cancer cases such as clear cell renal sarcoma renal artery sarcoma, rhabdoid renal tumor. These cancers have a significantly worse prognosis and require postoperative treatments different from nephroblastoma. The UK and Germany studies, members of the SIOP, showed that the incidence of pathology of nephroblastoma was 12% and 7.8%, respectively.

The relevance of diagnostic imaging studies to pathological results in our study is lower than that of SIOP. This difference may result from the nephroblastoma incidence of 75.8% in Children's Hospital 2, lower than that of SIOP, 85-90%. The incidence of clear cell sarcoma, rhabdoid renal tumor, which are very difficult to distinguish from nephroblastoma imaging studies, in our study are much higher than that of SIOP.

3.5. Locations of Wilms tumors

In our study, Wilms tumors were found in right, left and bilateral kidneys of 45.2%, 48.4% and 6.4%, respectively.

Most studies in Vietnam and abroad show no differences in the location of Wilms tumor in the right or left kidneys [1], [3]. According to Nevillet

and Arif N. Ali [4], Wilms tumors in bilateral kidneys account for about 4-7%. Tran Duc Hau shows the rate of 5.4% in bilateral kidneys [2] in Vietnam. These incidences are in line with our findings. A number of studies in the world have shown higher incidences of nephroblastoma in bilateral kidneys in children acquiring congenital malformations such as WAGR, Beckwith-Wiedemann syndrome and hemihypertrophy. However, 85% of pediatric patients children with WAGR or Beckwith-Wiedemann syndrome have a unilateral kidney tumor.

In our study, the intrarenal location of Wilms tumors were found in upper pole as 34%, lower pole 38%, and middle of the kidney 15%. In 6 cases (13%), the tumors were so big and compressed the renal parenchyma that we could not identify their original locations. There were regional lymphadenopathy in 4 cases. The lymph nodes were smaller than 1.2 cm, possibly inflammatory lymph nodes.

The literature also describes cases in which Wilms tumors originated out of the kidneys, but rare [10]. In our study, no cases of extrarenal Wilms tumors were found.

3.6. Distant metastasis

In our study, there were 3 cases of metastases (1 case of pulmonary metastasis, 1 case of liver metastasis, 1 case of peritoneal metastasis). Metastatic rates of 6.4% are similar to those of Abd El-Aal [4] but are lower than those of Breslow [5].

Table 2. Comparison of rates of metastasis

Studies	Cases	Distant metastasis	Rate (%)
Abd El-Aal [4]	62	4	6.5
Breslow [5]	1991	236	11.8
Our study	47	3	6.4

In three cases of distal metastasis demonstrated on imaging studies, our hospital was not eligible for biopsy and cell-specific identification of distant metastatic lesions. This is a limitation of our study, but after chemotherapy, all of these lesions have disappeared and this indicates that distant metastatic lesions are potentially sensitive to chemotherapy.

3.7. Stages

Table 3. Distribution of stages of disease and preoperative chemotherapy

	Preoperative chemotherapy		Total
Stages	**Yes**	**No**	
I	8 23.53%	5 38.5%	13 27.66%
II	19 55.89%	5 38.5%	24 51.06%
III	3 8.82%	1 17.69%	4 8.51%
IV	1 2.94%	1 2.94%	2 4.26%
V	4 11.76%	0 0%	4 8.51%
Total	35 100%	12 100%	**47** **100%**
Note: The above row is the case number, the bottom row is the percentage.			

Stage II accounts for the largest number when considering two groups of surgery with and without preoperative chemotherapy, including 9 cases in the age group considered for surgery without preoperative chemotherapy and 3 cases in the group from 6 months to 60 months without imaging studies suggesting Wilms tumors.

3.8. Classification of risk groups according to pathology

Table 4. Risk distribution by pathology

Risk	Preoperative chemotherapy		Rates %
	Yes	No	
Low	5 14.7%	1 7.69%	6 12.8%
Medium	25 73.5%	11 84.6%	35 74.5%
High	4 11.6%	2 15.4%	6 12.8%
Tổng	34 100%	13 100%	47 100%
Note: The above row is the case number, the bottom row is the percentage.			

The risk for Wilms tumors is mainly focused on stage II, with moderate risk. This result is consistent with other SIOP studies.

3.9. Surgical complications in groups of surgery with and without chemotherapy

Table 5. Rates of complications in groups of surgery with and without chemotherapy

Complications	With preoperative chemotherapy (n=34)	Without preoperative chemotherapy (n=13)	Total
Intraoperative tumor rupture	1/34 (2.94%)	3/13 (23.07%)	4/47 (8.51%)
Surrounding organ removal	1/34 (2.94%)	2/13 (15.38%)	3/47 (6.38%)
Inferior vena cava laceration	0/34 (0%)	2/13 (15.38%)	2/47 (4.26%)
Surrounding organ damage	0/34 (0%)	1/13 (7.69%)	1/47 (2.13%)
Total	2/34 **(5.89%)**	8/13 **(61.5%)**	10/47 (21.3%)

The complication rates of the surgical group without preoperative chemotherapy (61.5%) was 10 times higher than the surgical group with preoperative chemotherapy (5.89%). The common complication during surgery is tumor rupture. This indicates the effectiveness of preoperative chemotherapy in reducing surgical complications, including tumor rupture, resulting in reduction of stage III tumors. According to Ehrlich PF (2016) and colleagues, the rates of intraoperative complications is quite high, affecting the survival rate of pediatric patients (14.28%) [8]

3.10. Perirenal fat invasion

Table 6. Perirenal fat invasion

Perirenal fat invasion	Cases	Rates %
Yes	5	11.7
No	42	89.3
Total	47	100

Preoperative chemotherapy improves local factors in reducing the incidence of tumor ruptures and avoiding tumor cells left. Investigation of perirenal fat invasion is important in Wilms tumor staging. Once the tumors invade through the renal capsules, stage III will be established.

3.11. Intratumoral hemorrage

Table 7. Rates of intratumoral hemorrage

Intratumoral hemorrage	Cases	Rates %
Yes	35	74.5
No	12	25.5
Total	47	100

Wilms tumors have intratumoral haemorrhage rates as high as 74.5%. Surgery should be carried out carefully and gently to avoid intraoperative tumor rupture.

3.12. Tumor volumes

Table 8. Comparison of tumor volumes before chemotherapy and surgery

Wilms tumor volumes (cm^3)						**P**
Cases		**Mean**	**Median**	**Smallest**	**Largest**	
Before chemotherapy	27	554.6 ± 531.8	435.7	25.2	2836.2	**<0.001***
Before surgery	47	380.3 ± 518.0	255.4	2.8	2757.0	

(* : *Fisher test)*

The median value of tumor volume after chemotherapy was smaller than that before chemotherapy and the difference was statistically significant, with p <0.001. This is comparable to Tran Duc Hau's study[2] and 2001 SIOP [9]. This shows the effect of preoperative chemotherapy in reducing tumor volume.

3.13. Treatment results

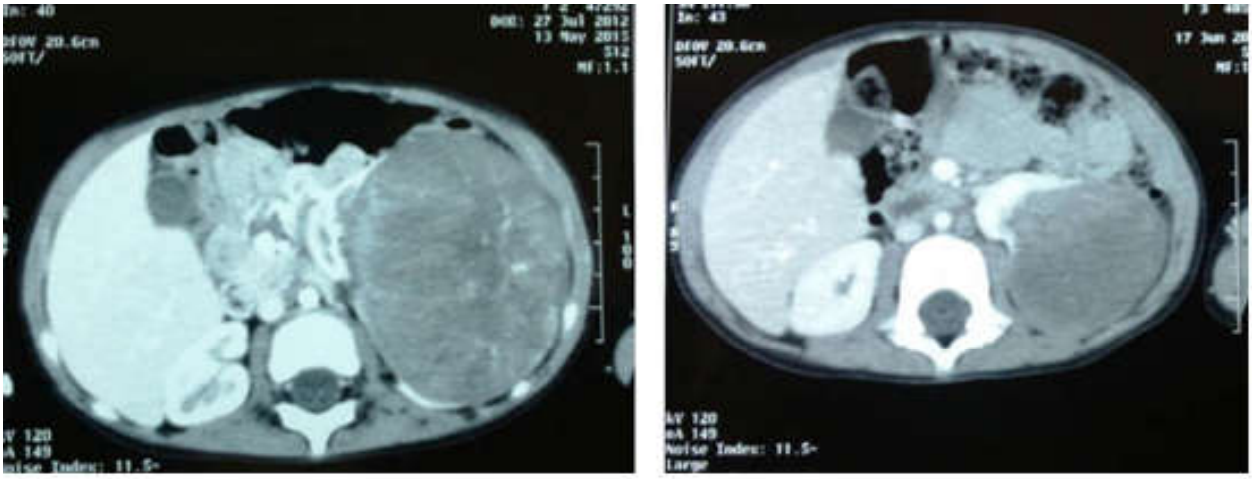
Until 30/06/2017, the follow-up of 47 patients (34 cases with preoperative chemotherapy, 13 cases without preoperative chemotherapy) is presented as follows:

- 39 patients were healthy, event-free survival no disease (82.9%).

- 43 living patients (91.5%) and 4 patients died (8.51%).

- 8 patients with complications (17.02%). Of which there were 2 cases of relapse (4.25%), 3 patients with distant metastasis (6.38%), 2 patients suffering toxic effects of chemotherapy (4.25%) and 1 patient abandoned treatment (2.13%).

Fig. 1



Tumor volumes before (V=191 ml) and after (V=63 ml) preoperative chemotherapy

" Source: Rơ Châm H. SHS 15043499"

Table 9. Comparison of survival rates in developed countries

Survival rates (%)	Our study (n=47)	SIOP 2001 (n=3686)	NWTS-4 (n=3335)	UK (n=714)
1 year - survival rate, event-free	82.9 %			
1 year – survival rate, overall	91.4 %			
5 year – survival rate, event-free		87 %	86 %	77.2 %
5 year – survival rate, overall		93 %	93,7 %	87.5 %

The estimated 1-year survival rates, event-free and overall, of our study were lower than those of the SIOP and NWTSG study groups, and higher than that of patients treated with SIOP algorithm in UK. These differences may come from the fact that our study is small in numbers of patients and short time in follow-up, leading to difficult for comparison. However our survival rate reached approximately 80-90% reflects good therapeutic efficacy of the regimen.

IV. CONCLUSIONS

The treatment results of nephroblastoma in accordance with 2001 SIOP regimen are relatively good. Healthy survival rate, event-free in a year is 82.9%; the overall survival rate was 91.5%. Two important factors that have prognostic value are the disease stage and the risk groups of pathology.

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