Clinical Features and Survival of Children with Wilms' Tumor in Lithuania

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Background. It is a first attempt to present and analyze the epidemiology and treatment results of Wilms' tumor (WT) from two different clinics iof n Lithuania for the last 10 years (1991–2000) and to compare them with the reports of the Ninth International Society of Pediatric Oncology Wilm's Tumor Trial and Study (SIOP-9) and the latest EUROCARE study.

Procedure. We have reported 47 new cases of WT. Patients' distribution according to age, gender, stage of the disease, clinical presentation at the diagnosis, and survival rates in correlation with histology and stage are presented.

Results. Among 47 newly diagnosed cases, the morbidity rates in boys were higher than in girls. Patients' average age at the time of diagnosis was 4 years. Postsurgical staging was the following: stage I was not observed in anybody (0%), II was found in 14 (30%), III in 27 (27%) and IV in 6 (15%). Among 35 cases analysed histologically in detail, one (3%) was classified as favorable, 26 (74%) were standard and 8(23%) unfavorable. The overall 5-year observed survival (OS) of all children diagnosed in 1991–2000 was 69%. The 5-year OS rates according to the stage were for II 92%, III 64% and IV 29%. OS for favorable histology was 100%, for standard 83%, and for unfavorable 48%.

Conclusions. We conclude that WT is still diagnosed at advanced stages in most cases in Lithuania. In comparison with the data of SIOP-9 and EORTIC, the survival is lower in our country. However, on starting to treat patients according to SIOP-93 protocols since 1997, the results are encouraging so far: remission is gained in most cases, relapse and death rates are decreasing. A further follow up will allow us to make statistically more significant conclusions on the survival.

Raktažodžiai: Wilms' tumor, children, SIOP, survival

INTRODUCTION

WT is the most common intra-abdominal solid tumor of childhood. Developments in surgery, radiation therapy, and chemotherapy have led to a dramatic improvement in the prognosis for most patients, and WT has become a paradigm for multimodal treatment of a pediatric malignant tumor (1). More than 80% of all children with WT can now be expected to have a long- term relapse-free survival (2).

In the present study, we report the epidemiological data and outcome of children diagnosed with WT in Lithuania in 1991-2000. The survival rates are compared among the subgroups of patients before and after 1997 when SIOP protocols were presented in our country, and with the outcomes observed by the SIOP-9 and EUROCARE.

MATERIALS AND METHODS

From 52 new cases of WT registered in Lithuania in 1991–2000, 42 were analyzed, while no information was available for 5 cases. They belong to the period 1991–1997.

Patients were identified according to age, clinical presentation at the time of diagnosis, sex, postsurgi-

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cal staging and histological type using the SIOP-9 Histologic Classification (3).

The survival was related to clinical stage and histological type. Survival curves were calculated using the Kaplan and Meier method (4).

The blood samples, kidney excretory urography, abdominal sonography, histopathological analyses of postsurgical material and breast X-ray examination were used for confirmation of WT diagnosis before 1997. However, at that time the histological type in most cases was not identified in detail. Only since 1997 it became possible to classify them according to Histopathological Classification as far as computer tomography became available since the same period of time.

In 1991–1997 the therapy included early radical nephrectomy, chemotherapy with vincristine (VCR), dactinomycine (AMD), and adriamycin (ADRIA) and radiation. Preoperative chemotherapy was administered in case of a very large tumor. The doses and regimens were stratified by age and stage. Since 1997 all patients have been treated according to SIOP WT 93 protocol.

RESULTS

The annual numbers of cases of WT in 1991–2000 are presented in Fig. 1.

Table shows clinical presentation at the time of diagnosis.

The average age at the time of diagnosis was 4 years. Among 47 analysed cases there were 19 girls and 28 boys. Age and sex distribution is presented in Fig. 2.

Among 35 histologically confirmed cases, 1 (3%) was classified as favorable, 26 (74%) as standard and 8 (23%) unfavorable according to the SIOP Histological Classification.

Fifure 3 shows the distribution of postsurgical stages.

In 1991–1997, of 29 patients 12 (41%) died. Three patients (25%) died because of resistance to chemotherapy and the other 9 (75%) died because

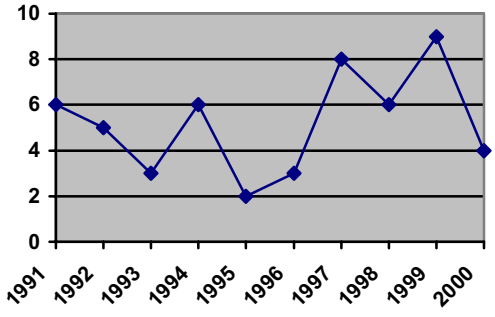


Fig. 1. Annual numbers of Wilms' tumor in 1991–2000 in Lithuania

Table. **Clinical presentation at the time of diagnosis**

Symptoms	No. of patients (%)
Palpable abdominal mass	47 (100%)
Fever	18 (38%)
Abdominal pain	13 (27%)
Hematuria	3 (6%)
Other symptoms: loss of weight, general intoxication, nausea, vomiting, diarrhoea, obstipation, infection of the urinary tract, etc.	11 (23%)
Hypertension	2 (4%)
Lung metastases	7 (15%)

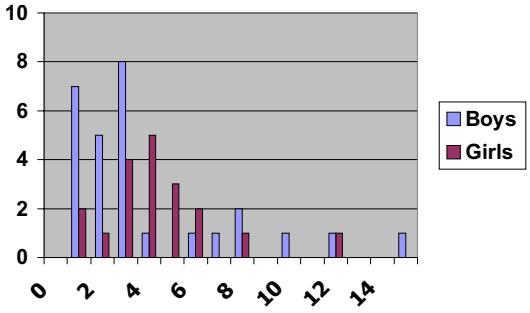


Fig. 2. Age and sex distribution of patients with Wilms' tumor

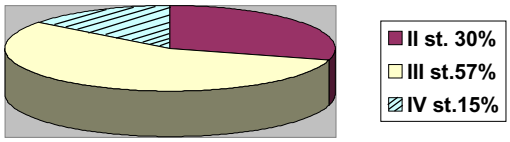


Fig. 3. Stage distribution of patients with Wilms' tumor

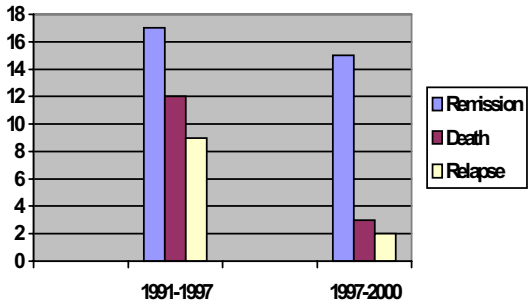


Fig. 4. Outcome of Wilms tumor in Lithuania

of recurrence. On average, the recurrence was detected 3.5 years after the date of diagnosis (Fig. 4).

In 1997–2000, of 18 patients 3(16%) died because of resistance to chemotherapy. Two patients (11%) showed recurrence: one of them had late extraabdominal relapse 2 years after the time of diagnosis,

the second one had early relapse with metastases to the bones with the favorable histology changed into a rhabdoid variant. Both of them have successfully completed the treatment (Fig. 4).

Data on overall survival in 1991–200 are preasented in Figs. 5–7.

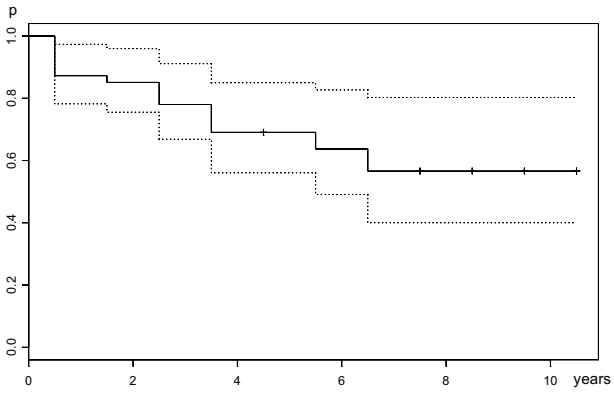
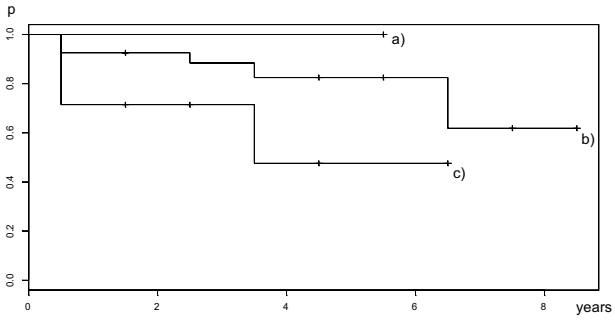


Fig. 5. Overall survival 1991–2000



a) favourable.
b) standard.
c) unfavourable.

Fig. 6. Overall survival according to histological subtypes

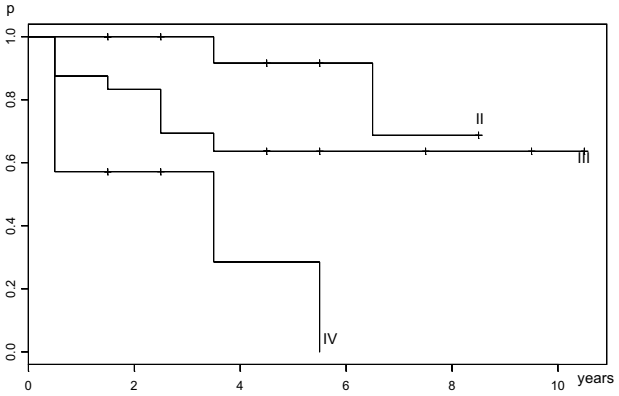


Fig. 7. Overall survival according to stage

DISCUSSION

In the European population, 97% of the malignant neoplasms of the kidney in childhood are WT (5). Mortality rates for childhood renal cancer recently have decreased considerably in most European countries (6), presumably due to improvements in treatment (7). According to the last EUROCARE study, survival of children with WT diagnosed in the former socialist countries was clearly inferior compared with the rest of Europe. The application of the latest advances may have been delayed (8). Our study could confirm this supposition.

A significantly greater difference was observed in the overall 5-year survival of WT between EUROCARE study (8) and the data of our clinic (83% and 69%, respectively). However, since 1997 there has been a marked improvement in survival rate when SIOP 93 has been applied for the treatment. OS increased up to 81%.

According to the recent SIOP-9 study (3) and our results 5-year survival rates according to histological subtypes were: 90% and 100% for favorable histology, 91% and 83% for standard, and 68% and 48% for unfavorable histology, respectively.

We connect such significant differences in OS with the accurate confirmation of WT, especially before 1997 when imaging techniques as CT and detail histology were introduced. Because of these reasons it was impossible to stratify the treatment by the most important prognostic factors (histology and exact stage). We suppose that the treatment was not intensive enough for the patients with high risk features.

CONCLUSIONS

In most cases WT in Lithuania is diagnosed at advanced stages. On starting to treat patients according to SIOP protocols the survival results have become encouraging: the incidence of relapse and death rate dramatically decreased after 1997.

Received 2 April 2002
Accepted 30 May 2002

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VAIKŲ SU VILMSO NAVIKU KLINIKINĖS YPATYBĖS IR IŠGYVENIMAS LIETUVOJE

S a n t r a u k a

Darbo tikslas – išnagrinėti Vilmso naviko (VN) epidemiologiją ir gydymo rezultatus remiantis dviejų skirtingų Lietuvos klinikų 10 metų ligos istorijų duomenimis ir palyginti juos su SIOP-9 VN tyrimo bei EUROCARE studijos duomenimis.

Retrospektyviai išnagrinėta 47 ligos istorijos. Ligoniai suskirstyti į atskiras grupes pagal amžių, lytį, ligos stadiją, kliniką. Taip pat analizavome išgyvenimo koreliaciją su histologiniu VN tipu bei ligos stadija.

Išnagrinėjus 47 ligos istorijas, nustatėme, kad berniukai VN serga dažniau. Amžiaus vidurkis nustatant diagnozę buvo 4 metai. VN stadijos po operacijos buvo šios: I stadija – nebuvo, II – 14 ligonių (30%), III – 27 (56%) ir IV – 6 (14%). 35 ligoniams buvo atliktas išsamus histologinis tyrimas: vienam ligoniui (3%) buvo nustatytas palankus histologinis variantas, 26 (74%) – standartinis ir 8 (23%) – nepalankus. Ligonių, kuriems VN buvo diagnozuotas 1991–2000 metais, bendras išgyvenimas sudarė 69%. Pagal stadijas išgyvenimas pasiskirstė taip: II stadija – 92%, III – 64% ir IV – 29%. Sirgusiųjų palankios histologijos grupės VN bendras išgyvenimas buvo 100%, standartinės – 83% ir nepalankios tik 48%.

Nustatėme, kad iki šiol VN Lietuvoje nustatomas išplitusios stadijos. Lyginant su SIOP-9 ir EORTIC duomenimis, mūsų ligoniai išgyvena trumpiau. 1997 metais pradėjus ligonius gydyti pagal SIOP-93 gydymo schemą, rezultatai labai pagerėjo: dažniau pasiekiama remisija, mažėja recidyvų ir mirštamumas.

Raktažodžiai: vaikai, Vilmso navikas, SIOP gydymo rezultatai