Cukurova Medical Journal
ÇUKUROVA ÜNİVERSİTESİ TIP FAKÜLTESİ

Cukurova Med J 2019;44(3):840-844
DOI: 10.17826/cumj.493064

ARAŞTIRMA / RESEARCH

Treatment results of Wilms tumour

Wilms tümöründe tedavi sonuçları

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Cukurova Medical Journal 2019;44(3):840-844.

Abstract

Purpose: The purpose of this study was to evaluate the treatment results of the patients with Wilms tumour (WT).

Materials and Methods: The clinical records of 21 children with WT treated between 2012 and 2017 were retrospectively reviewed. Age, nationality, symptoms, diagnostic and surgical methods, surgical complications, the stage of the disease, the status of neoadjuvant chemotherapy, radiotherapy status, presence of recurrent disease and histopathological characteristics of the tumour and outcome of the patients were analyzed.

Results: The female/male ratio was 2/1 and the mean age was 4.21±2.26 years. The most common physical examination finding was abdominal mass. The diagnosis was made with clinical examination and radiological investigation in 90.5% of the patients. Total nephroureterectomy was performed in all patients. The most common histopathological subgroup was classical Wilms Tumour that was detected in 81 % of the patients. 6.8 % of the patients had distant metastasis at the time of the diagnosis. The most common distant metastasis site was lungs. Overall survival (OS) of the patients was 85.7% and mean survival time was 36 months (2 months - 62 months). Advanced stage at diagnosis, presence of distant metastasis and diffuse anaplastic histology were associated with worse OS rates.

Conclusion: Similar to existing knowledge on outcome of patients with Wilms tumor, our results confirmed the negative effect of advanced stage, distant metastasis and diffuse anaplastic histology on survival. Further large-scale studies investigating molecular features of the tumor are needed to decide for proper treatment and to better predict outcome.

Keywords: : Wilms tumor, survival, children

Öz

Amaç: Bu çalişmanın amacı Wilms tümörlü (WT) hastaların tedavi sonuçlarını değerlendirmektir.

Gereç ve Yöntem: 2012-2017 yılları arasında WT tanılı 21 hastanın klinik kayıtları geriye dönük olarak incelendi. Yaş, uyruk, semptomlar, teşhis ve cerrahi methotlar, cerrahi komplikasyonlar, hastalığın evresi, neoadjuvan kemoterapi durumu, radyoterapi durumu, rekürren hastalığın varlığı, tümörün histopatolojik özellikleri ve hastaların sonuçları analiz edildi.

Bulgular: Kız/erkek oranı 2/1olup, ortalama yaş 4.21±2.26 yıldı. En sık saptanan fizik muayene bulgusu abdominal kitle idi. Hastaların %90,5'ine radyolojik bulgular ve klinik muayene ile tanı konuldu. Hastaların tamamına total nefroüreterektomi uygulandı. Hastaların %81'inde saptanan histopatolojik alt grup klasik Wilms tümörü idi. Hastaların %6,8'inde tanı anında uzak metastaz olup en sık uzak metastaz yeri akciğerdi. Hastaların genel sağkalımı (OS) %85,7 idi ve ortalama sağkalım süresi 36 aydı(2 ay-62 ay). Tanı anında ileri ever hastalık olması, uzak metastaz varlığı ve difüz anaplastik histoloji ile sağkalım oranları belirgin olarak etkilenmekteydi.

Sonuç: Literatürdeki verilere benzer şekilde, çalışmamızın bulguları Wilms tümöründe ileri evre, uzak metastaz ve yaygın anaplastik histolojinin sağkalım üzerindeki olumsuz etkilerini doğrulamıştır. Uygun tedaviye karar vermek ve prognozu daha kesin olarak belirleyebilmek için tümörün moleküler özelliklerini araştıran büyük ölçekli çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Wilms tumour, sağkalım, çocuklar

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Geliş tarihi/Received: 06.12.2018 Kabul tarihi/Accepted: 11.01.2019 Çevrimiçi yayın/Published online: 07.09.2019

INTRODUCTION

Wilms tumour, the most common renal tumor of childhood, constitutes 5.9 % of all pediatric cancers [1]. It is observed two times more in Europe than it is seen in Asian countries and it is more common in black race than in white race[2]. Wilms tumour is most frequently seen between the ages of 1 and 5 years and its peak age is 3. Although adult cases are reported, it is rarely reported in patients over 15 years[3].

The survival rates of the children with Wilms tumour had increased dramatically between the years of 1975 and 2010[4]. A better description of the biology of the disease, the existence of well-designed prospective studies, the use of more effective chemotherapeutic agents, the use of multimodal treatments, a better supportive care and improved screening methods can be mentioned among the reasons of this improvement. The purpose of this study was to evaluate the treatment results of the patients with Wilms Tumor.

MATERIALS AND METHODS

The files of 21 patients who had been operated between 2012 and 2017 were analyzed retrospectively after ethical committee approval (19.06.2018-Karar no:192.) Age, nationality, symptoms, physical examination findings, diagnostic and surgical methods, surgical complications, the stage of the disease, neoadjuvant chemotherapy (NC) status, histopathological characteristics of the tumour were recorded and survival analyze was performed.

The patients were treated in our hospital according to the protocol of Turkish Pediatric Oncology Group (TPOG) protocol [6]. NC included vincristine (1.4mg/m^2) for four weeks and actinomycin-d (15 microgram/kg) given for 5 days. After the postoperative period, chemotherapy was continued with or without doxorubicine or doxorubicine+etoposide in addition to vincristine and actinomycin-d and radiotherapy was given according to stage and histopathological characteristics of the disease.

The statistical analysis of the study was made by Statistical Package for Social Sciences version 20 (IBM Corp., Armonk, NY, USA). Demographic characteristics of the patients were given with descriptive statistics. Chi-square test was used to compare categorical measurements between groups. The Kolmogorov-Smirnov test was used to evaluate distribution pattern of the numeric variables. Mann-Whitney U test was used to compare two groups of numerical variables without normal distribution. Independent groups Student t test was used to make comparison between two groups with normal distribution. The statistical significance level (p) for all tests was <0.05.

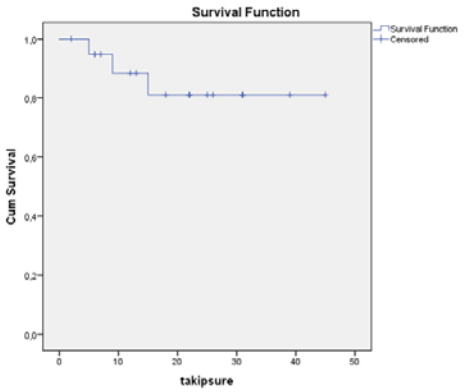

Figure 1. Overall survival of patients.

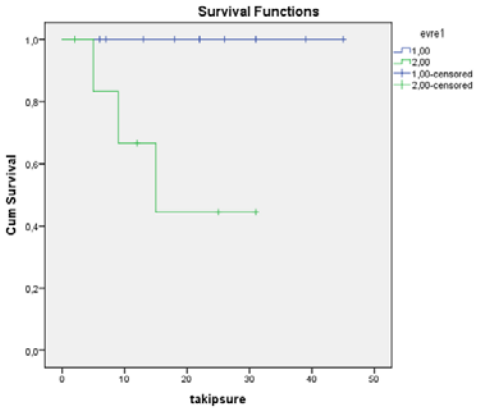

Figure 2. Overall survival according to early (stages 1-2) and advanced (Stages 3,4,5) stages.

RESULTS

There were 21 children with Wilms tumor treated in Adana City Training and Research Hospital between 2012 and 2017. The mean age of the patients was 4.21±2.26. 14 patients were female (66.7%) and 7 of

them were male (33.3%). 90.5 % of the patients applied to the hospital with a complaint of abdominal distention which was noticed by family members. Less common symptoms were abdominal pain, red-colored urine and fever. There were 12 Turkish, 9 Syrian patients. The demographical data and the tumour characteristics of the patients were shown in Table 1. The frequency of advanced stage (p=0.032), distant metastasis (p=0.046) and recurrence (p=0.046) were found significantly higher in Syrian patients compared to Turkish patients.

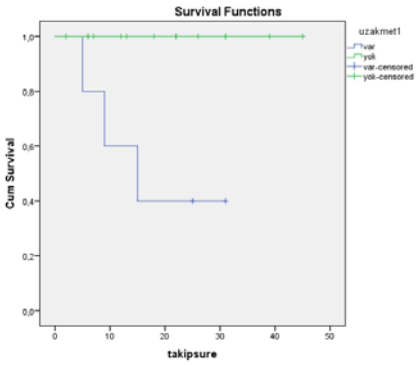

Figure 3. Overall survival according to distant metastasis status.

Neoadjuvant chemotherapy was given to 18 patients. Right or left total nephroureterectomy was performed in all patients depending on the location of the tumour. Total nephroureterectomy to one side and partial nephrectomy was performed to the other side in one patient with bilateral Wilms tumor. Surgical complication was experienced in 28.6% of the patients. The most common surgical complication was the injury of the surrenal gland. The details about the surgical complications were presented in Table 2.

It was found that overall survival (OS) of the patients was 85.7% and mean survival time was 36 months (2 months - 62 months) (Figure 1). The average survival rate was 40.9 months in Turkish patients and 21.22 months in Syrian patients and the difference in survival time according to nationalities was statistically significant (p=0.01). There was no statistically significant difference in OS rates according to gender, age, nationality, neoadjuvant chemotherapy, radiotherapy status, recurrent disease, existence of surgical complications (all p>0.05). OS was 100% in patients with early stages (stage 1 and 2) (n=13) and 62.5% in the group of advanced stages (Stages 3,4,5) (n=8). OS was significantly better in patients with early stage disease (p=0.05) (Figure 2).

Table 1. Demographic and clinical characteristics of patients

Variables		**N (21)**	**%**
Age Group	1 – 5 years old	17	81.0
	6 -10 years old	4	19.0
Gender	Male	7	33.3
	Female	14	66.7
Country	Turkey	12	57.1
	Syria	9	42.9
Diagnosis Method	Trucut	2	9.5
	Clinical+radiology	19	90.5
Stage	Stage 1	8	38.1
	Stage 2	4	19.0
	Stage 3	4	19.0
	Stage 4	4	19.0
	Stage 5	1	4.8
Pathology	Anaplasia	3	14.3
	Focal anaplasia	1	4.8
	Classical	17	81.0
Current Status of the Patients	On-treatment with disease	2	9.5
	Off-treatment without disease	15	71.4
	Exitus	3	14.3
	Lost	1	4.8
Side	Right	10	47.6
	Left	10	47.6
	Bilateral	1	4.8
Distant metastasis	Positive	6	28.6
	Negative	15	71.4
Total		21	100.0

Table 2. Surgical complications and results

Variables		**N (21)**	**%**
Side of the operation	Bilateral	1	4,8
	Right	10	47,6
	Left	10	47,6
Surgery Method	Total	21	100,0
	Subtotal	-	-
Surgical Complication	Yes	6	28,6
	No	15	71,4
Location of Surgical Complication	Adrenal	3	71,4
	Diaphragma	2	14,3
	Colon	1	9,5
	No	15	4,8

OS was significantly lower in patients with distant metastasis compared to patients without metastasis ($p<0.001$) (Figure 3). When the overall survival rates were considered according to histopathological characteristics, OS rate of patients with anaplasia (n=4) was 50% and without anaplasia (n=17) was 94.1%. OS was significantly worse in patients with anaplasia than patients without anaplasia ($p=0.046$).

DISCUSSION

Wilms tumour is the second most frequent intra-abdominal tumour in the childhood period and its prevalence is 1/10000. It is quite rare in the children under six months and older than 10 years [5]. Although Wilms tumour is seen in both genders at almost the same rate, female/male ratio was 2 in our study similar to other series reported by Akyüz et al and Israels et al[6,7]. Many of the children with Wilms tumour apply with abdominal mass that can be palped by family members or doctors during the physical examination. In our study, the most common application complaint was abdominal distension noticed by the family members similar to some other studies reported from high-income countries[8,9].

Neoadjuvant chemotherapy according to TPOG protocol has been adopted in treatment of Wilms Tumor at our centre. Preoperative chemotherapy provides some advantages to patients such as facilitation of the surgery and reduction of complications. However, it also has some disadvantages such as downstaging of the tumor and treatment for treatment without biopsy causes insufficient or excessive treatment of the disease. Today, SIOP (Societe Internationale d'Oncologie Pediatrique) group supports the preoperative treatment in Wilms Tumour while NWTSG (National Wilms Tumor Study Group) supports the surgical approach without preoperative treatment[10]. Low surgical complication rates can be attributed to neoadjuvant chemotherapy in our study.

Multidisciplinary treatment methods have led to OS rates of> 90% in patients with early stage disease[11]. However, management of high-risk patients such as anaplastic Wilms tumor has still been a challenge[12]. Overall survival in our study was lower compared to data of developed countries and better compared to underdeveloped countries[13,14,15]. Lower OS rates can be attributed to our study population's heterogeneity and high percentage of advanced stage disease. Since our hospital is a centre to which Syrian immigrants apply, almost half of our patients consisted of Syrian patients. Although advanced stage, metastatic and recurrent disease were more frequent among Syrian patients, their OS rates were not significantly lower compared to Turkish patients. However, OS time was significantly shorter in Syrian patients. In another study from our country by Akyüz et al, a better survival rate was reported with TPOG protocol[6]. The stage, the existence of anaplasia and the status of distant metastasis were the factors that affect the survival rate negatively in our study. Similar findings were reported in the literature[13,14].

The stage and histopathological characteristics of the tumor are still the most important factors in current Wilms tumor management strategies. Some biological markers such as p53 mutation, loss of heterozigocity on 11p15 that have affect on survival in Wilms tumor have also been identified[17]. Risk of recurrence was shown to be increased in presence of loss of heterozigocity on 11p15, 1p or 16q[18]. One of the major limitations of our study is lacking biological investigations. Some possible biomarkers that could be associated with lower OS rates might have been identified with proper methods.

Despite the significant improvement in survival rates of Wilms tumor, definition of distinct subgroups by identification of additional factors is required. Inclusion of biological evaluation of the tumor in decision-making at certain cornerstones of treatment may provide excellent long-term survival rates without causing major treatment-associated morbidity.

Yazar Katkıları: Çalışma konsepti/Tasarımı: İBC, ZÖ; Veri toplama: İBC; Veri analizi ve yorumlama: BYK; Yazı taslağı: İBC; İçeriğin eleştirel incelenmesi: BYK; Son onay ve sorumluluk: İBC, BYK, ZÖ; Teknik ve malzeme desteği: İBC; Süpervizyon: -; Fon sağlama (mevcut ise): yok.
Hakem Değerlendirmesi: Dış bağımsız.
Çıkar Çatışması: Yazarlar çıkar çatışması beyan etmemişlerdir.
Finansal Destek: Yazarlar finansal destek beyan etmemişlerdir.
Author Contributions: Concept/Design : İBC, ZÖ; Data acquisition: İBC; Data analysis and interpretation: BYK; Drafting manuscript: İBC; Critical revision of manuscript: BYK; Final approval and accountability: İBC, BYK, ZÖ; Technical or material support: İBC; Supervision: -; Securing funding (if available): n/a.
Peer-review: Externally peer-reviewed.
Conflict of Interest: Authors declared no conflict of interest.
Financial Disclosure: Authors declared no financial support

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